Types and Efficacy of Laboratory Tests for Diagnosing Peanut Allergy: A Systematic Review

Ahaleed Arkook[1], Lujain Arkook[2]

[1]. *Medical Laboratory Sciences Department- MLS program, Fakeeh College for Medical Sciences, Jeddah 21461, Saudi Arabia*

[2]. *MBBS General Practice, Medicine and surgery, university of Malta. Malta, MLT*

**Corresponding author: Ahaleed Arkook, Lujain Arkook, E-mail:ahaleed@gmail.com , lujain.arkook@gmail.com*

KEYWORDS

Peanut Allergy, Laboratory tests, Diagnostic Tests, Component-Resolved Diagnostics, Basophil activation test, Mast cell activation test.

ABSTRACT:

Background: Between 2 and 10% of people worldwide suffer from food allergies; the prevalence varies by age, location, and diagnostic technique. Challenges in the diagnosis of food allergies are said to be as common in Asia and Africa as they are in Western countries. Additionally, there is growing evidence that prevalence is increasing in developing countries. Double-blind food challenges are considered to be the gold standard in the diagnostic process, but they are risky and time-consuming. From objective symptoms to subjective ones (from urticaria and cough to severe systemic allergic reactions with wheezes or anaphylaxis), occurrences following the test were reported.

Objectives: In order to summarize and assess the different laboratory tests and their different parameters in the diagnosis of food allergies, particularly peanut allergies, we carried out this systematic review. These tests included the mast cell activation test (MAT), specific immunoglobulin E (sIgE) tests, component-resolved diagnostics (CRD), and the basophil activation test (BAT).

Methods: We conducted a comprehensive search in PubMed, Web of Science, and Scopus to identify studies evaluating laboratory tests for diagnosing peanut allergy. We selected studies according to inclusion and exclusion criteria. Data on diagnostic performance metrics were extracted. The risk of bias was assessed using the QUADAS-2.

Results: The inclusion criteria were met by 11 research studies with 1170 participants. When compared to other current laboratory tests such as the skin prick test, sIgE, and basophil activation test (BAT), the mast cell activation test (MAT) was found to be the most accurate diagnostic tool for peanut allergy diagnosis. It may even be able to replace the conventional oral food diagnostic tests (OFCs). However, it is novel and still under research, and its cost and accessibility are still restricted. By using BAT, we may use CD63 peanut/anti-IgE and CD-sens to determine the severity and threshold of allergic reactions during OFCs.

Conclusion: Mast cell activation test offers superior accuracy in the diagnosis of peanut allergy and can help confirm diagnoses. A multi-test approach that incorporates these tools can enhance diagnostic accuracy, reduce the risk of overdiagnosis, improve patient management, and decrease the need for risky OFCs.

Introduction

Approximately 1-3% of children worldwide are affected by peanut allergies [1], and around 0.5-1.5% of adults have peanut allergies [2]. The prevalence of peanut allergies has increased over the last few decades, particularly in developed nations [3]. Peanut allergy often lasts a lifetime, the patient is susceptible to its consequences and events that could be from some objective symptoms to a high systemic severe reaction like anaphylaxis [4]. For children and their caregivers, of course, having this allergy decreases the quality of life for the patient, Since peanuts is commonly favored by many people. Parents of children with peanut allergies experience constant anxiety about the possibility of their children accidentally ingesting peanuts, especially in unsupervised environments, even at routine activities like having lunch at a friend's house or going to school can become sources of anxiety [5]. On the other hand, there is a need for more easy, feasible, accurate, and not risky diagnostic tests to detect and diagnose this allergy. As we know, misdiagnosis may result in unnecessary food restrictions and poor quality of life, it's worth noting that children with peanut allergies don't experience an improvement in their quality of life

by eating other nut foods that they don't have an allergy to [6], while failing to diagnose a true allergy may put patients' lives at risk of allergy events, these events vary from one patient to the other. Peanut allergy occurs when the immune system overreacts to peanut proteins, usually involving immunoglobulin E (IgE) antibodies [7]. When someone with a peanut allergy eats peanuts, these IgE antibodies cause the release of chemical substances like histamine, causing reactions that can range from mild itching to severe anaphylaxis. However, diagnosing a true peanut allergy isn't always simple because having IgE antibodies doesn't always mean a person will have symptoms of allergy when they eat peanuts [8]. Although skin prick tests (SPT) and specific IgE (sIgE) blood tests are frequently used to diagnose peanut allergies, they have numerous limitations [9], so doctors frequently need to confirm the diagnosis after performing these tests by OFCs, the gold standard.

Symptoms of the allergy may be like other conditions in their presentation, such as food intolerances or non-IgE-mediated allergies [10]. Due to these difficulties, physicians typically use a mix of clinical history, laboratory testing, and potentially dangerous oral food challenges (OFCs) to confirm a peanut allergy [11]. During an OFC, the patient eats small amounts of peanuts under medical supervision to see if a reaction occurs. Although OFCs are thought to be the gold standard test for allergy diagnosis, they are expensive, time-consuming, and can result in serious reactions [12]. There are many lab tests available to test and diagnose peanut allergy. Every test has its pros and cons. The most common tests include:

1. Specific IgE (sIgE) Tests: These blood tests measure IgE antibodies that react to peanut proteins. Despite being widely accessible, they may produce false-positive or false-negative results.
2. Skin Prick Tests (SPT): In this test, a small quantity of peanut extract is applied to the skin, and the area is pricked to see if a reaction occurs. It is a quick and somewhat inexpensive clinical test, but cross-reactivity with other allergens can lead to false positives.
3. Component-Resolved Diagnostics (CRD): This test detects IgE antibodies to specific peanut proteins, like Ara h 1, Ara h 2, Ara h 3, Ara h 6, Ara h 8, and Ara h 9; each one has its role in the diagnosis, as we will discuss.
4. Basophil Activation Test (BAT): This test measures how basophils respond to peanut allergens. It's very accurate but requires specialized equipment, so it's not widely available.
5. Mast cell activation test (MAT): it is a novel approach to diagnosing food allergies, particularly peanut allergy.

Diagnosis and identification of peanut allergy is complex, and a clear understanding of available diagnostic tests is essential for improving patient care. This systematic review aims to overview and evaluate the efficacy of different types of laboratory tests used to diagnose peanut allergy. Accurate diagnosis can improve patient care, reduce unnecessary food restrictions, and ease the anxiety experienced by patients and their families. This review will explore important questions about the accuracy, reliability, and practical use of these tests.

Methods

Eligibility Criteria

Studies that satisfied these requirements were eligible for inclusion:

- **Population:** Adults or children diagnosed or suspected of having peanut allergy.
- **Index test:** Studies that evaluated laboratory diagnostic tests for peanut allergy, including serum-specific immunoglobulin E (sIgE) testing, component-resolved diagnostics (CRD), basophil activation tests (BAT), and mast cell activation tests (MAT).
- **control:** Studies that compared laboratory tests to a reference standard, oral food challenge (OFC), which is considered the gold standard for diagnosing peanut allergy and the most accurate.

- **Outcomes:** Studies that report different diagnostic metrics and their accuracy outcomes, including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and area under the receiver operating characteristic curve (AUC).
- **Study Design:** Diagnostic accuracy studies, prospective cohort studies, or randomized controlled trials.

The following studies were excluded:

- Studies didn't evaluate diagnostic tests for peanut allergy.
- primarily evaluated tests that were clinical like skin prick test, conjunctival provocation test, or oral mucosal brush biopsy for the diagnosis of peanut allergy.
- Studies not specific to peanut allergy.
- paper conferences and reviews or book chapters case reports.
- Studies without a reference standard (e.g., oral food challenge).
- Animal studies or in vitro studies.
- publications in languages other than English.

Search Strategy:

We searched the literature in multiple electronic databases to identify relevant studies that met our inclusion criteria. PubMed, Scopus, and Web of Science were searched. The search was performed using a combination of keywords and Medical Subject Headings (MeSH) terms related to peanut allergy and diagnostic tests. The search strategy on PubMed included the following MeSH terms: "(("Nut and Peanut Hypersensitivity/diagnosis"[Mesh]) OR ("Peanut Hypersensitivity/diagnosis"[Mesh]))" and the clinical trials filter was applied. On Scopus and Web of Science, we used the following keywords with Boolean terms: "((peanut allergy) AND ((diagnostic test) OR (laboratory test) OR (IgE) OR (component-resolved diagnostics) OR (basophil activation test) OR (mast cell activation test))".

Study Selection

Two independent reviewers (Reviewer 1 and Reviewer 2) conducted the study selection process. Initially, Rayyan, a semi-intelligent online program, was used to screen the titles and abstracts of all identified studies for relevance [13]. Discrepancies between reviewers were resolved by discussion, and a third reviewer was consulted if consensus was not reached. Full-text articles were retrieved for studies that met the inclusion criteria or where there was uncertainty. A PRISMA flow diagram (Figure 1) was created to document the selection process using RevMan [14].

Data Extraction

Data were extracted by two reviewers using a pre-designed data extraction Excel sheet. There was a third reviewer who confirmed the extracted data.

Extracted information included:

- Study characteristics: study ID (last name of the first author et al. plus year of publication), country, study design, sample size, evaluated test parameter, primary outcome of the study, and key findings.
- Diagnostic tests: Type of test (e.g., sIgE, CRD, BAT), its different parameters.
- Risk of bias: The QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies 2) tool, which is appropriate for evaluating studies that assess a diagnostic test, is used to assess methodological quality and risk of bias.

Risk of Bias Assessment

Two independent reviewers (XXXXXX)(XXXXXXX) assessed the quality of the included studies using the QUADAS-2 tool, which evaluates four key domains:

1. Patient selection
2. Index test (the laboratory test)
3. Reference standard (oral food challenge the gold standard)
4. Flow and timing (delays between index test and reference standard)

Every domain received a risk of bias rating of low, high, or unclear**.**

Results

Study Selection

The initial literature search yielded [1486] studies from online databases (PubMed, Scopus, and Web of Science). [238] duplicate records were eliminated, leaving [1248] studies for screening of the abstract and title. [25] studies were chosen for full-text review based on the inclusion and exclusion criteria. Finally, [11] studies met the eligibility criteria and were included in the systematic review.

A PRISMA flow diagram outlining the study selection process is provided in Figure 1.

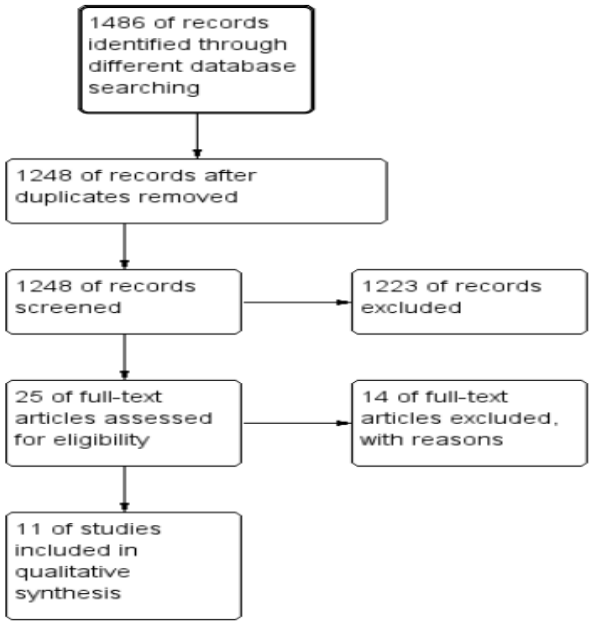

Figure 1 shows Prisma flow diagram

Characteristics of Included Studies

The [11] included studies comprised a total of [1170] participants, with sample sizes ranging from [42] to [200].

The diagnostic tests evaluated included:

- Serum Specific IgE (sIgE) or Component-Resolved Diagnostics (CRD) (n = [5])
- Basophil Activation Test (BAT) (n = [4])
- Mas cell activation test (MAT) (n= [2])

Detailed characteristics of each included study are summarized in Table 1

Table 1 shows the study characteristics of the included studies.

Study ID	study characteristics						
	country	population	design	sample size	primary outcome	diagnostic test parameter	key finding
Dang et al. 2012[15]	Australia	In Melbourne, Australia, 131 council-run immunization sessions were used to select 11–15-month-old infants.	Prospective cohort study	200	To ascertain whether Ara h 2 testing could increase. The precision of peanut allergy diagnosis and so, eliminate the necessity for an oral food challenge (OFC).	. Ara h 2	Ara h 2 plasma sIgE test results are more accurate than whole peanut plasma sIgE levels and may be a new diagnostic method that can differentiate between peanut allergy and tolerance, perhaps lowering the requirement for an OFC.
Glaumann et .al. 2012[16]	Sweden	Children between the ages of 4 and 19 who were sent to Stockholm, Sweden's Sach's Children's Hospital	prospective study	38	To assess the antibodies to peanut allergen components and the basophil allergen threshold sensitivity (CD-sens) in relation to DBPCFC in the diagnoses of peanut allergy in children.	basophil allergen (CD-sens parameter) and antibodies to peanuts component	A negative CD-sens to peanut ruled out peanut allergy in this investigation. The immunoassay for IgE-antibody to the peanut components and CD-sensing to peanut assays seem to be safe, efficient, and cost-effective complements to DBPCFC.
Santos et al. 2014[17]	UK	Children with non-peanut-sensitized nonallergic (NA), peanut allergy (PA), or peanut sensitization but tolerance (PS)	prospective study	104	to evaluate the effectiveness of the basophil activation test (BAT) as a peanut allergy diagnostic marker.	basophil activation test (BAT) parameters	BAT decreased the need for OFCs and outperformed other diagnostic tests in differentiating between peanut allergy and tolerance, especially in challenging situations.
Santos et al 2015[18]	UK	This study included consecutive patients who were in a study about the use of BAT in the diagnosis of peanut allergy Peanut Allergy and Sensitization study (which included children who had been not included in Learning Early About Peanut Allergy [LEAP] study after receiving a positive oral peanut challenge result) were included in this study\.	a prospective study	49	To evaluate how well the basophil activation test (BAT) predicts the degree of reaction and cutoff point of peanut sensitivity during oral food challenges (OFCs)	basophil activation test (BAT)parameters	The severity of allergic reactions to peanuts is correlated with basophil reactivity, while the threshold is correlated with basophil sensitivity (CD-sens). The degree and threshold of allergy reactions during OFCs can be estimated by CD63 peanut/anti-IgE and CD-sens readings.
Kukkonen et al. 2015[19]	Finland	Children aged 6 to 18 who may have a peanut allergy at Helsinki University Skin and Allergy Hospital	a double-blind placebo-controlled study	102	to improve diagnoses for moderate-to-severe peanut allergies and develop an oral peanut challenge with defined allergen activity	Component-resolved diagnostics	In order to differentiate between severe allergy and mild symptoms, co-sensitization to Ara h 2 and Ara h 6 was linked to severe reactions. There was no diagnostic value added by SIgE to Ara h 8.
Veen et al. 2016[20]	Netherland	consecutive patients who attended to their outpatient clinic	prospective cohort study	72	assessment the usefulness of component-resolved diagnostic testing in patients with peanut allergies	Component-resolves diagnostics (Ara h 1, 2, 3, 6, 8, 9	This study demonstrates that for the diagnosis of peanut allergy, component-resolved diagnostics is not more effective than skin prick testing or sIgE to peanut extract.
Bahri et al. 2018[21]	UK	population sensitized with peanuts and underwent DBPCFCs	prospective cohort study	42	To evaluate a novel diagnostic test (MAT).	MAT (a robust tool)	This study demonstrated the superiority of MAT over other diagnostic tests already in use.
Hemmings et al 2020[22]	UK	People who participated in the study were either sensitive to peanuts but tolerant of them, or neither sensitized nor allergic to peanuts.	prospective cohort study	100	Evaluation of Ara h 2 and Ara h 6's diagnostic value and relative significance in peanut allergy	Ara h 2 and Ara h6	The most accurate IgE for peanut allergy diagnosis is Ara h 2-specific IgE and Ara h 6-specific IgE. Despite some cross-reactivity with Ara h 6, Ara h 2 is the predominant conglutin in peanut allergy in the United Kingdom.
Duan et al. 2021[23]	Canada, Austria	Individuals with tree nut and/or peanut allergies or sensitivities ranging in age from 6 months to 17 years.	prospective study	197	To find out if the basophil activation test (BAT) is useful for identifying tree nut and peanut allergies	CD63 expression parameter (BAT)	In children who are sensitive to many nuts, the basophil activation test can predict the clinical state of peanut and tree nut allergies

							and may lessen the requirement for high-risk OFCs in patients.
Kansen et al. November 2020[24]	Netherland	Adults who had a peanut DBPCFC included 70 new patients (2012-2019) and 84 individuals from prior research (2002-2012).	prospective study	154	To confirm a previously discovered Ara h 2 cutoff level with 100% positive predictive value (PPV) in persons with suspected peanut allergy and assess the diagnostic utility of (combined) peanut components.	Ara h 1, 2, 3, 6, and 8 were measured using ImmunoCAP	The discriminative ability of sIgE to Ara h 2 and Ara h 6 is equally good.
Zbären et al 2024[25]	unclear	112 individuals who were prospectively enrolled in the MONA project and had clear clinical data on the peanut allergic status (80) children and adolescents with peanut allergies and 32 nonallergic (controls).	prospective cohort study	112	This study's main objective was to evaluate the diagnostic efficacy of the whole blood-based BAT versus the serum-based Hoxb8 MAT.	Hoxb8 MAT	Comparable to the fresh whole blood-based BAT, the Hoxb8 MAT showed extremely strong diagnostic precision in patients prospectively evaluated for peanut allergy. Furthermore, it proved useful in accurately classifying BAT non-responders as either allergic or nonallergic.

Diagnostic Accuracy Results

1. Serum Specific IgE (sIgE) and Component-Resolved Diagnostics (CRD)

An Ara h 2 sIgE level of 0.46 kUA/L provides 95% specificity and 73% (95% CI, 66% to 84%) sensitivity, while a whole peanut sIgE level of 6.2 kUA/L provides 95% specificity with a significantly lower sensitivity of 44% (95% CI, 34% to 54%; P <.001), according to Dang et al. (2012). This indicates that specific sIgE Ara h 2 plasma test levels offer higher diagnostic accuracy than total peanut plasma sIgE levels.

Ninety-five (62%) of the patients in Kansen et al.'s November 2020 study had peanut allergy, and the best predictors of allergy were specific IgE to Ara h 2 and Ara h 6, with an AUC (95%CI) of 0.85 (0.79-0.91) and 0.85 (0.79-0.92), respectively. sIgE Ara h 2 with 52% sensitivity and 100% specificity at a cutoff level more than or equal to 1.75 kUA/L with 100% PPV sIgE NPV 56% (59/105). Ara h 6 has 46% sensitivity and 100% specificity with 100% PPV, with NPV 55% (47/85) at a cutoff level more than or equal to 1.80 kUA/L.

In Kukkonen et al. 2015, sIgE to Ara h 6 AUC 0.98 (95% CI, 0.96–1.00) with 95% sensitivity and 95% specificity is the best marker of moderate-to-severe allergy. SIgE to Ara h 2 AUC 0.96 (95%CI, 0.93-0.99) at cutoff point 1.8 kU/L with 80% sensitivity and 95% specificity. Upon measuring sIgE to Ara h 2 and Ara h 6 together, all (100%) severe reactions at low doses could be diagnosed. sIgE to Ara h 8 or 9 showed no significant differences.

In Hemmings et al. 2020 also showed that Ara h 2 sIgE and Ara h 6sIgE showed the highest diagnostic accuracy for peanut allergy when compared to total peanut IgE and other peanut allergens, unlike other studies. Despite some degree of cross-reactivity with Ara h 6, Ara h 2 is the predominant conglutin in peanut allergy in the UK.

2. Basophil Activation Test (BAT)

The BAT optimal diagnostic cutoffs in Santos et al. (2014) demonstrated 98% negative predictive value, 95% positive predictive value, and 97% accuracy. BAT made it possible to cut the number of necessary OFCs by two-thirds.

According to Santos et al. (2015), patients with CD63 peanut/anti-IgE levels of 1.3 or higher were more likely to experience severe reactions (relative risk, 3.4; 95% CI, 1.8-6.2). Additionally, this study discovered that patients who had a CD-sens value of 84 or higher were more likely to react to peanut protein 0.1 g or less (relative risk, 1.9; 95% CI, 1.3-2.8).

In Glaumann et al. 2012, ninety-two* percent of patients who were positive for DBPCFC were positive for CD-sens to peanut and Ara h 2**. In this study, peanut allergy was ruled out by a negative CD-sens.

*One child was not tested in CD-sens (peanut).

**Two children were low responders.

High sensitivity and specificity (95.3% vs. 93.2%), good positive predictive values (PPV), and negative predictive values (96% vs. 91%) were seen in the most consistent percentage CD expression (0.001-1000 ng/mL protein) for peanuts in Duan et al. 2021.

3. Mast cell activation (MAT)

In Bahri et al. 2018, MAT AUC at its optimal cut-off value of 6.3 showed 97% (95% CI, 83-100) sensitivity and 92% (95% CI, 62-100) specificity.

BAT %CD at its optimal cut-off value of 7.8 showed 80% (95%CI, 61-92) sensitivity and 89% (95% CI, 52-100) specificity.

Ara h 2 at its optimal cut-off value of 1.64 showed 77% (95% CI, 58-90) sensitivity and 83% (95% CI, 52-98) specificity.

IgE to peanut optimal cut-off value 3.8 showed 83 (95% CI, 65-94) sensitivity and 92% (95% CI, 62-100) specificity.

Note: the optimal cut-off value was determined by Youden index.

According to Zbären et al. (2024), when compared to existing SPT and sIgE tests, the diagnostic accuracy of Hoxb8 MAT was highest at allergen concentrations ≥100 ng/mL, with an area under the

curve (AUC) of 0.97, 93% sensitivity, and 96% specificity. And when compared to BAT, Hoxb8 MAT showed comparable diagnostic efficacy. Furthermore, the Hoxb8 MAT correctly classified sera from BAT non-responders as allergic and nonallergic. There were two low responders, as we noted in Glaumann et al. (2012), so it was not possible to compute a CD-sens value numerically.

Risk of Bias result

Using the QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies) tool, which assesses four important domains—patient selection, index test, reference standard, and flow and timing—the risk of bias in the included studies was evaluated. The risk of bias (ROB) and applicability in each domain were evaluated, and studies were categorized as having low, high, or unclear risk in each domain. All studies demonstrated a low risk of bias across the four domains (patient selection, index test, reference standard, and flow and timing). There were no concerns regarding applicability. This suggests that the included studies provide reliable and valid data for assessing diagnostic accuracy. A detailed risk of bias summary is provided in Figure 2.

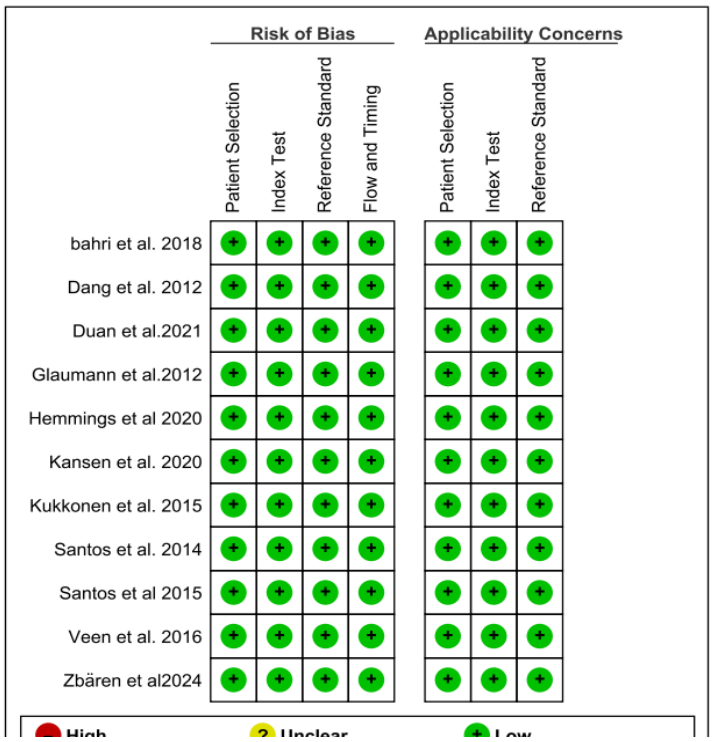

Figure 2 shows the ROB assessment summary using RevMan program.

Discussion

Summary of Findings

This systematic review evaluated and overviewed the diagnostic accuracy of different types of laboratory tests for diagnosing peanut allergy, including serum-specific IgE (sIgE), Component-Resolved Diagnostics (CRD), and the Basophil Activation Test (BAT) and Mast cell activation test (MAT). Our results indicate that while each of these tests demonstrates diagnostic utility, their performance varies significantly in terms of sensitivity and specificity.

Ara h 2 plasma sIgE test levels are more accurate than whole peanut plasma IgE protein levels and may become a new diagnostic tool that can differentiate between peanut allergy and peanut tolerance, potentially reducing the need for an OFC. The discriminative ability of sIgE to Ara h 2 and Ara h 6 is equally good compared to total peanut IgE. This suggests that co-sensitization to Ara h 2 and Ara h 6 is linked to severe reactions and can differentiate between mild symptoms and severe allergies. Component-resolved diagnostics is not better than sIgE to peanut extract or skin prick testing for peanut allergy diagnosis, according to Veen et al. 2016.

BAT proved to have a greater superiority to other tests in distinguishing between peanut allergy and tolerance and limited the need for food challenge tests. In some cases, there may be low responders, and these low responders could be classified by the Hoxb8 MAT. The severity of allergic reactions to peanuts is linked to basophil reactivity, the threshold of allergic reactions could be predicted by basophil sensitivity (CD-sens). The degree of allergic reactions during OFCs can be estimated using CD63 peanut/anti-IgE and CD-sens values. When compared to OFCs, the CD-sensing test for peanuts and the immunoassay for IgE-antibody to the peanut components seem to be safe, efficient, and economical.

Although MAT is still mostly in the research stage, it has the potential to be a useful diagnostic tool for difficult food allergy situations, such as peanut allergy. When compared to current allergy diagnostics, the mat robust can provide better diagnostic results. AND The Hoxb8 MAT demonstrated a very good diagnostic precision in patients prospectively assessed for peanut allergy, comparable to the fresh whole blood-based BAT. Additionally, it demonstrated its value for accurate classification of BAT non-responders into allergic and nonallergic individuals.

Comparison with Existing Literature

Our findings are consistent with other previous studies that show DBPCFC increases the cost of living directly and indirectly according to Cerecedo et al.(2014)[26], the limitations of conventional tests like SPT and sIgE in distinguishing between sensitization (presence of IgE antibodies) and clinical allergy (symptomatic reactions). For example, studies by Sicherer et al. (2018) [27] reported that SPT and sIgE have high sensitivity but lower specificity, which may lead to overdiagnosis when used in isolation. A meta-analysis by Jin et al. (2019) [28] demonstrated that the combination of clinical history and patient-reported symptoms greatly increases the diagnostic accuracy of SPT and sIgE. This integrated approach is supported by our review, which suggests that in order to improve diagnostic precision, laboratory test interpretation should be done in conjunction with clinical context. For whole peanut extract, Wang et al. (2018) [29] discovered that Ara h 2-specific IgE offered better specificity than conventional sIgE testing. According to their review, using component-resolved diagnostics can minimize patient risk by reducing the requirement for oral food challenges.

Mast cell activation (MAT), a novel diagnostic tool under research in the field of allergy diagnosis, in our review it shows the most accurate diagnostic results compared to standard diagnostic tests.

Clinical Implications

The results of this review have several implications for clinical practice:

1. Multi-Test Approach: No single laboratory test is definitive for diagnosing peanut allergy. Combining SPT, sIgE, and CRD can enhance diagnostic accuracy, with BAT serving as a confirmatory test in challenging cases.
2. Component-Resolved Diagnostics (CRD): Given the high specificity of Ara h 2, CRD should be considered in clinical algorithms for diagnosing peanut allergy, particularly when SPT or whole peanut sIgE results are ambiguous.
3. Reduce Overdiagnosis: The use of CRD, BAT, and MAT can help minimize overdiagnosis and unnecessary dietary restrictions by distinguishing between sensitization and true clinical allergy.

Limitations of the Review:

This review has several limitations that should be considered:

- We did not put a table of participant characteristics because this data was lacking in most of the included studies and only reported the main character of the included participants.
- Publication Bias: Despite a detailed comprehensive search strategy, there is a possibility of publication bias, as studies with negative results may not have been published.
- Limited Data for MAT: The number of studies evaluating the Mast cell activation Test was limited, which may affect the robustness of our conclusions regarding its diagnostic accuracy.

Recommendations for Future Research:

Standardization of Testing Protocols: Future studies should adopt standardized protocols for performing and interpreting diagnostic tests to reduce heterogeneity and improve comparability.

More research on the Mast cell activation test (MAT) is required.
Conducting large, multicenter studies can enhance the generalizability of findings and provide more reliable estimates of diagnostic accuracy.

Conclusion

This systematic review highlights that traditional tests like SPT and serum IgE remain useful in initial screening. Component-resolved diagnostics (Ara h 2 or Ara h 6) and basophil Activation Test (BAT) are useful for more accurate diagnosis and predicting the severity of the allergic reactions, Mast cell activation test offers superior accuracy in the diagnosis of peanut allergy and can help confirm diagnoses. A multi-test approach that incorporates these tools can enhance diagnostic accuracy, reduce the risk of overdiagnosis, improve patient management, and decrease the need for risky OFCs. Further research is needed to address existing limitations and standardize diagnostic strategies for peanut allergy.

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Conflict of Interest

There is no conflict of interest with anyone else.

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