Scoping Review of Diagnostic Delay in people with Autoimmune Blistering Diseases

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Abstract

Objective: The objective of this scoping review is to determine which autoimmune blistering diseases (AIBDs) have diagnostic delays and the reasonings behind these. Alongside this, it will look at which AIBDs have the most significant diagnostic delays and the effects this can have on patients' treatment and care satisfaction.

Introduction: Due to the rare nature of AIBDs, and the tendency to mimic other inflammatory dermatoses such as eczema, urticaria and other skin conditions such as scabies prior to blistering, there is the potential for both misdiagnosis and delay in correct diagnosis of the conditions (time between onset of symptoms and confirmation of diagnosis). This delay in diagnosis can lead to severe skin changes and symptoms as well as requiring more intensive treatments, leading to increased risk of side effects such as diabetes and osteoporosis. It is hoped that a scoping review into these delays can help increase clinical awareness of the conditions allowing for quicker diagnosis and improved patient care.

Inclusion criteria: Studies will be included if they are on people over the age of 18 years, with no geographical limits being set, with any paediatric patient being excluded from the study. To be included, the exposure must include a histopathological diagnosis of an AIBD or a misdiagnosis of another skin condition which then led to a further diagnosis of an AIBD. If studies only have other forms of blistering condition, or a diagnosis not confirmed via histopathology, then they will be excluded from the search. The outcomes included in the review, will be reasons for the delay in diagnosis, time taken between onset of symptoms and diagnosis, number of misdiagnosis and the impacts of delayed treatment, specifically side effects of the therapies. Alongside this patient satisfaction and causes of misdiagnosis will also be included. If studies are about participants diagnosed for the first time with no delay, then they will be excluded from the review.

Methods: Three databases will be searched as part of the review, with MEDLINE, EMBASE and PsycINFO all being used. These searches will be conducted in November 2025. Once the searches are conducted, the papers will be downloaded onto Endnote and then transferred onto the online

software Rayann, allowing multiple reviewers to screen both title and abstracts as well as full texts. Data will then be extracted through using a data extraction table.

Keywords: Dermatitis herpetiformis; Autoimmune blistering; Misdiagnosis; Pemphigoid; Pemphigus

Introduction

Autoimmune blistering diseases (AIBDs) are a group of rare conditions in which autoantibodies cause severe blistering on the patient's skin, and in some cases, mucous membranes. These autoimmune conditions are uncommon and therefore clinical recognition can be limited. Furthermore, they can resemble other inflammatory dermatoses such as eczema, urticaria and nodular prurigo, alongside other conditions such as scabies and generalised pruritic. These factors all contribute to delayed referral from primary care to tertiary care and therefore lead to a delay in diagnosis (time between onset of symptoms and confirmation of diagnosis) due to the conditions requiring histopathological diagnoses for confirmation (1, 2).

These delays in diagnosis lead to more severe blistering and changes to the patient's skin, alongside more severe symptoms. This means that more aggressive therapeutics will be used to treat the conditions leading to severe side effects such as diabetes and osteoporosis. If these diagnostic delays were reduced, then milder treatment interventions could be used earlier reducing the risk of severe side effects, as well as avoiding inappropriate treatments and the need for hospitalisation. These would improve patient satisfaction ratings in their care, whilst also reducing financial burdens for healthcare systems.

A recent international survey explored the unmet needs in pemphigoid diseases from the perspective of patients, clinicians and researchers. A total of 135 participants were included in the study, with data on patient satisfaction showing that 50% of patients were unsatisfied with patient care during the diagnostic process. This was mainly due to misdiagnosis and long diagnostic delays. Six patients visited more than five doctors before a correct diagnosis was made, highlighting the frequency of these diagnostic delays(3).

A preliminary search of MEDLINE was conducted and no current or underway systematic reviews or scoping reviews on the topic were identified.

The aim of the review is to understand diagnostic delay in people over the age of 18 with an autoimmune blistering disease, including which of the diseases are associated with longer diagnostic delay. Alongside this, the aim is to investigate what causes these diagnostic delays, with a hope that the review can improve clinical knowledge and recognition of these diseases to improve patient satisfaction and reduce side effects associated with more severe treatments.

Objectives:

1) To determine for which AIBDs there tends to be a delay in diagnosis
2) To determine factors which lead to delay in diagnosis

3) To determine average delay in diagnosis

Review question

Do patients over the age of 18 with an autoimmune blistering disease experience diagnostic delay globally?

- Do these delays differ between different AIBDs?
- What are the reasons behind these diagnostic delays?
- What impact do these delays have on patient care and treatment?

Inclusion criteria

Participants

Patients over the age of 18 will have a histopathological diagnosis of an autoimmune blistering disease globally. They will also be eligible if they have had a misdiagnosis of another skin condition which then led to further diagnosis of an AIBD. Any patient under the age of 18, with another skin condition or a diagnosis without histopathological confirmation will be excluded from the study.

Concept

Papers will be included if they have data on the length of diagnostic delay of an AIBD, or if they include reasons behind these delays. They will also be included if there are multiple misdiagnosis eventually leading to an AIBD, as well as the impact these delays in treatment have had on patient satisfaction and therapeutic side effects. If patients have been diagnosed first time with no delay, then they will be excluded from the review.

Context

There will be no geographical limits on papers to be included, to gain a global picture of diagnostic delays. A dermatology referral will be required for a confirmed diagnosis.

Types of sources

This scoping review will consider quantitative analytical observational studies including retrospective cohort studies, case-control studies and analytical cross-sectional studies. In addition to these, descriptive observational studies will also be included, such as case series, individual case reports and descriptive cross-sectional studies.

This scoping review will not consider both experimental and quasi-experimental study designs including randomized controlled trials, non-randomized controlled trials, before and after studies and interrupted time-series studies. Furthermore, systematic and scoping reviews have also been excluded from this review. The review also excludes expert opinion, animal studies, background information and conference abstracts. This is to ensure that primary data is used for the review.

Methods

The proposed scoping review will be conducted in accordance with the JBI methodology for scoping reviews (4).

Any deviations from the protocol will be reported and justified in the appropriate section of the methods.

Search strategy*:*

The search strategy will aim to locate both published and unpublished studies. A two-step search strategy will be utilized in this review. First an initial limited search of MEDLINE (PubMed), EMBASE and PsycINFO was used and change as appropriate was undertaken to identify articles on the topic. The text words contained in the titles and abstracts of relevant articles, and the index terms used to describe the articles were used to develop a full search strategy for report the name of the relevant databases/information sources *(see Appendix I*). The search strategy, including all identified keywords and index terms, will be adapted for each included database and/or information source.

Studies published in any language and in any country will be included. Studies published since inception of the databases will be included.

Three databases were used in the final search, MEDLINE, EMBASE and PsycINFO. All three databases were searched using the online OVID platform. Unpublished articles will be identified via ProQuest Dissertations & Theses (available via NUsearch).

Study/Source of evidence selection

Following the search, all identified citations will be collated and uploaded into EndNote 21, before being transferred into the online software Rayann and duplicates removed. Following a pilot test, titles and abstracts will then be screened by two independent reviewers on Rayann for assessment against the inclusion criteria for the review. Potentially relevant sources will be retrieved in full and assessed in detail against the inclusion criteria by three independent reviewers. Reasons for exclusion of sources of evidence at full text that do not meet the inclusion criteria will be recorded and reported in the scoping review. Any disagreements that arise between the reviewers at each stage of the selection process will be resolved through discussion, or with an additional reviewer. The results of the search and the study inclusion process will be reported in full in the final scoping review and presented in a PRISMA flow diagram (5).

Data extraction

Data will be extracted from papers included in the scoping review by two or more independent reviewers using a data extraction tool developed by the reviewers (Appendix 2). The data extracted will include specific details about the participants, concept, context, study methods and key findings relevant to the review questions.

Data analysis and presentation

A narrative synthesis will accompany the tabulated and charted results and will describe how the results relate to the reviews objective and questions.

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Conflicts of interest

None

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Appendices

Appendix I: Search strategy

MEDLINE (via Ovid)

Pemphigus (MH) OR **Pemphigoid, Bullous** (MH) OR **Pemphigoid, Benign Mucous Membrane** (MH) OR **Pemphigus, Benign Familial** (MH)

OR

- Autoimmune blistering diseases
    - Conditions

OR

- Autoimmune bullous diseases
    - Conditions

OR

- Autoimmune skin diseases
    - Conditions

OR

- Bullous pemphigoid

OR

- Mucous membrane pemphigoid

OR

- Epidermolysis bullosa acquisita

OR

- Dermatitis herpetiformis

OR

- Linear IgA bullous dermatosis

OR

- IgA pemphigus

OR

- Pemphigus vulgaris

OR

- Pemphigus foliaceus

AND

- Diagnosis

OR

- Diagnostic

OR

- Diagnostic pathway

AND

- Misdiagnosis

- Delay

OR

- Time

1st search 30/10/25 = 716

EMBASE (Via Ovid)

Pemphigus (MH) OR **Bullous pemphigoid** (MH) OR **Pemphigoid** (MH) OR **mucous membrane pemphigoid** (MH)

OR

- Autoimmune blistering diseases
    - Conditions

OR

- Autoimmune bullous diseases
    - Conditions

OR

- Autoimmune skin diseases
    - Conditions

OR

- Bullous pemphigoid

OR

- Mucous membrane pemphigoid

OR

- Epidermolysis bullosa acquisita

OR

- Dermatitis herpetiformis

OR

- Linear IgA bullous dermatosis

OR

- IgA pemphigus

OR

- Pemphigus vulgaris

OR

- Pemphigus foliaceus

AND

- Misdiagnosis

OR

- Delay

1st Search 10/11/25 = 279

PsycINFO (Via Ovid)

- Autoimmune blistering diseases
    - Conditions

OR

- Autoimmune bullous diseases
    - Conditions

OR

- Autoimmune skin diseases
    - Conditions

OR

- Bullous pemphigoid

OR

- Mucous membrane pemphigoid

OR

- Epidermolysis bullosa acquisita

OR

- Dermatitis herpetiformis

OR

- Linear IgA bullous dermatosis

OR

- IgA pemphigus

OR

- Pemphigus vulgaris

OR

- Pemphigus foliaceus

AND

- Misdiagnosis

- Delay

OR

- Time

1st Search 11/11/25 = 4 papers

Appendix II: Data extraction instrument