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A Systematic Review of Bullous Pemphigoid and HLA-DQA1

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Abstract

There is growing evidence suggesting that specific HLA-DQA1 alleles are associated with increased odds of developing bullous pemphigoid. However, this evidence remains inconclusive, thus, a meta-analysis is needed to synthesize the available literature and provide a comprehensive overview of the association between HLA-DQA1 and bullous pemphigoid. The ultimate goal of this research is to provide valuable insights into identifying carriers of the condition.

Troubleshooting

Administrative Information

1 **Tilte:**

"A Systematic Review of Bullous Pemphigoid and HLA-DQA1"

Registrations:

protocols.io

2 **Authors (in order):**

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Principal Investigator: Leading Edge Dermatology
Dr. Elyse Julian, D.O.

3 **Amendments**

Amendments will be provided, as necessary.

Support

Sources: There are no sources of financial support for this research.
Institution: Lake Erie College of Osteopathic Medicine - Bradenton
Principal Investigator: Elyse Julian, D.O.
Role of Principal Investigator: Oversight of Research

Introduction

4 **Rationale**

There is growing evidence suggesting that specific HLA-DQA1 alleles are associated with increased odds of developing bullous pemphigoid. However, this evidence remains inconclusive, thus, a meta-analysis is needed to synthesize the available literature and provide a comprehensive overview of the association between HLA-DQA1 and bullous pemphigoid. The ultimate goal of this research is to provide valuable insights into identifying carriers of the condition.

5 **Objectives**

1. To systematically review literature on the association between bullous pemphigoid and HLA-DQA1 alleles.
2. To identify the HLA-DQA1 alleles that are associated with an increased or decreased odds of developing bullous pemphigoid.
3. To identify gaps in the current literature and highlight areas for future research.

Methods

6 **Eligibility Criteria**

Inclusion Criteria:
1. Studies that investigate the association between HLA-DQA1 and bullous pemphigoid in human subjects.
2. Studies published after the year 2000 will be included in the data analysis.
3. Studies published in the English language.
4. Studies accessible through open access or institutional access.

Exclusion Criteria:
1. Studies not published in the English language.
2. Studies which do not have all information needed to conduct a proper review.
3. Studies with confusing, unintelligible, or difficult-to-interpret data.
4. Studies that investigate other autoimmune disorders or skin conditions.

7 **Information Sources**

Databases used for this study include PubMed/MEDLINE, Google Scholar, Embase and Cochrane Library. Institutional access will be used when available for journals which may not be open access. Data will be gathered for approximately a few weeks to a month.

8 **Search Strategy**

The search strategy will incorporate relevant terms such as: "Bullous Pemphigoid," and "HLA-DQA1," "genetic predisposition to disease," and related terminology. To address potential limitations, the search will require both HLA-DQA1 and bullous pemphigoid to appear in the article. Additionally, a manual review of the reference lists of identified articles will be performed. To ensure data quality, searches will be restricted to articles published in English, and results will be filtered based on the predetermined inclusion and exclusion criteria. The search process will be conducted by three independent reviewers. A fourth reviewer will be available to resolve any discrepancies.

9 Study Records

9.1 Data Management

The search results will be listed in a shared document, which will be utilized to manage sources and data. Duplicates will be removed and the remaining articles will be screened for eligibility using the inclusion and exclusion criteria listed below.

9.2 Selection Process

During the selection process, three independent reviewers will screen the titles and abstracts of the articles identified in the search to determine their relevance to the research topic. Articles that are deemed potentially eligible will have their full text retrieved and reviewed for inclusion. To be included in the review, studies must contain all relevant data items or enough data to calculate the data items and be specific to individual HLA-DQA1 alleles. A minimum of three articles are required to include an HLA-DQA1 for meta-analysis. Alleles will be excluded if a minimum of three viable studies cannot be identified. Moreover, the specific HLA-DQA1 allele must be studied in isolation in the article.

9.3 Data Collection Process

Data will be collected from individual studies by three researchers. The gathered data will be placed on a single shared Excel document. Any questions related to the authenticity or accuracy of the data are referred to the other researchers involved in the study. If a consensus cannot be reached, the Principal Investigator will be consulted for the final decision.

10 Data Items

The data items collected include:
1. Study design (Case control, cohort, etc.)
2. HLA-DQA1 allele investigated

3. Population characteristics of the sample used
4. Number of controls
5. Number of controls with the HLA-DQA1 alleles
6. Number of cases of bullous pemphigoid
7. Number of cases with bullous pemphigoid and HLA-DQA1 alleles
8. Calculable or provided odds ratio with associated confidence intervals of each individual allele

11 **Outcomes and Prioritization**

The study objectives will guide the data collection process, with a focus on identifying HLA-DQA1 alleles that meet the inclusion criteria in at least three eligible studies. To ensure consistency and reliability of results, only alleles with low heterogeneity ($I^2 \leq$ 25%) and statistical significance will be included in the final analysis.

12 **Risk of Bias in Individual Studies**

The NIH Quality Assessment of Case-Control Studies Tool may be used for risk of bias assessment. Doi plots and/or an LFK index will be measured with MetaXL as a quantitative measure of bias.

Data Synthesis

13 A: Revman 5.4 and MetaXL will be used for statistical analysis. Revman will be used for sample analysis based on sample size and MetaXL will be used for analysis based purely on odds ratio with associated confidence intervals.

B: Odds ratios and confidence intervals will be assessed. I^2 will also be used to examine heterogeneity. Heterogeneity which shows an I^2 above 50% will be considered high heterogeneity. p values must be below 0.05 to provide enough evidence of a difference between odds.

Revman citation:
The Cochrane Collaboration. (2020). Review Manager (RevMan) [Computer Program]. Version 5.4.

Barendregt, JJ., Doi SA. (2017). MetaXL User Guide Version 5.3. Retrieved from: http://www.epigear.com/index_files/MetaXL%20User%20Guide.pdf

14 **Meta-bias(es)**

The GRADE system will be used to assess the strength of the body of evidence.

Citation for criteria:
Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, Guyatt GH, Harbour RT, Haugh MC, Henry D, Hill S, Jaeschke R, Leng G, Liberati A, Magrini N, Mason J, Middleton P, Mrukowicz J, O'Connell D, Oxman AD, Phillips B, Schünemann HJ, Edejer T, Varonen H, Vist GE, Williams JW Jr, Zaza S; GRADE Working Group. Grading quality of evidence and strength of recommendations. BMJ. 2004 Jun 19;328(7454):1490. doi: 10.1136/bmj.328.7454.1490. PMID: 15205295; PMCID: PMC428525.