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Protocol: MHC class I and dengue hemorrhagic fever: a systematic review of HLA-A*24 and HLA-B*44

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This project will examine the effect of two MHC class I alleles, HLA-A*24 and HLA-B*44 on dengue hemorrhagic fever susceptibility. A systematic review will be conducted comparing the HLA-A*24 and HLA-B*44 via subgroup analysis and generation of forest plots.

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Title

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Registration

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Authors

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3.2 Dr. Teresa Pettersen is the PI of the research. Andrew Cook and Dylan Thibaut are first and second reviewers.

Amendments

4 Amendments to the protocol will be provided if necessary.

Support

5 No funding was acquired for this research.

Introduction

6

6.1 The association of HLA alleles with dengue fever and dengue hemorrhagic fever is a topic of research interest. Dengue fever has been evaluated for associations with HLA alleles. In this study, we investigate the role of HLA

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class I alleles, HLA-A*24 and HLA-B*44 in a more severe form of the disease, dengue hemorrhagic fever.

6.2 This review investigates the role of HLA-A*24 and HLA-B*44 alleles in susceptibility or protection to dengue hemorrhagic fever compared to healthy control group. These results are compared to the role HLA-A*24 and HLA-B*44 contribute to protection or susceptibility to dengue fever.

Methods

7

7.1 Patients possessing HLA-A*24 or HLA-B*44 that were diagnosed with dengue hemorrhagic fever (DHF) or dengue fever (DF), including primary or secondary infection.

A systematic review will be performed. Studies from 2000 - 2022 will be included. Only studies published in English will be used. This study will be performed starting in May 2022.

7.2 Google Scholar database will be used in the literature review.

7.3 The search terms will be used in Google Scholar, "HLA Dengue Fever", "HLA Dengue Hemorrhagic Fever". "HLA-A*24 Dengue Hemorrhagic fever", "HLA-A*24 Dengue fever", "HLA-B*44 Dengue Hemorrhagic fever", "HLA-B*44 Dengue fever". Limitations on study publication date from 2000-2022 will be applied.

7.4 A shared document will be used to manage records of sources and data collected. This data will be transferred to Review Manager 5.4 for further analysis.

7.5 Two independent reviewers selected studies in this research according to the following criteria.

Inclusion criteria: Patients possessing HLA-A*24 or HLA-B*44 that were diagnosed with dengue hemorrhagic fever (DHF) or dengue fever (DF), including primary or secondary infection. Studies using odds ratio or sufficient data available to calculate an odds ratio.

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Exclusion criteria: Studies including patients diagnosed with dengue shock syndrome (DSS). Patients diagnosed according to the 2009 WHO guidelines of severe dengue and dengue. Studies in a foreign language, studies using animals as subjects, and studies not using odds ratio or studies with insufficient data available to calculate odds ratios.

7.6 Data will be extracted from studies independently.

7.7 HLA-A*24 and HLA-B*44 allele frequencies of patients with dengue fever, dengue hemorrhagic fever, and healthy control populations will be gathered.

7.8 Outcomes: Determining odds of dengue hemorrhagic fever and dengue fever given presence of HLA-A*24 or HLA-B*44.

7.9 Risk bias assessment: The NIH quality assessment of case-control studies tool, and DOI plot will be used.

7.10 HLA-A*24 and HLA-B*44 allele frequency data among those with dengue hemorrhagic fever will be compared to those with the given allele who are healthy. This will be repeated with dengue fever as well. This data will be inputted into Review Manager 5.4 to generate odds ratios from each study. These odds ratio will then be used to create forest plots. If a study contains multiple populations, these will be combined into one odds ratio. I^2 will be used in consideration for heterogeneity. MetaXL software can be used for any other tests necessary not covered by this program.

7.11 The Grading of Recommendation, Assessment, Development and Evaluation (GRADE) system will be used in the evaluation of the strength of the body of evidence.

Current Research Stage

8 Current stage of research: preliminary planning and protocol creation.

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