A Scoping Review of Enterovirus D-68

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Objective

To create a scoping review on enterovirus D-68 (EV-D68) that will serve as a useful tool to guide future research with the aim of filling critical information gaps and supporting the development of public health preparedness activities.

Introduction

EV-D68 is a non-polio enterovirus, primarily resulting in respiratory illness, with clinical symptoms ranging from mild to severe. Infection has also been associated with severe neurological conditions like acute flaccid myelitis (AFM). EV-D68 was first discovered in 1962, with infrequent case reports until 2014 at which point a widespread multi-national outbreak mostly affecting the pediatric population occurred across North America, Europe, Southeast Asia and Africa. This outbreak was associated with an increase in AFM, with cases being reported in Canada, the United States, Norway, and France. With this new and emerging threat, public health and other organizations were called upon to implement response measures such as establishment of case definitions, surveillance mechanisms, and recommendations for clinical and public health management. The response to the 2014 outbreak in Canada highlighted several important EV-D68 evidence gaps including a lack of risk factor and clinical information available for non-severe cases, and uncertainty around seasonal, cyclical and secular trends. Given the increased reporting of EV-D68 cases associated with severe outcomes, it's critical that public health establishes what is known about EV-D68 in order to support decision-making, education and other preparedness activities and to highlight priority areas for future research to fill critical knowledge gaps. Scoping reviews provide a reproducible and updateable synthesis research methodology to identify and characterise all the literature on a broad topic as a means to highlight where evidence exists and where there are knowledge gaps. In order to systematically characterise the EV-D68 knowledge base, a scoping review was conducted to map the current body of evidence.

Methods

A literature search of published and grey literature on EV-D68 was conducted on May 1, 2017. A standardized search algorithm was implemented in four bibliographic databases: Medline, Embase, Global Health and Scopus. Relevant grey literature was sought from *a priori* identified sources: the World Health Organization, United States Centers for Disease Control and Prevention, the Public Health Agency of Canada, the European Centre for Disease Prevention and Control, and thesis registries. Two-level relevance screening (title/abstract followed by full-text) was performed in duplicate by two independent reviewers using pretested screening forms. Conflicts between the reviewers were reconciled following group discussion with the study team. English and French articles were included if they reported on EV-D68 as an outcome. There were no limitations by date, publication type, geography or study design. Conference abstracts were excluded if they did not provide sufficient outcome information to characterize. The articles were then characterized by two independent reviewers using a pretested study characterization form. The descriptive characteristics of each article were extracted and categorized into one of the following broad topic categories: 1) Epidemiology and Public Health, 2) Clinical and Infection Prevention and Control (IPC), 3) Guidance Products, 4) Public Health Surveillance, 5) Laboratory, and 6) Impact. The Epidemiology and Public Health category contained citations describing prevalence, epidemiological distribution, outbreak data and public health mitigation strategies. Clinical and IPC citations included details regarding symptoms of EV-D68 infection, patient outcomes, clinical investigation processes, treatment options and infection prevention and control strategies. The Guidance category included citations that assess risk, provide knowledge translation or provide practice guidelines. Public Health Surveillance citations provided details on surveillance systems. Citations in the laboratory category included studies that assessed the genetic characteristics of circulating EV-D68 (phylogeny, taxonomy) and viral characteristics (proteins, viral properties). Lastly, the Impact category contained citations describing the social, economic and resource burden of EV-D68 infection. Each broad topic category was subsequently characterised further into subtopics.

Results

The search yielded a total of 384 citations, of which 300 met the inclusion criteria. Twenty-six of forty-three potentially relevant grey literature sources were also included. Preliminary literature characterization suggests that the majority of the published literature fell under the topic categories of Epidemiology, Clinical, and Laboratory. There were limited published articles on public health guidance, IPC, surveillance systems and the impact of EV-D68. The grey literature primarily consisted of webpages directed towards the public (what EV-D68 is, how to prevent it, what to do if ill, etc.). This scoping review work is presently underway and a summary of the full results will be presented at the 2018 Annual Conference.

Conclusions

The body of literature on EV-D68 has increased since the 2014 outbreak, but overall remains small and contains knowledge gaps in some areas. To our knowledge, this scoping review is the first to classify the entirety of literature relating to EV-D68. It will serve as a useful tool to guide future research with the aim of filling critical information gaps, and supporting development of public health preparedness activities.

Keywords

Enterovirus D68; Scoping review; EV-D68

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