Comprehensive Literature Review of the Humanistic Burden of Clostridium (Clostridiodes) difficile Infection

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Abstract: Background: Clostridiodes (formerly Clostridium) difficile infection (CDI) is an anaerobic, spore-forming bacterium with manifestations including diarrhea, pseudomembranous colitis and toxic megacolon. Despite general understanding that CDI may be associated with marked burden on patients' health, there has been limited information available on the humanistic burden of CDI. The objective of this literature review was to summarize the published data on the humanistic burden of CDI globally, in order to better inform future research efforts and increase awareness of the patient perspective in this disease. Methods: A comprehensive literature review of the past 15 years (2002-2017) was conducted using MEDLINE, Embase and Cumulative Index of Nursing and Allied Health Literature. Additional searches were conducted from conference proceedings (2015-2017). Articles selected were studies specifically designed to examine the humanistic burden of illness associated with adult patients with CDI. Results: Of 3,325 articles or abstracts identified, 33 remained after screening and full text review. Sixty percent (60%) were published in 2016 or 2017. Data from the United States or Western Europe were most common. Data from Brazil, Canada, China and Spain also exist. Thirteen (13) studies used validated patient-reported outcomes instruments, mostly EQ-5D utility and SF-36 generic instruments. Three (3) studies used CDI-specific instruments (CDiff32, CDI-DaySyms). The burden of CDI impacts patients in multiple health-related quality of life (HRQOL) domains. SF-36 domains with the largest decrements compared to other GI diarrheal diseases (IBS-D and Crohn's) were role physical, physical functioning, vitality, social functioning, and role emotional. Reported EQ-5D utilities for CDI ranged from 0.35-0.42 compared to 0.65 in Crohn's and 0.72 in IBS-D. The majority of papers addressed physical functioning and mental health domains (67% for both). Across various studies patients reported weakness, lack of appetite, sleep disturbance, functional dependence, and decreased activities of daily lives due to the continuous diarrhea. Due to lack of control over this infection, CDI also impacts the psychological and emotional quality of life of the patients. Patients reported feelings of fear, anxiety, frustration, depression, and embarrassment. Additionally, the type of disease (primary vs. recurrent) may impact mental health. One study indicated that there is a decrement in SF-36 mental scores in patients with recurrent CDI, in comparison to patients with primary CDI. Other domains highlighted by these studies include pain (27%), social isolation (27%), vitality and fatigue (24%), self-care (9%), and caregiver burden (0%). Two studies addressed work productivity, with 1 of these studies reporting that CDI patients had the highest work productivity and activity impairment scores among the gastrointestinal diseases. No study specifically included caregiver self-report. However, 3 studies did provide mention of patients' worry on how their diagnosis of CDI would impact family, caregivers, and/or friends. Conclusions: Despite being a serious public health issue there has been a paucity of research on the HRQOL among those with CDI. While progress is being made, gaps exist in understanding the burden on patients, caregivers, and families. Future research is warranted to aid understanding of the CDI patient perspective.

Keywords: burden, Clostridiodes, difficile, humanistic, infection

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