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A Comprehensive Review: Inflammatory Bowel Disease And Its Global Perspective

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Abstract:

Inflammatory bowel disease (IBD), comprising ulcerative colitis (UC) and Crohn's disease (CD), represents a persistent gastrointestinal inflammatory condition. Initially labeled as a "Western disease," IBD was predominantly associated with Western lifestyles, but a shift in dietary and lifestyle patterns has led to a noticeable rise in Asian populations. The global prevalence of IBD reached 6.8 million cases in 2017, with a subsequent decrease to 4.9 million cases in 2019, showcasing a dynamic occurrence. The multifactorial pathogenesis involves genetic susceptibility, environmental factors, and an aberrant immune response to the gut microbiota. IBD is classified into CD, affecting any part of the gastrointestinal tract, and UC, limited to the colon and rectum. A third category, IBD-unspecified (IBD-U), is utilized when the inflammation's origin is unclear. Complications, including strictures, fistulas, and colorectal cancer, emphasize the disease's severity. Treatment options range from aminosalicylates to biologics, with emerging therapies and a focus on the mucosal antibacterial barrier offering potential advancements. Global healthcare organizations, recognizing IBD as a global ailment, aim to summarize epidemiological patterns to guide interventions. In study on global burden of disease 40 million cases were reported, prevalence of more than 1 percent of total global incidence has been seen worldwide, 41.00 thousand deaths, and 1622.50 thousand DALYs globally in 2019. While advancements have been made, further research is crucial to improve prevention and treatment strategies. The shift in the pathogenic focus towards mucosal antibacterial barriers presents a potential avenue for future developments, offering hope for enhanced outcomes and improved quality of life for individuals affected by IBD.

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Keywords: Inflammatory Bowel Disease, Ulcerative Colitis, Crohn's Disease, Gut microbiota

Introduction

Define Inflammatory bowel disease

Inflammatory bowel disease (IBD) encompasses Crohn's disease (CD) and Ulcerative Colitis (UC), representing a persistent inflammatory condition affecting the gastrointestinal tract. Initially labeled as a condition linked to Western lifestyles, it was often referred to as the "Western disease." Approximately 1 million individuals in the United States and 2.5 million in Europe are estimated to be affected by IBD. However, shifting dietary and lifestyle patterns have led to a noticeable rise in IBD incidence within Asian populations. The origin of IBD exhibits significant diversity, marked by unpredictable episodes of relapses and remissions. Notably, there is currently no definitive clinical remedy for IBD. Individuals grappling with IBD must navigate life with this enduring chronic ailment, necessitating the rebuilding of their lives. This prolonged experience with the disease can substantially compromise the quality of life (QoL) for those affected by IBD.[1,2]

Prevalence of IBD Globally

Inflammatory bowel disease (IBD) represents a worldwide health issue, displaying differing levels and patterns in various countries and regions.[3] In the year 2017, the global tally of inflammatory bowel disease (IBD) reached 6.8 million cases.[4] The standardized prevalence rate adjusted for age rose from 79.5 per 100,000 individuals in 1990 to 84.3 per 100,000 individuals in 2017.[4] Nevertheless, by the year 2019, the global count of inflammatory bowel disease (IBD) cases stood at 4.9 million. The age-standardized prevalence and incidence rates demonstrated a decline from 73.23 and 6.1 in 1990 to 59.2 and 4.9 in 2019, respectively.[5]

Global morbidity and mortality due to IBD

In 2019, inflammatory bowel disease (IBD) emerged as a substantial global health issue, with an estimated total of around 4.9 million cases worldwide.[6] Incidence Rate: The age-standardized incidence rate of inflammatory bowel disease worldwide in 2019 was recorded at 4.97 per 100,000 person-years. Mortality Rate: In 2019, the age-standardized mortality rate for inflammatory bowel disease globally stood at 0.54 per 100,000 person-years. In 2019, the age-standardized rate of Disability-Adjusted Life Years (DALYs) attributable to inflammatory bowel disease globally was 20.15 per 100,000 person-years.[3]

Types of Inflammatory bowel disease

Inflammatory bowel disease (IBD) is a persistent and recurrent inflammatory condition affecting the gastrointestinal tract. It is commonly classified into two primary forms: Crohn's disease (CD) and Ulcerative colitis (UC).[7,8]

Crohn's Disease (CD): This form of inflammatory bowel disease can impact any segment of the gastrointestinal tract, spanning from the oral cavity to the rectum. It is distinguished by transmural inflammation, signifying that the inflammation might permeate the complete thickness of the bowel wall. Manifestations can exhibit considerable diversity, commonly encompassing abdominal pain, diarrhea, weight loss, and malnutrition.[9]

Ulcerative Colitis (UC): UC is confined to the colon and rectum. It is identified by inflammation and ulcers in the innermost lining of the colon and rectum. Common symptoms encompass diarrhea mixed with blood and mucus, abdominal pain, a pressing need to defecate, and weight loss.[9]

Additionally, there exists a third classification referred to as IBD-unspecified (IBD-U), utilized when it is uncertain whether the inflammation arises from Crohn's disease (CD) or Ulcerative Colitis (UC).[7]

The development of inflammatory bowel disease (IBD) is influenced by multiple factors, encompassing genetic susceptibility, environmental elements, and an abnormal immune response to the gut microbiota. Despite notable progress in comprehending the condition, the precise cause remains unidentified, and a definitive cure is presently unavailable. Treatment endeavors focus on mitigating inflammation, addressing symptoms, and enhancing the overall quality of life.[10]

Severity of IBD

Inflammatory bowel disease (IBD) is a persistent inflammatory disorder of the gastrointestinal (GI) tract, characterized by a cyclical pattern of relapses and remissions. It includes both ulcerative colitis (UC) and Crohn's disease (CD). The degree of severity in IBD can be assessed through diverse clinical indices, although there is a scarcity of validated tools for appraising IBD severity in studies reliant on administrative claims.[11]

The severity of inflammatory bowel disease (IBD) is influenced by various factors, such as the effect of the illness on the individual, the overall disease load, and the progression of the condition. These criteria are interrelated, with their correlations and interactions not consistently being proportional or mutually exclusive.[12]

Evaluating the influence of the illness on the individual involves an assessment of clinical symptoms, quality of life, fatigue, and disability. The disease burden is gauged by indicators like inflammatory markers (such as C-reactive protein), mucosal lesions, upper gastrointestinal engagement, and the extent of the disease. Factors contributing to the disease course encompass structural damage, historical aspects or the extension of intestinal resection, perianal disease, frequency of flares, and the emergence of extraintestinal manifestations.[12]
A research effort formulated and authenticated an index for measuring the severity of inflammatory bowel disease (IBD) utilizing data from administrative claims in the United States. This study identified autonomous factors that can predict hospitalizations related to IBD, and these predictors were employed in devising severity indices for IBD. These indices serve the purpose of forecasting outcomes associated with IBD by leveraging databases of administrative claims.[11]

Global distribution of IBD

The reported escalation in the global impact of inflammatory bowel disease (IBD) necessitates regular updates of methodologies and datasets to enhance precision in estimating figures for guiding healthcare policies. In 2019, the worldwide count of IBD cases reached about 4.9 million. While the age-standardized prevalence and incidence rates declined from 73.23 and 6.1 in 1990 to 59.2 and 4.9 in 2019, respectively, the highest rates were observed in North America, with the lowest rates reported in Oceania.[5]
Regions with a high socio-demographic index (SDI) exhibited the highest age-standardized prevalence rate, although these rates showed a decline in 2019 when compared to figures from 1990. Conversely, the age-standardized prevalence and incidence rates experienced an increase in middle, low middle, and low SDI quintiles over the three decades. Globally, the age-standardized rates for deaths, disability-adjusted life years (DALYs), years lived with disability (YLD), and years of life lost (YLL) demonstrated a decrease from 1990 to 2019. Within the same timeframe, the total count of individuals with inflammatory bowel disease (IBD) in India doubled from 0.13 million to 0.27 million, with the age-standardized incidence rate rising from 2.23 to 2.34.[5]

Major causes of IBD

The precise origin of inflammatory bowel disease (IBD) remains unidentified, yet it is believed to arise from an intricate interplay among genetic, environmental, microbial, and immune factors[13-15] Genetic Aspects: Extensive research has recognized more than 200 genetic loci linked to inflammatory bowel disease (IBD), underscoring a substantial genetic contribution. Nevertheless, these genetic elements in isolation do not account for the entirety of the risk associated with IBD, implying the participation of additional factors.[13] Environmental Elements: Factors in the environment, including diet, smoking, and early-life exposure to antibiotics, have been identified as contributors to the advancement of inflammatory bowel disease (IBD).[16] A Western-style diet and lifestyle have been linked to a heightened occurrence of inflammatory bowel disease (IBD).[13] Microbial Factors: The gut microbiota plays a pivotal role in the onset of inflammatory bowel disease (IBD). An observed imbalance in the gut microbiota, termed dysbiosis, has been noted in individuals with IBD.[13] Specific pathogens or viruses have the potential to induce a persistent inflammatory response, culminating in the development of inflammatory bowel disease (IBD).[17] Immune Aspects: Inflammatory bowel disease (IBD) is marked by an aberrant immune response within the gastrointestinal tract. This response entails the infiltration of neutrophils and macrophages that release cytokines.[13] An impaired mucosal immune response to commensal bacteria is implicated in the development of inflammatory bowel disease (IBD), particularly Crohn's disease (CD).[17]

Major Complications arises due to IBD

Inflammatory bowel disease (IBD), encompassing both Crohn's disease (CD) and ulcerative colitis (UC), may result in various complications, affecting both the intestines and other organs outside the gastrointestinal tract.[18-21] Intestinal Complications: These encompass strictures, fistulas, abscesses, and colorectal cancer. Strictures, a frequent complication of Crohn's disease (CD), can result in bowel obstruction. Fistulas, abnormal connections between distinct parts of the intestine or between the intestine and other organs, are also prevalent in CD. Abscesses, pockets of pus, can develop in regions affected by disease activity. Both CD and ulcerative colitis (UC) elevate the risk of colorectal cancer.[18] Extraintestinal Complications:
These complications can impact diverse bodily systems. Frequently observed extraintestinal manifestations encompass arthritis, skin disorders such as erythema nodosum and pyoderma gangrenosum, eye issues like uveitis and episcleritis, and liver conditions like primary sclerosing cholangitis.[19] Complications Associated with Surgery: Individuals with inflammatory bowel disease (IBD) frequently undergo surgery due to complications of the disease or ineffectiveness of medical treatment. Postoperative complications may involve anastomotic leak, wound dehiscence, pelvic sepsis, perianal fistula, anastomotic stricture, small bowel

obstruction, and various infectious complications.[20] Drug-Induced Complications: Treatment for inflammatory bowel disease (IBD) may give rise to adverse effects. For instance, the use of corticosteroids may lead to osteoporosis, and the administration of immunosuppressive drugs can heighten the susceptibility to infections and specific cancers.[18] Renal Complications: Inflammatory bowel disease (IBD) can result in complications affecting the kidneys, such as nephrolithiasis, tubulointerstitial nephritis, and glomerulonephritis.[21]

Current available treatment for IBD

Management of IBD focuses on symptom control, sustaining remission, and enhancing the overall quality of life. The selection of treatment modalities is contingent upon the type, location, and severity of the disease.[19,22] Aminosalicylates: These are commonly employed for mild to moderate cases of UC. Instances encompass mesalamine, sulfasalazine, balsalazide, and olsalazine.[19] Corticosteroids: These are used for moderate to severe IBD. Examples include prednisone and budesonide.[19] Immunomodulators: These are used for moderate to severe IBD that doesn't respond to other treatments. Examples include azathioprine, 6-mercaptopurine, and methotrexate.[19] Biologics: These are used for moderate to severe IBD that doesn't respond to other treatments. Examples include anti-TNF agents (infliximab, adalimumab, etc.), anti-integrins (vedolizumab), and anti-interleukins (ustekinumab).[19,22] Janus Kinase (JAK) Inhibitors: These are a new class of drugs used for moderate to severe IBD. An example is tofacitinib.[22] Other Treatments: Other treatments under development include sphingosine-1-phosphate receptor modulators and other small molecules.[19,22]

View of global health care organization on IBD

Inflammatory bowel disease (IBD) is acknowledged as a global ailment by healthcare entities worldwide. The incidence of IBD is on the rise, particularly in developing nations, and this upward trend is anticipated to persist due to shifts in dietary and lifestyle practices. Global healthcare organizations are committed to summarizing the latest epidemiological trends of IBD at national, regional, and global levels to garner attention and delineate measures to alleviate the disease burden. They compile data on IBD's incidence, prevalence, mortality, and disability-adjusted life years (DALYs) across diverse countries and territories.

The Global Burden of Disease Study 2019 documented a total of 404.55 thousand incident cases, 4898.56 thousand prevalent cases, 41.00 thousand deaths, and 1622.50 thousand DALYs attributed to IBD globally in 2019. The age-standardized DALYs showed a decrease from 27.2 in 1990 to 20.15 per 100,000 individuals in 2019. Regions with a high socio-demographic index consistently exhibited notable age-standardized rates over the past three decades. In 2019, high-income North America registered the highest age-standardized rates, followed by Western Europe and Australasia. An understanding of shifts in epidemiological patterns is crucial to furnish evidence for mitigating the escalating IBD burden. This knowledge aids global healthcare organizations in formulating and executing strategies for the prevention, early detection, and management of IBD.[23]

Research areas for further improvement in IBD Prevention and Treatment

The advancement of IBD treatment has been significant; however, a substantial portion of patients either does not respond to existing treatments or experiences a loss of response, necessitating the exploration of new therapeutic strategies. Traditional treatments focus on symptom control through pharmacotherapy, encompassing aminosalicylates, corticosteroids, immunomodulators, and biologics, supplemented by general measures or surgical resection if needed. Novel therapeutic avenues are emerging, including small molecules, apheresis therapy, enhanced intestinal microecology, cell therapy, and exosome therapy. Patient education plays a role in enhancing the effectiveness of IBD treatment.[19]

Looking ahead, the attention to the pathogenesis has now pivoted towards the antibacterial barrier within the mucosa in both Crohn's disease (CD) and ulcerative colitis (UC). Implementing this innovative concept demands an entirely new strategy but holds promise in moving closer to a cure for these debilitating diseases. In cases where incomplete immune modulation falls short in achieving crucial endpoints—such as stopping disease activity and progression—this shift may prove to be more effective.[24]

Discussion

Inflammatory Bowel Disease (IBD) is a complex and chronic inflammatory gastrointestinal disorder, primarily comprising Ulcerative Colitis (UC) and Crohn's Disease (CD). Historically labeled as a "Western disease," the incidence of IBD is progressively rising globally, challenging the previous perception that linked it predominantly to western habits. This discussion aims to explore the global prevalence, severity, complications,

causes, and available treatments for IBD, emphasizing the perspectives of healthcare organizations and areas for further research and improvement.

IBD poses a significant global health concern with an estimated 6.8 million cases worldwide in 2017. However, recent data from 2019 indicates a decrease in the global prevalence to 4.9 million cases, highlighting a dynamic nature in its occurrence. While traditionally higher in Western countries, the prevalence rates have been on the rise in Asia, suggesting a shift in the geographical distribution of IBD cases.

IBD is categorized into Crohn's Disease (CD) and Ulcerative Colitis (UC), with a third category known as IBD-unspecified (IBD-U). CD can affect any part of the gastrointestinal tract and is characterized by transmural inflammation, while UC is limited to the colon and rectum, featuring inflammation and ulcers in the innermost lining. The multifactorial pathogenesis involves genetic susceptibility, environmental factors, and an aberrant immune response to the gut microbiota.

The global impact of IBD extends beyond prevalence, with significant morbidity and mortality rates. Complications can be intestinal, extraintestinal, surgery-related, drug-induced, and renal. Complications such as strictures, fistulas, and colorectal cancer underscore the severity of the disease, requiring comprehensive management strategies.

Treatment options for IBD include aminosalicylates, corticosteroids, immunomodulators, biologics, and Janus Kinase (JAK) inhibitors. Healthcare organizations, recognizing IBD as a global disease, aim to summarize epidemiological patterns to guide prevention and management strategies. The Global Burden of Disease Study 2019 reported 404.55 thousand incident cases, 4898.56 thousand prevalent cases, 41.00 thousand deaths, and 1622.50 thousand DALYs of IBD globally in 2019.

Despite advancements, there is a need for further research to improve prevention and treatment strategies. Emerging therapies, patient education, and a focus on the mucosal antibacterial barrier are identified as potential areas for future developments. A shift in the pathogenic focus towards mucosal antibacterial barriers may bring us closer to a cure for IBD, emphasizing the importance of innovative approaches.

Conclusion:

Inflammatory Bowel Disease remains a challenging global health concern, impacting millions worldwide. The dynamic trends in prevalence, the variety of complications, and the ongoing quest for effective treatments underscore the need for a multidimensional approach. Healthcare organizations play a pivotal role in understanding epidemiological patterns, guiding interventions, and shaping global strategies. Continued research and innovative therapeutic strategies offer hope for enhanced outcomes and improved quality of life for individuals living with IBD.

Abbreviations:

1. CD: Crohn's Disease
2. DALYs: Disability-Adjusted Life Years
3. GI: Gastrointestinal
4. IBD: Inflammatory Bowel Disease
5. SDI: Socio-Demographic Index
6. UC: Ulcerative Colitis
7. YLD: Years Lived with Disability
8. YLL: Years of Life Lost

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