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Mini Review

History and Prevalence of Ulcerative Colitis: A Review

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Abstract

The first description of ulcerative colitis (UC) dates back to 1859. It is one of the two main types of inflammatory bowel disease. This disease affects the colonic mucosal layer where inflammation causes superficial damage. In the latter part of the 18th century, only the symptoms were recognized but little was known about its cause and treatment. But in 19th century with diagnostic advances, it was known that the disease caused ulcerations in mucosal lining which led to effectiveness in treatment. The early 20th century saw an expansion in understanding of UC and it was differentiated from other gastrointestinal diseases. There was better awareness about the disease pathophysiology and role of immune system. A surge in genetic research and gut microbiome provided the needed information about the causes of the disease. With all this knowledge, there is a definite improvement in quality of life of Ulcerative Colitis patients. This article summarizes the advances in knowledge about ulcerative colitis and its prevalence.

Keywords: ***ulcerative colitis, inflammatory bowel disease, Crohn's disease, immune system, gastrointestinal disease.***

Introduction

Ulcerative colitis is an autoimmune disease that affects the colon. It is one of the two main forms of inflammatory bowel disease, the other being Crohn's disease. Though, it presents in adolescence and early adulthood, but can also start in childhood [1]. It is a lifelong disease and has a strong emotional as well as social impact on the patients. In UC, the immune system of the body targets the healthy cells that line the colon, which leads to inflammation and ulcers in the large intestine (colon).

History

In 1793, Matthew Baillie's work titled 'Morbid Anatomy of Some of the Most Important Parts of the Human Body' offered evidence that individuals were falling victim to ulcerative colitis in the later years of the 18th century [2]. Unlike an investigation into the causes, characteristics, progression, and "outcomes" of the disease, this presentation directly showcased postmortem pathological anatomical alterations, detailing organ by organ [3]. It was Sir Samuel Wilks who initially discussed the disease in the year 1859, stating that it was "simple ulcerative colitis [4]." Earlier to this time, it was not differentiated from dysentery. Samuel Wilks differentiated it from bacterial dysentery. He stated that there was a significant difference between the two. However, this distinction was rarely differentiated while the patient was still alive until around 20 years ago; necropsies more commonly made this finding. He described the inflammation of the colon and distal section of the ileum in 1859 under the name ulcerative colitis [4]. Wilks's autopsy revealed a transmural ulcerative inflammation of the colon and terminal ileum in a 42-year-old woman who died after several months of diarrhoea and fever. This was later identified as Chrons disease [5]. The work of Wilks was later confirmed by Sir Arthur Hurst [6]. Wilks and Moxon's 1875 case report describing ulceration and inflammation of the whole colon in a young woman who succumbed to severe bloody diarrhea an early instance of ulcerative colitis [7]. After that pathological and clinical features of the disease were closely noted by Wilks & Moxon (1875) [7], Allchin (1885) [8] and Hale-White (1888) [9].

In the year 1745, Prince Charles, suffered from ulcerative colitis and he successfully managed his symptoms by adopting a diet free of a milk and dairy products [10]. In 1888, following the rise of the germ theory, Sir William Hale White from London (1857-1949) provided an extensive record of cases he had directly witnessed. These instances highlighted occurrences of "ulcerative colitis" that defied association with any recognized causes, such as "tumors, dysentery, tuberculosis, typhoid, and similar factors." [11]. It is from this report that the term "ulcerative colitis" entered into the broader

medical lexicon. The year 1909 marked a pivotal moment in the understanding of UC. In January of that year, Royal Society of Medicine in London convened a symposium. At this gathering, over 300 cases of ulcerative colitis (UC), sourced from multiple hospitals in London, were presented and subjected to comprehensive analysis and discussion [12]. Then in March of 1909, an article titled "Address on the natural history of ulcerative colitis and its bearing on treatment was published in British Medical Journal authored by Herbert P. Hawkins [13]." This lecture, which was presented before the Bristol Medico-Chirurgical Society emphasized the pivotal role of comprehending the natural progression of the disease. He illustrated the disease through case studies and put forth the notion that identifying the "active bacterial agents" accountable for the disease was important for effective management of the disease.

In the decades following 1909, the medical field experienced remarkable advancements in understanding ulcerative colitis. During this period, significant contributions were made to the understanding of ulcerative colitis. Lewisohn's comprehensive demonstrations of familial susceptibility [14], Hewitt's identification of the connection between UC and polyps [15], and Wangensteen's recognition that it could serve as an early indicator of colon cancer [16] were among the noteworthy breakthroughs. In 1923, Helmholz provided the initial account of ulcerative colitis which included children from 8 to 15 years [17]. During the span of 1930s and 1940s, numerous reports established a connection between UC and psychiatric conditions [18]. Wittkower's study for instance found that out of 40 patients 28 experienced emotional trauma before the onset of UC [19]. A significant milestone during this era was Sloan's comprehensive analysis of the clinical features of 2000 UC patients published in 1950 [20]. Moreover, psychotherapy demonstrated its potential in resolving some cases of UC and aiding remission in others [21]. Thus, ulcerative colitis was recognized as a disease with the development of modern technology. The positive responses observed with ACTH and adrenal steroids during the 1950s spurred curiosity in immunological mechanisms [22]. This interest continued to grow in the 1960s when the effectiveness of the immunosuppressive drug mercaptopurine (6-MP) was established in treating patients with UC [23]. Later it was summarized that ulcerative colitis is caused by the interaction of the four etiological determinants, that is genetic endowment, constitutional vulnerability, intrapsychic processes, and the external environment [24]. Currently, the role of emotions and stress in human diseases has expanded into the field of neuroscience [25], and is now involving neuroimmune interactions as the basis of the emotional contributions to IBD. Recent researches have shown that IBD symptoms can cause significant mental stress. Current guidelines therefore encourage clinicians to manage both psychosocial and organic manifestations of IBD [26].

The Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) initiative provided recommendations regarding therapeutic targets in IBD back in 2015. These were again revised in December 2020 through STRIDE consensus. This consensus established that the objectives for treating ulcerative colitis (UC) should encompass a combination of clinical and endoscopic results [27,28]. There are a large number of therapeutic targets which are being explored in treatment of ulcerative colitis. These are in various clinical phases -sphingosine-1-phosphate receptor modulators (such as ozanimod and etrasimod), JAK inhibitors (such as upadacitinib), anti-leukocyte integrins (such as etrolizumab and abrilumab), monoclonal antibodies (such as mirikizumab) and faecal microbiota transplantation [29].

Prevalence of Ulcerative Colitis

Inflammatory bowel disease has increased in prevalence in newly industrialized nations whose societies have become more westernized moving into 21st century. Though incidence of UC is stabilizing in Western nations, but still the disease burden is heavy because prevalence exceeds 0-3% [30]. The prevalence among kids older than 10 is on the rise [31]. IBD is more common in developed nations than in developing nations, but evidence indicates that it is spreading unevenly across the globe [32,33]. UC is becoming more common in both adult [30] and pediatric populations [34]. According to a study by Kaplan et al. (2019) UC has its highest prevalence in North America, Europe and Australia, while a substantial rise in cases is seen in Africa, Asia and South America [35]. In Italy the available estimates of incidence rely on relatively modest population samples. The incidence of UC varies within the range of approximately 10 [36,37] to 15 cases per 100,000 inhabitants per year [38-40].

Incidence rates of between 21 and 32.2/100,000 were reported in studies utilising UK data from the 1990s [41-43], and prevalence estimates between 328 and 409/100,000 [41,44-46]. While other studies revealed an ongoing increase in incidence rates [47,48], the study suggested that rates have stabilised in the Western world. The prevalence estimates in two recent UK studies (2020) which removed a substantial number of uncertain diagnoses from general practise, were much higher, at 725-781/100,000 [49,50]. A 2020 study in UK reported a prevalence of 12.6/100,000 person years (95% confidence interval (CI) 11.4-13.9) [50]. Importantly, prevalence appears to be rising with a recent data from the Lothian region highlighting a point prevalence of 432/100,000 [51]. The incidence of UC in Kuwait area was 2.8 per 100,000 people per year, according to the authors. The incidence of pediatric IBD was 2.6 per 100,000 people per year, according to another study from Kuwait [52].

In the observational study of individuals with inflammatory bowel disease (IBD) in Oman, it was documented that the occurrence of ulcerative colitis (UC) stood at a rate of 1.35 cases per 100,000 individuals annually [53]. Abdul-Baki et al. (2007) gathered information from IBD patients in Beirut and documented an average yearly occurrence of 4.1 cases per 100,000 individuals for ulcerative colitis (UC), 1.4 cases per 100,000 individuals for Crohn's disease (CD), resulting in a combined annual IBD incidence of 5.5 cases per 100,000 individuals [54].

In India many regional differences have been reported in the prevalence of UC and CD. While initial studies from Haryana by Khosla et al. reported 42.8/100,000 patients in 1986 [55]. In the year 2003, Sood et al. reported 44.3/100,000 from Punjab [56]. This was a far lower prevalence of nearly one-third to one sixth of IBD studies compared to western countries of Canada, North America or UK [41,57,58]. Another survey in 2012 which was a national survey showed equal prevalence of UC in northern and southern states of India [59]. These findings suggest that the true burden of inflammatory bowel disease in the Indian subcontinent is still not clear and more studies are needed to better understand the regional differences in the prevalence of IBD in India.

Gender: The gender distribution of IBD varies globally, with Western countries showing a female preponderance in both CD and UC [58,60]. In India, the majority of studies have indicated a higher incidence of ulcerative colitis (UC) and Crohn's disease (CD) in males [60,61]. This has been attributed to factors such as migration from villages to cities and social inhibitions affecting women's attendance at hospitals. However, a study from Central India has not shown any gender difference [62].

Age: In Western countries, inflammatory bowel disease (IBD) exhibits a two-peak occurrence pattern, with significant cases emerging between ages 20-39 and 60-79 [63]. The median age at which Crohn's disease (CD) is diagnosed precedes that of ulcerative colitis (UC) by approximately ten years. Moreover, the age distribution pattern observed in India mirrors that of other Asian nations [64] with the mean age at the time of diagnosis of UC and CD being closer to 40 years [65], with no bimodal distribution [66]. In a multicentric study conducted in Kerala, it was observed that among adults, Crohn's disease (CD) happened at a younger age compared

to ulcerative colitis (UC), while this pattern was reversed in children [67].

Conclusion

Today, a lot more is known about ulcerative colitis than way back in 1800s. With advances in understanding the pathophysiology of ulcerative colitis, many critical questions still need an answer. One of them will be identifying the core cause and triggers that lead to this disease, combined with environmental factors. The field of medical research is constantly advancing, and so it is very likely that the future will bring forth a wide range of new therapeutic options for patients with ulcerative colitis. This will include biologics and immunomodulators, microbiome-based therapies, gene editing and advanced therapies, digital health and nutritional therapies.

List of Abbreviations

UC: Ulcerative Colitis
ACTH: Adrenocorticotropic hormone
IBD: Inflammatory bowel disease
STRIDE: Selecting Therapeutic Targets in Inflammatory Bowel Disease
JAK Inhibitor: Janus kinase Inhibitor
CD: Crohn's disease

Declarations

Ethical Approval and Consent to participate

Not Applicable

Consent for publication

All authors give consent for this publication

Conflicts of Interest

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