

Introduction

Inflammatory bowel disorders (IBD), including ulcerative colitis (UC) and Crohn's disease (CD), are chronic remitting disorders with unpredictable courses and variable responses to therapy. The diagnosis of IBD is based on clinical, radiologic, endoscopic and histological findings. Immunological, environmental, infectious (*Yersinia enterocolitica*) and genetic factors have been postulated to increase the risk for developing IBD¹.

Crohn's Disease

CD is primarily a disease of older children and young adults and is rare in infancy. Few epidemiological studies have been conducted to find the incidence of CD in the general population. In the Scandinavian population alone, the incidence of IBD is 7 per 100,000, with CD at 1.3 per 100,000². CD can affect any part of the intestine, and the lesions are often patchy and occasionally very extensive. Histologically, CD is characterized by a transmural inflammatory infiltrate composed predominantly of lymphocytes and macrophages. Macrophage aggregates are often seen in biopsy specimens, but well developed granulomas are present in only 50% resected specimens³.

CD can also manifest itself along with other disorders like Henoch-Schonlein purpura⁴. Vasculitis is a uncommon complication of CD, however, few cases have been reported of cutaneous polyarteritis nodosa with CD⁴. A milder form of Perianal CD exists and can vary from mild asymptomatic disease to a severe disabling disorder⁵.

Studies in monozygotic twins and Jewish population indicates influence of genetic factors on the pathogenesis of CD⁶. The mode of inheritance seems to be complex and heterogenous, with candidate loci of IBD located on chromosomes 2, 6, 12, and 16⁷.

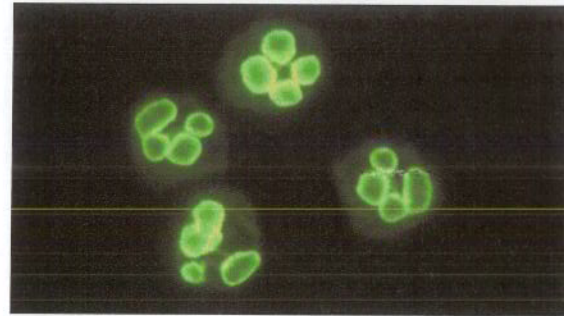


Figure 1. pANCA reaction using immunofluorescence method

Benefits of early diagnosis:

1. Decreases the long term morbidity of CD, which includes delayed puberty, short height, diminished bone density, vitamin and mineral deficiency⁸.
2. Leads to early involvement of pediatric surgeons in the treatment process, leading to surgical intervention in early diagnosed cases when CD is localized. This results in improving growth, better disease control and quality of life for the patient⁹.

Therefore readily available, non-invasive serological tests that can screen for IBD and discriminate CD from UC are desperately needed⁸.

Useful autoantibody markers include:

- **Anti-*Saccharomyces cerevisiae* mannan antibodies (ASCA).**
- **Perinuclear anti-neutrophil cytoplasmic antibodies (pANCA).**

ASCA of IgG and IgA isotype are present in 60% of cases with CD¹. The ASCA's are directed against phosphopeptidomannan present in the yeast (*S. Cerevisiae*) cell walls¹⁰. It has been suggested that combined evaluation of ASCA and pANCA increases the positive predictive value, in comparison to individual assessment of CD cases by ASCA and UC cases by pANCA⁵.

Summary

Recently, complicated serological testing algorithms have been proposed for diagnosis of IBD and to improve discrimination between CD and UC¹. In summary, we recommend that all suspected cases of IBD be tested for pANCA and ASCA (G and A). Further, at risk first degree relatives of CD and UC patients can be tested for ASCA to evaluate their genetic predisposition towards CD.

Ulcerative Colitis

UC affects pediatric and adult population alike. Few epidemiological studies have been conducted to find the incidence of UC in the general population. In the Scandinavian population alone, the incidence of IBD is 7 per 100,000, with UC at 3.2 per 100,000². Genetic predisposition and high prevalence rates are observed in familial clusters in Caucasians and Jews. There is equal preponderance in males and females¹¹. Although UC is primarily confined to the colon and rectum, patients can also develop systemic symptoms like cutaneous, ophthalmic, hepatobiliary and arthritic lesions¹². Bloody diarrhea is the most prevailing symptom, accompanied by rectal urgency and tenesmus. Some patients can present with severe exacerbation and such acute attacks are followed by periods of remission. Persistent Th2 T cell activation (dysfunction, possibly initiated by infectious bacteria like *Campylobacter*, *shigella*, or *Entamoeba Histolytica*) results in production of antibodies directed against colon epithelial cells, bacteria, and milk-derived proteins¹³. Th2 secreted cytokine IL-8 leads to neutrophil migration to the site of inflammation in the intestinal lumen. These activated neutrophils release reactive oxygen metabolites which injure local mucosal tissue, leading to abscesses formation and multiple ulceration. After several cycles of tissue damage and healing, mild submucosal fibrosis sets in and if it persists, toxic megacolon may result, leading to dilation and perforation of the colon¹⁴.

Benefits of early diagnosis:

1. Treatment of severe UC reduces the occurrence of toxic megacolon.
2. Chronicity of UC leads to **colorectal cancer**¹⁵ Cancer screening and colonoscopy is then recommended once every two years for all UC cases. This can be avoided if UC can be diagnosed early and treated successfully.
3. UC is currently treated successfully by several medications. First line therapy for UC is aminosalicylates, Followed by corticosteroids if the aminosalicylates are ineffective. Immunosuppressive agents like azathioprine and cyclosporine can be used in case of steroid-refractory disease¹⁶. Appropriate consumption of absorbable carbohydrates and fish oils has been shown to be effective in controlling UC and its exacerbations¹⁷. If all drug therapy fails the only treatment is surgery (Proctocolectomy).

pANCA occurs in 62% of UC patients and in only 5-6% of Crohn's patients, these antibodies serve as a good discriminatory marker to diagnose and differentiate between CD and UC¹ (see table above).

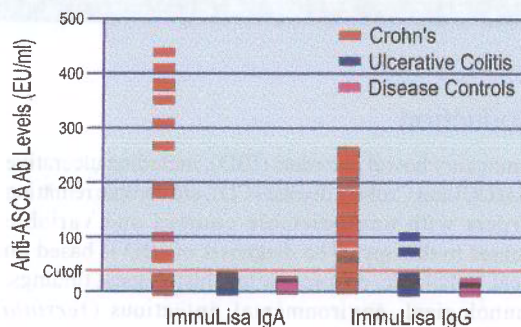


Figure. Discrimination of CD and UC using IMMCO ELISA method.

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