Evaluation of Role of Beta 2 Microglobulin and P- ANCA in the diagnosis of Ulcerative Colitis and their Correlation to Disease Activity

Thesis

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List of Abbreviations

Abb.	Full term
5-ASA	*5-aminosalicylate*
6-MP	*6- mercaptopurine*
ACG	*American College of Gastroenterology*
ADA	*Adalimumab*
ADA	*anti-drug antibodies*
AIH	*Autoimmune hepatitis*
ANCA	*Antineutrophil Cytoplasmic Antibodies*
anti-CBir1	*Antibody against flagellin expressed by Clostridial phylum*
AS	*Ankylosing Spondelitis*
ASCA	*Anti-Saccharomyces cerevisiae Antibodies*
ATG16L1	*Autophagy-related protein 16-1*
AZA	*Azathioprine*
B2-M	*Beta 2 microglobulin*
Budesonide-MMX	*Multi-matrix system (MMX) technology.*
CARD15	*Caspase recruitment domain-containing protein 15*
CBC	*Complete blood count*
CD	*Chrons disease*
CDAI	*Crohns disease activity index*
COX-2	*Cyclo oxygenase inhibitor*
CRP	*C- Reactive Protein*
CsA	*Cyclosporine*
CTE	*Computed tomography enterography*
DAE	*Device-assisted enteroscopy*
EIMs	*Extra intestinal manifestations*
EN	*Erythema nodosum*
ESR	*Erythrocyte Sedimentation Rate*
FC	*Fecal calprotectin*
FN	*Fecal Neopterin*
HIV	*Human immunodeficiency virus*
HLAB27	*Human leukocyte antigen (HLA) B27 (subtypes B*2701-2759)*

List of Abbreviations (Cont...)

Abb.	Full term
IBD	*Inflammatory bowel disease*
IBD1	*Inflammatory bowel disease protein 1*
IBD5	*Inflammatory bowel disease 5*
IBS	*Irritable bowel syndrome*
ICE	*Interleukin (IL)-1 converting enzyme*
IFX	*Infliximab*
IgG	*Immunoglobulin G*
IL	*Interleukin*
IL23R	*Interleukin 23 receptor*
IMs	*Immunomodulators*
IRR	*Incidence rate ratio*
IUS	*Intestinal ultrasound*
IV	*Intravenous*
MPV	*Mean platelet volume*
MRI	*Magnetic resonance imaging*
MTX	*Methotrexate*
NK	*Natural killer cells*
NOD2	*Nucleotide-binding oligomerization domain-containing protein*
NSAIDs	*Non-steroidal anti-inflammatory drugs*
OmpC	*Outer membrane protein C*
PE	*Push enteroscopy*
PG	*Pyoderma gangrenosum*
PLT	*Platelet count*
PSC	*Primary sclerosing cholangitis*
RA	*Rheumatoid arthritis*
RDW	*Red blood cell distribution width*
SBCE	*Small bowel capsule endoscopy*
SBFT	*Small bowel follow through*
SLE	*Systemic lupus erythematosus*
SpA	*Spondeloarthritis*
Th	*T helper cell*

List of Abbreviations (Cont...)

Abb.	Full term
TNF-a	*Tumour necrosis factor alpha*
TNFRs	*Tumor necrosis factor receptors*
TPMT	*Thiopurine methyl transferase*
UC	*Ulcerative colitis*
UGI	*Upper castrointestinal*
VTE	*Venous thromboembolism*
WBC	*White blood cell*

ABSTRACT

Regarding the P-ANCA in the four different study groups; that most of active UC cases (80 %) had positive P-ANCA while only 15 % of the inactive cases had positive P-ANCA and the difference was highly statistically significant. All cases of IBS-control and normal-control had negative PANCA.

Most of positive P-ANCA ulcerative colitis cases (42.1%) had extensive disease involvement, (31.6%) had left sided colitis, (21.1%) had proctosigmoiditis and only (5.3%) have pancolitis.

We also found most of P-ANCA positive ulcerative colitis patients (52.6%) had moderate endoscopic activity and (21.1%) had severe endoscopic activity, while only (10.5%) had mild activity.

Lastly, we found higher mean Beta 2 microglobulin (B2-M) levels in positive PANCA ulcerative colitis patients than in negative PANCA patients and the difference was highly significant.

Keywords: *Immunoglobulin G – Infliximab - Tumour necrosis factor alpha*

INTRODUCTION

Inflammatory bowel disease (IBD), which includes Crohn's disease (CD) and ulcerative colitis (UC), is a chronic condition marked by recurrent episodes of inflammation in the gastrointestinal tract. The anatomic location and degree of inflammation determine the predominant symptoms ***(Angriman I et al., 2007).*** Exacerbations are characterized by symptoms of diarrhea, urgency of defecation and occasionally rectal bleeding and abdominal pain. The aim of treatment is to induce and maintain disease remission ***(Hanauer SB, 2006).***

Diagnosis of IBD has historically been based on a combination of clinical history and examination, blood parameters, radiology and endoscopy ***(Smith L and Gaya D, 2012).*** The current gold standard for assessing intestinal inflammation is endoscopy with biopsies. This technique allows visual inspection of the gastrointestinal tract, and mucosal biopsy specimens can be obtained for histological examination. The location, extent, and severity of disease can be established with this procedure, but it is invasive, it cannot examine the entire gastrointestinal tract. This examination is painful and requires both a skilled operator and an uncomfortable preparatory regimen ***(Paduchova Z and Durackova Z, 2009).***

Disease activity in IBD is determined using both direct and non-invasive laboratory markers. However, endoscopic examination is still the gold-standard diagnostic test ***(Mowat C et al., 2011)*.** Laboratory markers such as C reactive protein (CRP), erythrocyte sedimentation rate (ESR), white blood count (WBC) and platelet count, albumin and fecal calprotectin have been investigated in IBD with different aims including diagnosis, disease activity, response to therapy, and estimate of relapse with a wide range of sensitivity and specificity ***(Costa F et al., 2005)*.**

Unfortunately, an ideal marker for IBD that is easy, cheap, rapid to perform, disease specific, and having prognostic merit against relapse or recurrence of the disease has not yet been identified ***(Vermeire S et al., 2006)*.**

The serologic panel for IBD is rapidly expanding. So far, antineutrophil cytoplasmatic antibodies (ANCA) and anti-Saccharomyces cerevisiae mannan antibodies (ASCA) are the most widely studied markers and remain the best characterized markers in IBD. Antineutrophil cytoplasmic antibodies (ANCAs) are antibodies for granules of neutrophil cytoplasm; it is first reported in UC patients in 1990 ***(Rump A et al., 1990)*.** The ANCA+ve/atypical P-ANCA –ve phenotype is characteristic of CD, while the ASCA –ve/atypical P-ANCA +ve phenotype is seen primarily in UC ***(Papp M et al., 2007)*.**

Beta 2 microglobulin (B2-M) is a low-molecular-weight protein released by activated T and B lymphocytes. The estimated half-lifetime is short (2 h) ***(Bjerrum OW et al., 1990).*** Beta 2 microglobulin has been shown to increase in several inflammatory and hematologic disorders, such as systemic lupus erythematosus (SLE), acquired immunodeficiency syndrome, multiple myeloma, lymphoma and leukemia ***(Yang J et al., 2006).***

Patients with IBD, serum B2-M level is associated with active disease. B2-M level may be considered a useful marker of IBD and could be a potential indicator of disease activation. B2-M serum level provides additional data to supplement existing markers such as CRP and ESR ***(Yilmaz B et al., 2014).***