بسم الله الرحمن الرحيم

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بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى مسئولية عن محتوى هذه الرسالة.

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Assessment the Role of Non Invasive Biomarkers as an Early Predictors of Mucosal Healing in Ulcerative Colitis Patients Treated with the Biological Therapy

Thesis

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Shaimaa Abdelrahman Ahmed

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List of Abbreviations

Abb.	Full term
5ASA	*Aminosalicylates*
6-MP	*6-mercaptopurine*
ADA	*Adalimumab*
ANCA	*Antineutrophil cytoplasmic antibodies*
ASCA	*Anti– Saccharomyces cerevisiae antibodies*
AXR	*Abdominal x ray*
AZA	*Azathioprine*
B2-M	*Beta 2 microglobulin*
BE	*Barium enema*
BUS	*Bowel ultrasound*
CD	*Crohn's disease*
CRP	*C-reactive protein*
CRP/ALB	*C-reactive protein/albumin ratio*
CsA	*Cyclosporine*
CTC	*CT colonography*
CTE	*CT enterography*
ECCO	*European Crohn and Colitis Organization guidelines*
EH	*Endoscopic healing*
ERCP	*Endoscopic retrograde cholangiopancreatogram*
ESR	*Erythrocyte sedimentation rate*
FC	*Fecal calprotectin*
IBD	*Inflammatory bowel disease*
IFX	*Infliximab*
IL-8	*Interleukin-8*
IQR	*Inter-quartile range*
MCS	*Mayo clinic score*
MES	*Mayo endoscopic score*
MH	*Mucosal healing*

List of Abbreviations (Cont…)

Abb.	Full term
MRCP	*Magnetic Resonance cholangio pancreaticography*
MRI	*Magnetic Resonance Imaging*
NLR	*Neutrophil-to-lymphocyte ratio*
NLR	*Neutrophil-to-lymphocyte ratio*
NSAID	*Non-steroidal anti-inflammatory drug*
PLR	*Platelet-to-lymphocyteratio*
PMBCs	*Peripheral blood mononuclear cells*
QOL	*Quality of life*
RA	*Rheumatoid arthritis*
ROC	*Receiver operating characteristic curve*
TNFα	*Tumor necrosis factor alpha*
UC	*Ulcerative colitis*
VTE	*Venous thromboembolism*
WBC	*White blood cells*

INTRODUCTION

The inflammatory bowel disease (IBD) comprises two types, namely, the ulcerative colitis (UC) and Crohn's disease (CD). They are a spectrum of chronic idiopathic autoimmune inflammatory disorders with remission and relapses, primarily affecting the gastrointestinal system ***(Machado et al., 2013).***

IBD occur with different frequencies around the world. The countries reporting for the highest incidence of UC are the United States, the United Kingdom and Sweden, IBD have always seemed to be rare in the Middle East and Northern Africa. No accurate registry of patients had ever studied the exact prevalence of CD and UC in these populations. In Mediterranean countries, the prevalence of UC was estimated to be 5/100000 in urban areas ***(Matsuoka et al., 2018).***

UC is characterized by confluent mucosal inflammation and erosions starting from the anal verge and extending to a variable extent, where patients often complain of diarrhea associated with rectal bleeding, abdominal tenderness, and weight loss ***(El-Atrebi et al., 2021).***

Etiopathogenesis of IBD comprises genetic components, environmental factors, microbial flora of the gut, and immune responses. However, the main mechanism seems to be the bacterial antigens gaining access to the antigen-presenting cells

through the impaired epithelial barrier ***(Ordás and Eckmann, 2012).***

Ulcerative colitis (UC) is characterized by a neutrophil-mediated inflammation of the gut. Indeed, European Crohn and Colitis Organization guidelines (ECCO) have highlighted how the grade of neutrophilic infiltration is necessary for the diagnosis of this pathological condition and for the evaluation of histological activity ***(Sandborn et al., 2015).***

Thus, colonoscopy is necessary to collect mucosal biopsies and assess neutrophilic infiltration for the diagnosis and during follow-up to evaluate treatment response and predict long-term outcome, although histological healing is still debated. However, colonoscopy is an invasive, costly, and not always well-tolerated examination for patients ***(Mumolo et al.***, ***2018).***

Apart from endoscopic interventions, disease severity can be also assessed using less-invasive biomarkers, including blood count, ESR, CRP and fecal calprotectin ***(Alexander et al., 2007).***

In fact, systemic inflammation is characterized by a change in the levels of circulating white blood cells (WBC), and in particular it induces an increase in circulating neutrophils that is accompanied by a relative decrease in the percentages of lymphocytes ***(Gökmen et al., 2015).***

In this regard, an increasing body of evidence has suggested that the neutrophil-to-lymphocyte ratio (NLR) can be a useful biomarker of many systemic inflammation responses and in the oncologic setting ***(Goodman et al., 2015).***

There is also some evidence of a possible role of this simple biomarker in the UC setting, in particular concerning disease severity, but no sufficient studies have tested the value of this parameter in predicting therapeutic response to medical treatment ***(Torun et al., 2012).***

Furthermore, the platelet-to-lymphocytes ratio (PLR) has recently been correlated to the prognosis of malignancies and to disease activity in rheumatologic diseases, but data on its role in UC patients are lacking ***(Zhang et al., 2018).***

Medical therapy of IBD is complex as the disease etiology is multifactorial and the primary aim of pharmacotherapy is to dampen the generalized inflammatory response, thereby relieving symptoms. The specific goals of treatment in IBD include the control of acute exacerbation, maintenance of remission, treatment of specific complications, and surveillance of malignant transformation ***(Brunton et al., 2018).***

Many drugs are used in the treatment of IBD including mesalamine derivatives, glucocorticoids and immunomodulators, in addition to the biologics that are derived partly or completely

from living biological sources such as animals and humans ***(D'Haens and Sartor, 2014).***

The most widely used biologics are the TNF-α inhibitors such as adalimumab, certolizumab, golimumab, and infliximab, which are highly effective in the treatment of both UC and CD. The other biological agents in IBD include the integrin receptor antagonists, namely, vedolizumab and natalizumab, and IL-12 and IL-23 antagonist (Ustekinumab) ***(Chan et al., 2017).***