Laboratory Markers of Inflammatory Bowel Disease

Essay

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List of Abbreviations

ACD	Anaemia of Chronic Disease
AJ	Adherence junctions
AJC	Apical junctional complex
ANCA	Antineutrophil cytoplasmic antibodies
APCs	Antigen- presenting cells
ASCA	Anti-Saccharomyces cervisiae
CARD-15	Caspase recruitment domain family, member 15
CDAD	Clostridium difficile-associated disease
CBC	Complete blood count
CD	Crohn's disease
CD	Cluster of differentiation
COX-2	Cyclooxygenase-2
CRC	Colo rectal cancer
CRP	C- reactive protein
CT scan	Computed Tomography scan
DLG5	Discs large homolg 5
E-Coli	Escherichia Coli
EGE	Eosinophilic gastroenteritis
ELISA	Enzyme-Linked Immunosorbent Assay
ESR	Erythrocytic sedimentation rate
FBDs	Functional Bowel Disorders
GALT	Gut associated lymphoid tissue
GIT	Gastroinstinal tract
Hb	Haemoglobin
HLA	Human leucocyte antigen

HMG	High Motility Group
HRT	Hormon replacement therapy
IBD	Inflammatory bowel disease
IBS	Irritable bowel syndrome
IC	Intermediate colitis
ICOS	Induible T cells Co stimulator
Ig A	Immunoglobuline A
Ig G	Immunoglobuline G
IFN	Interferon
IFT	Intestinal function tests
IGG	Immunoglobulin G
IL	Interluken
IL-R	Interleukin receptor
IL-RA	Interleukin receptor antagonists
Kd	Kilo Dalton
LPS	Lipo polysaccharids
M2-PK	M2-Pyruvate Kinase:
MAdCAM	Mucosal addressin cell adhesion molecule
MDR1	Multi drug resistance 1
MDS	Myelodysplastic syndrome
MRI	Magnetic Resonance Imaging
NF kb	Nuclear Factor kb
NDDIC	National Digestive Diseases Information Clearinghouse
NIF	Neutrophil Immobilising Factors
NSAIDs	Non steroidal anti-inflammtory drugs
OCTN 1	Organic cation tranporter 1
OCs	Oral contraceptives
OMPc	E.coli Outer Membrane Porine

PANCA	Perinuclear antineutrophil cytoplasmic antibodies
PCR	Polymerase chain reaction
PMNe	Polymorphonuclear neutrophil elastase
PPARG	Peroxisone proliferative activated receptor gamma
SC	Schistosoma colitis
SLC22A4	Solute carrier family member 22 A4
STfR	Serum transferrin receptor
TGF	Transforming growth factor
TH1	T – helper 1
TH2	T- helper 2
TJs	Tight junctions
TfR	Transferrin receptor
TLRs	Toll- like receptors
TNF	Tumour necrosis factor
TR 1	Type1 regulator T cell
UC	Ulcerative Colitis
US	Ultra Sound
WBCs	White blood cells count.
WHO	World Health Organization

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Inflammatory bowel disease **(IBD)** is a group of diseases characterized by non-specific inflammation of the gastrointestinal tract **(GIT)**. Two major forms are recognized; Crohn's disease **(CD)** which can affect any part of the GIT, most commonly the ileum and the ascending colon; and Ulcerative Colitis **(UC)** which affects only the large bowel. Both are more common in Western countries **(Peter et al., 2000).**

The exact etiologies remain uncertain, results from research in animal models, human genetics, basic science and clinical trials have provided important new insights into the pathogenesis of chronic, idiopathic, relapsing, and immune-mediated intestinal inflammation. These studies indicate that Crohn's disease and ulcerative colitis are heterogeneous diseases characterized by various genetic abnormalities **(Sartor., 2006).**

Laboratory markers have been investigated in inflammatory bowel disease (IBD) for diagnostic and differential diagnostic purposes, for assessment of disease activity and risk of complications, for prediction of relapse, and for monitoring the effect of therapy. Markers of inflammation {especially C reactive protein (CRP)} correlates well with disease activity in Crohn's disease and has the potential to select responders to biological therapies introduced for treatment of IBD **(Egan et al., 2006).**

Many Crohn's disease (CD) patients develop complications (fistulae and abscesses), and require surgery, often repeatedly and at variable instances. Identifying serological markers that determine their early or repeated manifestation can enable implementing more aggressive preventive strategies **(Amre et al., 2006).**

Novel fecal markers such as (Calprotectin) and other leukocyte proteins can be used to monitor disease activity in patients with CD as well as in UC, moreover they provide a rapid and non invasive tool to discriminate patients with IBD from those with Irritable bowel syndrome (IBS) **(Vermeire et al., 2006) .**

Aim of the work:

The aim of this essay is to highlight the laboratory markers that have been recently used for diagnosis, differential diagnosis and prognosis of IBD.

I – Historical view:-

Inflammatory bowel diseases were described by Giovanni Battista Morgagni (1682-1771) ,and by the Polish surgeon Antoni Leśniowski in 1904 (leading to the use of the eponym "Leśniowski-Crohn disease" in Poland) then by the Scottish physician T. Kennedy Dalziel in 1913 **(Crohn et al ., 1932 ; and Blumberg ., 2008).**

Burrill Bernard Crohn, an American gastroenterologist at Mount Sinai Hospital, described fourteen cases in 1932, and submitted them to the American Medical Association under the term "Terminal ileitis": A new clinical entity". Later on, he along with colleagues Leon Ginzburg and Gordon Oppenheimer published the case series as "Regional ileitis": a pathologic and clinical entity **(Crohn et al., 1932; and Blumberg., 2008).**

II-Epidemiology:

The epidemiological studies are aimed to better define the burden of illness, to explore the mechanism of association with environmental factors, and to identify new risk factors **(Lakatos., 2006).**

The incidence rate of UC varies greatly between 0.5-24.5/10^5 inhabitants, while that of Crohn's disease varies between 0.1-16/10^5 inhabitants worldwide, with prevalence rates of IBD reaching up to 396/10^5 inhabitants. A further difference is that the previously reported predominance of UC is diminishing, as CD is becoming more prevalent **(Lakatos., 2006).**

The average annual incidence of Intermediate colitis (IC) [patients with features of both diseases] ranges 1.6 to 2.4/100,000 versus 7.3 to 13.6/100,000 for UC. At the time of initial diagnosis of inflammatory bowel disease (**Geboes et al., 2003)**.

The incidence varies according to:

A-Geographical distribution:

Inflammatory bowel diseases are a public health problem in developed countries as 1 per 1000 people suffers from these diseases. Most of affected people are young adults **(Podolosky and Daniel ., 2002).**

IBD is traditionally considered to be common in the Western world, and its incidence has sharply increased since the early 1950s. In contrast, until the last decade, low prevalence rates have been reported from other parts of the world including Eastern Europe, South America, Asia and the Pacific region **(Vernier et al., 2005).**

Recent trends indicate a change in the epidemiology of IBD within previously low incidence areas, now reporting a progressive rise in the incidence, while in West European and North American countries the figures have stabilized or slightly increased, with decreasing incidence rates for ulcerative colitis. Some of these changes may represent differences in diagnostic practices and increasing awareness of the disease **(Lakatos., 2006).**

In Middle-East IBD is traditionally reported to be high among Jews coming from the United States and Northern Europe. In Israel, the incidence is somewhat lower and Ashkenazi Jews have a higher incidence than Sephardic Jews. In 2000, Niv et al., reported an annual incidence of $5.04/10^5$ for UC for a ten-year follow-up period between 1987-1999. The prevalence rate rose from $121.0/10^5$ to $167.2/10^5$ **(Niv et al., 2000).**

In contrast, Arab countries in the Middle East are still reporting low incidence rates. A prospective hospital-based study from Saudi Arabia reported an estimated incidence of $0.5/10^5$ and prevalence of $5.0/10^5$ for IBD in children in 1993-2002 **(El Mouzan., 2006; and El Ghamdi et al., 2004)**

In Egypt, colitis is a common clinicopathological entity, a study during the period from 1975-1985 on 786 patients with colonic diseases revealed that 32.7% of the cases showed colonoscopic polyposis most of them were schistosomal. Colonic masses were detected in 8.4%of the cases (schistosomal or adenocarcinoma). Colonic ulcerations were detected in 8.2% of cases (ulcerative colitis, schistosomal ulcers and adenocarcinoma of the colon). Schistosomal colitis (sc) was detected in 7.7%of cases.) **(Thakeb et al, 1987).**

The prevalence of IBD in Egypt is 152,234 to 76,117,421 at 2004 according to The National Digestive Diseases Information Clearinghouse (NDDIC) which is a service of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). NIDDK is part of the National Institutes of Health under the U.S. Department of Health and Human Services**(US Census Bureau, International Data Base, 2004).**

The differences in incidence rates among various geographical areas suggest a role of certain environmental factors. It is known that the incidence differs among different ethnic groups living in the same geographic region **(Lakatos et al., 2006).**

B-Age:

The peak incidence of ulcerative colitis occurrs between the ages of 15 and 25y, it is thought to be a bimodal distribution in age of onset with a second peak in incidence occurring in the 6th decade of life **(Hanauer., 2006).**

It is important but difficult to study the epidemiology of IBD in children. Although both UC and CD are rare below the age of 11 years, the upper age limit varies between 14 and 17 years of age. The incidence of these diseases increases rapidly after adolescence. The incidence of IBD, in particular CD had

increased over the last ten years. Furthermore, upper gastrointestinal involvement is reported to be more common in children with CD **(Gopal et al., 2006).**

Siblings or children of people with Crohn's disease are 3 to 20 times more likely to develop the disease **(Tysk et al., 1998).**

C-Sex:

The male-to-female ratio is approximately equal for both ulcerative colitis and Crohn disease **(Lakatos., 2006).**

III-Pathogenesis of Inflammatory Bowel Disease:

In the decades since the major forms of IBD were defined on the basis of clinical manifestations, investigators have been challenged to identify the fundamental pathophysiologic processes underlying these enigmatic disorders, and clinicians have struggled to provide effective therapy for the often dismaying clinical manifestations. Clinical experience has led to the generally accepted notion that Crohn's disease and ulcerative colitis are distinct, if not discrete, entities. And stem possibly from acommon mechanism with an exact etiology that remains obscure **(Hanauer., 2006).**

A-The major forms of IBD are:

1-Crohn's disease (CD):

Regional Enteritis; Granulomatous Ileitis or Ileocolitis:

CD is a lifelong inflammatory disease that damages the digestive tract lining. It can occur anywhere in the digestive tract and may occur simultaneously in different locations **(Stange et al., 2006).**