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بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى

مسئولية عن محتوى هذه الرسالة.

ملاحظات:





Serum Calprotectin as a Potentially Sensitive Biomarker for Inflammatory Bowel Disease in Egyptian Patients

Thesis

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قَالَ

سَبَّحَانَكَ لَا إِلَهَ إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
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List of Abbreviations

| Abb. | Full term |
|----------------|---|
| AA..... | <i>Amino Acid</i> |
| AIEC..... | <i>Adherent Invasive Escherichia coli</i> |
| ANCA..... | <i>Anti-neutrophil cytoplasmic antibodies</i> |
| ASCA..... | <i>Antisaccaromyces cerevisiae</i> |
| ATG16L1..... | <i>Autophagy related 16 like 1</i> |
| AUC..... | <i>Area Under Curve</i> |
| Ca..... | <i>Calcium</i> |
| Cal..... | <i>Calprotectin</i> |
| C-ANCA..... | <i>Cytoplasmic Anti-neutrophil cytoplasmic antibodies</i> |
| CBC..... | <i>Complete blood picture</i> |
| CD..... | <i>Crohn's Disease</i> |
| Creat..... | <i>Creatinine</i> |
| CRP..... | <i>C- Reactive Protein</i> |
| D..... | <i>Day</i> |
| DAMPs..... | <i>Damage Associated Molecular Patterns</i> |
| EBV..... | <i>Epstein-Barr Virus</i> |
| ELISA..... | <i>Enzyme-Linked Immuno Sorbent Assay</i> |
| ESR..... | <i>Erythrocyte Sedimentation Rate</i> |
| FC..... | <i>Fecal calprotectin</i> |
| GAWAS..... | <i>Genome Wide Association studies</i> |
| Hb..... | <i>Hemoglobin</i> |
| HHV6B..... | <i>Human Herpes Virus type 6</i> |
| HP..... | <i>Helicopacter pylori</i> |
| HS..... | <i>Highly significant</i> |
| IBD..... | <i>Inflammatory Bowel Disease</i> |
| Ig..... | <i>Immunoglobulin</i> |
| IIF..... | <i>Indirect Immunofluorescence</i> |
| IL..... | <i>Interleukin</i> |
| ILCs..... | <i>Innate lymphoid cells</i> |
| INF..... | <i>Interferon</i> |
| IQR..... | <i>Inter quartile Range</i> |
| IRGM Gene..... | <i>Immunity-related GTPase family M protein</i> |

List of Abbreviations cont...

| Abb. | Full term |
|--------------------------------|--|
| <i>LPS</i> | <i>Lipopolysaccharides</i> |
| <i>MAPK</i> | <i>Mitogen-activated protein kinase</i> |
| <i>mL</i> | <i>Milli Liter</i> |
| <i>Mn</i> | <i>Manganese</i> |
| <i>Mo</i> | <i>Month</i> |
| <i>MRP</i> | <i>Myeloid- related protein</i> |
| <i>NADPH</i> | <i>Nicotinamide Adenine Dinucleotide Phosphate</i> |
| <i>NK cells</i> | <i>Natural Killer cells</i> |
| <i>NK- KB</i> | <i>Nuclear factor kappa-B</i> |
| <i>nL</i> | <i>Nano Liter</i> |
| <i>NOD like receptor</i> | <i>Nucleotide-binding oligomerization domain like receptor</i> |
| <i>NS</i> | <i>Non significant</i> |
| <i>OD</i> | <i>Optical denisty</i> |
| <i>PAMPs</i> | <i>Pathogen Associated Molecular Patterns</i> |
| <i>P-ANCA</i> | <i>Perinuclear Anti-neutrophil cytoplasmic antibodies</i> |
| <i>PLT</i> | <i>Platelet</i> |
| <i>PSC</i> | <i>Primary sclerosing cholangitis</i> |
| <i>RA</i> | <i>Rheumatoid Arthritis</i> |
| <i>RAGE</i> | <i>Receptor for advanced glycation end products</i> |
| <i>RNA</i> | <i>Ribonucleic Acid</i> |
| <i>ROC</i> | <i>Receiver Operating Curve</i> |
| <i>ROS</i> | <i>Reactive oxygen species</i> |
| <i>S</i> | <i>Significant</i> |
| <i>SES-CD</i> | <i>Simple Endoscopic Score for Crohn's Disease</i> |
| <i>SPSS</i> | <i>Statistical Package for Social Sience</i> |
| <i>Th cell</i> | <i>T helper cell</i> |
| <i>TLR4</i> | <i>Toll Like Receptor 4</i> |

List of Abbreviations *cont...*

| Abb. | Full term |
|------------------|------------------------------|
| <i>TNF</i> | <i>Tumor Necrosis Factor</i> |
| <i>UC</i> | <i>Ulcerative Colitis</i> |
| <i>uL</i> | <i>Micro Liter</i> |
| <i>Wk</i> | <i>Week</i> |
| <i>Zn</i> | <i>Zinc</i> |

INTRODUCTION

Inflammatory Bowel Disease (IBD), mainly Ulcerative Colitis (UC) and Crohn's disease (CD), are a group of disorders characterized by prolonged inflammation of the gastrointestinal tract. Although the etiology of IBD is not well understood, environmental, genetic and immunologic factors have been considered to play the major role in etiology of the disease. It is believed that IBD is the result of a dysregulated immune response to the host intestinal microflora in the genetically susceptible individuals (*Wallace et al., 2014*).

Currently, colonoscopy is the gold standard method for initial diagnosis (which provides a macroscopic and microscopic description of the mucosa through biopsies), assessment of the disease burden, and evaluation of response to treatment. Even so, the colonoscopy is an invasive, expensive, and difficult-to-prepare patient method. Thus, the development of more convenient, inexpensive, and non-invasive assessments are crucial for IBD (*Norouzinia et al., 2017*).

As the incidence of IBD increases, the health and financial burden of the disease also increases. These changes make the role of IBD biomarkers further crucial. Serum markers of acute phase response such as C-reactive protein (CRP) and Erythrocyte Sedimentation Rate (ESR) have been widely investigated as biomarkers of IBD. However, they are not specific to IBD as their levels are also increased in various

conditions such as infections, other autoimmune disorders and malignancy (*Iskandar and Ciorba, 2012*). Serum calprotectin, as a novel bloodbased biomarker of IBD, has been investigated in several investigations (*Tayebeh et al., 2019*).

Calprotectin is a calcium- and zinc-binding protein consisted of two small anionic proteins, S100A8, and S100A9. Its expression has been identified in the early differentiation stage of a variety of immune cells including macrophages, granulocytes, and monocytes, following their activation by damage-associated molecular patterns (DAMPs) or pathogen-associated molecular patterns (PAMPs). Calprotectin release weakens the cell–cell contacts and as a result, the permeability of endothelium will be modified leading to the leukocyte extravasation (*Ehrchen et al., 2009*). Serum calprotectin has been reported as a promising biomarker in monitoring IBD patients and may be more convenient in routine practice and more acceptable to patients (*Fukunaga et al., 2018*).

AIM OF THE WORK

The aim of this work is to evaluate serum calprotectin as a biomarker for IBD in Egyptian Patients.