ABSTRACT

Background*:* Gastroesophageal reflux disease (GERD) is one of the most prevalent gastrointestinal disorders, and its prevalence is increasing worldwide. It is a condition that develops by reflux of the stomach contents into the esophagus, and causes troublesome symptoms, such as heartburn and regurgitation. The aim of this work is to evaluate the serum level of IL4 in patients with GERD and patients with refractory GERD.

Patients and methods: The study included two groups of patients, Group-1 including 25 patients with GERD symptoms who didn't receive treatment or who received treatment for less than 8 weeks with improvement of symptoms and Group-2 including 25 Patients with refractory GERD and who received PPIs for more than 8 weeks without improvement of symptoms. **Results**: Serum Interleukin-4(IL4) level was elevated in patients with refractory GERD more than patients with GERD, Serum IL4 level was elevated in patients with Barrett's esophagus more than patients with Reflux oesophagitis.

Conclusion: The study has concluded that : Serum Interleukin-4(IL4) level was elevated in patients with refractory GERD more than patients with GERD, Serum IL4 level was elevated in patients with Barrett's esophagus more than patients with Reflux oesophagitis, Pathological features that we found in patients with GERD were moderate reflux oesophagitis (52%), mild reflux oesophagitis (40%) and severe reflux oesophagitis (8%), while in patients with refractory GERD there were severe reflux oesophagitis (56%), Barrett's esophagitis (28%) and moderate reflux oesophagitis (16%).

Key words: GERD, Refractory GERD, Interleukin-4, IL4, Reflux oesophagitis, Barrett's esophagus.

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List of Abbreviations

5-HT4 .....5-hydroxytryptamine-4
AL2+ .....Aluminum
ALT.....Alanine Aminotransferase
APC .....Argon Plasma Coagulation
AST.....Aspartate Aminotransferase
ATP.....Adenosine Triphosphate
B cells .....B Lymphocytes
BE.....Barrett's Esophagus
Ca .....Calcium
CanDys.....Canadian Dyspepsia
CBC .....Complete Blood Count
CBT .....Cognitive Behavioral Therapy
CCB .....Calcium Channel Blocker
Cl.....Chloride
Cm.....Centimeter
COPD.....Chronic Obstructive Pulmonary Disease
Creat .....Creatinine
CYP2C19 (P450 2C19) ....Cytochrome P450 2C19
D2.....Dopamine 2
DGER.....Duodenogastroesophageal Reflux
DIS .....Dilated Intercellular Spaces
DNA .....Deoxyribonucleic Acid
EAC .....Esophageal Adenocarcinoma
EE.....Erosive Esophagitis
EGD .....Esophagogastroduodenoscopy
ENT .....Ear, Nose, Throat
EoE.....Eosinophilic Esophagitis

List of Abbreviations

EST.....Electrical Stimulation Therapy
FDA .....Food and Drug Administration
g/dL .....Grams Per Deciliter
GEJ .....Gastroesophageal Junction
GERD.....Gastroesophageal Reflux Disease
GI .....Gastrointestinal
GIT .....Gastrointestinal Tract
H.....Hydrogen
H. pylori.....Helicobacter Pylori
H2RAs .....Histamine-2 Receptor Antagonists
HCL .....Hydrochloric Acid
HCO3.....Bicarbonate
HDL-C.....High Density Lipoprotein Cholesterol
HH .....Hiatus Hernia
HRQL.....Health-Related Quality of Life
IBS.....Irritable Bowel Syndrome
IFN-γ .....Interferon-γ
IL.....Interleukin
INR .....International Normalized Ratio
IPG .....Implantable Pulse Generator
K.....Potassium
LES.....Lower Esophageal Sphincter
LESP.....Lower Esophageal Sphincter Pressure
M receptors.....Muscarinic Receptors
mEq/L.....Milliequivalents Per Liter
Mg2+ .....Magnesium
Mii.....Multichannel Intra-Luminal Impedance

List of Abbreviations

mins .....Minutes

mm of Hg .....Millimeters of Mercury

mm .....Millimeter

MUSE.....Medigus Ultrasonic Surgical Stapler

Na .....Sodium

NAB .....Nocturnal Acid Breakthrough

NERD.....Non Erosive Reflux Disease

NSAIDs .....Non-Steroidal Anti-Inflammatory Drugs

P value .....Probability Value

Pg .....Picogram

PGE .....Prostaglandin E

PMNLs .....Polymorphonuclear Leukocytes

PPIs .....Proton Pump Inhibitors

PT.....Prothrombin

PTT.....Partial Thromboplastin Time

QOL .....Quality of Life

RE .....Reflux Esophagitis

ROC curve.....Receiver Operator Characteristic Curve

SD.....Standard Deviation

SSR.....Sustained Symptom Response

SSRI .....Selective Serotonin Reuptake Inhibitors

T cells .....T lymphocytes

TCAs.....Tricyclic Antidepressants

TEA .....Transcutaneous electrical acustimulation

Th cells .....T Helper Cells

TIF.....Transoral Incisionless Fundoplication

List of Abbreviations

TLESR .....Transient Lower Esophageal Sphincter Relaxation

TNF-α .....Tumor Necrosis Factor-α

U/L.....Unit per Liter

vs.....Versus

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INTRODUCTION

Gastroesophageal reflux disease (GERD) is one of the most prevalent gastrointestinal disorders, and its prevalence is increasing worldwide. It is a condition that develops by reflux of the stomach contents into the esophagus, and causes troublesome symptoms, such as heartburn and regurgitation ***(Yu-Min et al., 2017).***

Heartburn and regurgitation are the cardinal and most common symptoms of GERD. They are the typical symptoms of GERD ***(Orlando, 2010).***

GERD may manifest atypically with extra-oesophageal symptoms as respiratory symptoms (cough, wheezes like asthma and recurrent upper respiratory tract infections), ENT symptoms (hoarseness of voice, globus sensation, postnasal drip, otitis media, dental erosions, sore throat, gingivitis, halitosis, aphthous ulcers and water brash), cardiac symptoms like pericordial or chest pain that may mimic anginal pain and multiple unexplained symptoms, which may be associated with psychological distress ***(Richard et al., 2015).***

Patients with GERD, especially with chronic disease, may present complications as esophagitis, Barrett's esophagus and peptic stricture ***(Sudha et al., 2018).***

Although PPIs are currently the most effective treatment for GERD and its complications, patients with nonerosive reflux disease (NERD) and patients with erosive esophagitis (EE) may remain symptomatic on standard therapy after 8 weeks of treatment. Patients with continued symptoms despite PPI treatment are considered to have refractory GERD ***(Mermelstein et al., 2018).***

Recently refractory GERD is generally defined as the persistence of typical symptoms that do not respond to stable, twice-daily PPI dosing during at least 12 weeks of treatment. Up to 30% of GERD patients experience refractory GERD ***(Mermelstein et al., 2018).***

There are many potential causes and factors related to refractory GERD that vary in incidence, clinical importance, and symptom severity and frequency. Poor compliance and adherence should first be assessed before further evaluation is decided. The most common mechanisms for refractory GERD include functional bowel disorders, weakly acidic reflux, and residual acid. Factors related to metabolism and bioavailability play a limited role in PPI failure. GERD-like symptoms may also be due to a variety of other disorders, such as eosinophilic esophagitis (EoE), pill-induced esophagitis, infectious esophagitis, and achalasia, which should be considered in the differential diagnosis of patients with unremitting symptoms ***(Mermelstein et al., 2018).***

Barrett's esophagus is the condition in which a metaplastic columnar mucosa replaces an esophageal squamous mucosa damaged by gastroesophageal reflux disease (GERD). Barrett's esophagus are major risk factors for esophageal adenocarcinoma ***(Stuart and Rhonda, 2014).***

Cytokines are a peptide signaling molecules, play an important role in the damage of tissues and can demonstrate pro-inflammatory as well as anti-inflammatory activity ***(Vladimir et al., 2015).***

In addition to direct stimulation by intraluminal reflux contents, the esophageal epithelial layer is also exposed to factors produced by chronic inflammatory cells from the basal side ***(Jing et al., 2016).***

Studies have shown an increase in proinflammatory TH1 cytokines in reflux esophagitis compared to BE, whereas TH2 cytokines are predominant in BE. There is increase in IL-4 in BE ***(Jing et al., 2016).***

Aim of the Work

The aim of this work is to evaluate the serum level of IL4 in patients with GERD and patients with refractory GERD.