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List of Abbreviations

5HT4	5-Hydroxytryptamine 4 Receptors
BMI	Body Mass Index
CD4	Cluster of Differentiation 4
CLA	Cutaneous Lymphocyte Antigen
CM	Cow Milk
CMA	Cow Milk Allergy
CMPA	Cow Milk Protein Allergy
CRD	Component-Resolved Diagnostics
EG	Eosinophilic Gastroenteritis
EGJ	Esophago-gastric Junction
EoE	Eosinophilic Esophagitis
FA	Food Allergy
FD	Functional Dyspepsia
FDA	Food and Drug Administration
FEIA	Fluorescent Enzyme Immunoassay
FGIDs	Functional Gastrointestinal Disorders
FPIEC	Food-Protein Induced Enterocolitis
FPIES	Food Protein Induced Enterocolitis Syndrome
GEJ	Gastro Esophageal Junction
GER	Gastro-Esophageal Reflux
GERD	Gastro-Esophageal Reflux Disease
GIT	Gastro-Intestinal Tract
H2RA	Histamine-2 Receptor Antagonists
HDL	High Density Lipoprotein
HPF	High Power Field
HRQL	Health Related Quality of Life Questionnaire

List of Abbreviations(Cont.)

IgA	Immunoglobulin A
IgE	Immunoglobulin E
IL-4	Interleukin 4
LA	Los Angeles Classification System
LES	Lower Esophageal Sphincter
MCH	Major Histocompatibility Complex
MEN	Multiple Endocrine Neoplasia
NERD	non erosive reflux disease
NSAIDs	Non-Steroidal Anti-Inflammatory Drugs
OAS	Oral Allergy Syndrome
OFC	Oral Food Challenge Test
OIT	Oral Immunotherapy
PNU	Protein Nitrogen Unit
PPIs	proton pump inhibitors
QOL	Quality Of Life
RAST	Radioallergosorbent test
RFE	Radiofrequency Energy
SCIT	Subcutaneous Immunotherapy
SCJ	Squamocolumnar Junction
SEB	Staphylococcal Enterotoxin B
SLIT	Sublingual Immunotherapy
SPT	Skin Prick Test
TGF	Transforming Growth Factor
Th2	T-helper 2 cells
TLESR	Transient lower esophageal sphincter relaxation

List of Abbreviations(Cont.)

TNF	Tumor Necrosis Factor
TVP	Textured Vegetable Protein
VCAM-1	Vascular Cell Adhesion molecule 1
ZES	Zollinger-Ellison Syndrome

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Introduction

Gastro-esophageal reflux disease (GERD) is a condition that develops when the reflux of stomach contents causes troublesome symptoms and/or complications (*Vakil et al., 2006*). GERD prevalence is high, occurring in 14% to 20% of the urban population in the United States (*Dent et al., 2005*), a figure equivalent to that in other countries (*Moraes-Filho et al., 2005*).

In addition to its morbidity, the importance of GERD has been emphasized as there is a significant limitation to the health-related quality of life, such as permanent discomfort to the patient with repeated visits to the doctor, as well as high costs of investigations and treatment(*De Sousa et al.,2006*).

While heartburn, regurgitation, and difficulty swallowing are the most common GERD-related complaints, GERD can manifest a variety of other symptoms. This recognition has led to a broader definition of GERD-related symptomatology, which can include laryngitis, cough, asthma, and dental erosions(*Vakil et al., 2006*).

Regurgitation or aspiration of gastric juice in GERD can cause extra GIT manifestations as chronic cough, dental erosion, recurrent pneumonitis, or idiopathic pulmonary fibrosis. In one cohort of patients with idiopathic pulmonary fibrosis, 67 percent were later diagnosed with GERD(*Sweet et al.,2007*).

Atypical manifestations of GERD may present in the form of chronic sinusitis, posterior laryngitis, nocturnal choking, chronic hoarseness, otitis media, idiopathic pulmonary fibrosis, and asthma(*Richter,1996*).

Epidemiological evidence suggests that 34-89 percent of asthmatics have GERD (irrespective of the use of bronchodilators)(*Sontag et al., 1990*). Physiologic changes caused by asthma and chronic cough promote acid reflux. GERD is also considered by many investigators as a factor contributing to airway inflammation. The association of GERD with asthma/chronic cough and vice versa has been supported by a large number of experimental and clinical findings. This clarifies that there is a link between GERD and allergy(*Theodoropoulos et al.,2002*).

Few studies discussed the relationship between GERD and food allergy but still the link between them not been well studied or investigated. One study showed the role of serum interleukin 4 (IL-4) and tumor necrosis factor alpha (TNF- α) in pathogenesis of the reflux symptoms in children with primary acid gastro-esophageal reflux (GER) and acid GER secondary to cow's milk allergy (CMA) and concluded that The highest mean serum IL-4 and TNF- α concentrations were observed in children with GER secondary to CMA and in children in control group (with cow's milk allergy and/or other food allergy (FA) diagnosed-CMA/FA) before the treatment administration(*Semeniuk et al.,2012*). Another study took patients with CMA and suspected GERD and found that

CM exposure increases the number of weakly acidic reflux episodes. CM challenge during 48-hour multichannel intra-luminal impedance-pH monitoring identified a sub-group of patients with allergen-induced reflux (*Borrelli et al.,2012*).

The estimated prevalence of food allergy is 2-8% in the pediatric population and approximately 2% in adults. Food accounts for 90% of allergic reactions. Cows' milk protein,egg, peanut, soya and wheat are the most common causative foods in infants and young children; peanuts,tree nuts, fish and shellfish are the most common causative foods in older children and adults. The development of food allergy requires an immunological reaction directed to a food antigen. This reaction may involve immunoglobulin E (IgE) or T lymphocytes (T-cells) or some components of both IgE and T-cells (mixed IgE/non-IgE reaction)(*Motala,2008*).

In at least a subset of infants with these functional disorders, improvement after dietary elimination of specific food proteins has been demonstrated. Gastrointestinal food allergy should therefore be considered in the differential diagnosis of infants presenting with persistent regurgitation, constipation or irritable behaviour, particularly if conventional treatment has not been beneficial. The diagnosis of food protein-induced gastrointestinal motility disorders is hampered by the absence of specific clinical features or useful laboratory markers(*Heine,2008*).

Aim of the Work

The aim of this work is to study the prevalence of food allergy in adult patients with GERD of unknown etiology.

CHAPTER (1):FOOD ALLERGY

Definition:

Food allergy is an immune system reaction that occurs soon after eating a certain food. Even a tiny amount of the allergy-causing food can trigger symptoms and signs such as digestive problems, hives or swollen airways. In some people, a food allergy can cause severe symptoms or even a life-threatening reaction as anaphylaxis. It's easy to confuse a food allergy with a much more common reaction known as food intolerance. While bothersome, food intolerance is a less serious condition that does not involve the immune system(*Gupta et al.,2013*).

- People with a food intolerance may have digestive symptoms such as diarrhea, bloating and stomach cramps. This may be caused by difficulties digesting certain substances, such as lactose. However, no allergic reaction takes place(*NHS,2014*).

Important differences between a food allergy and a food intolerance include:

- The symptoms of a food intolerance usually only occur several hours after eating the food but food allergy can occur within few minutes.
- Eating a larger amount of food to trigger an intolerance but food allergy can occur with minimal amount of food.
 - Unlike an allergy, a food intolerance is never life-threatening(*NHS,2014*).

Historical view of food allergy:

Over two thousand years ago Hippocrates wrote about the negative effects that food could have on different people:

For cheese does not prove equally injurious to all men, for there are some who can take it to satiety, without being hurt by it in the least, but, on the contrary, it is wonderful what strength it imparts to those it agrees with; but there are some who do not bear it well, their constitutions are different, they differ in this respect, that what in their body is incompatible with cheese, is roused and put in commotion by such a thing; and those in whose bodies such a humor happens to prevail in greater quantity and intensity, are likely to suffer the more from it. But if the thing had been pernicious to the whole nature of man, it would have hurt all” (*Lundy,2007*).

Historically, physicians were recognized for being able to treat their patients’ illnesses by diet manipulation. That means that throughout history, doctors treated illness by changing a patient’s diet. An example of this written approximately 200 years ago and credited to Matthew Baillie is as such:

“To judge of the true skill and merit of a physician requires a competent knowledge of the science of medicine itself; but to gain the good opinion of the patient or his friends, there is perhaps no method so ready as to show expertness in the regulation of the diet of the sick. Discretion and judgment will, of course, be required; the