



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكرو فيلم

بسم الله الرحمن الرحيم



HANAA ALY



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم



شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



HANAA ALY



شبكة المعلومات الجامعية
التوثيق الإلكتروني والميكروفيلم

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات



يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار



HANAA ALY



Screening for Celiac Disease among Patients with Chronic Kidney Disease

Thesis

Submitted for partial Fulfillment of Master Degree in Pediatrics

Submitted by

Doha Ahmad Anwar

Ain Shams University

M.B, B.Ch

Supervisors

Prof. Magid Ashraf Abdel Fattah Ibrahim

Professor of Pediatrics

Faculty of Medicine - Ain Shams University

Prof. Ahmed Mohamed Hamdy

Professor of Pediatrics

Faculty of Medicine - Ain Shams University

Dr. Ragia Marei Ali Said

Assistant Professor of Pediatrics

Faculty of Medicine - Ain Shams University

Faculty of Medicine

Ain Shams University

2019

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

Acknowledgment

*First and foremost, I feel always indebted to **ALLAH**,
the Most Kind and Most Merciful.*

*I'd like to express my respectful thanks and
profound gratitude to **Prof. Magid Ashraf Abdel
Fattah Ibrahim**, Professor of Pediatrics - Faculty of
Medicine- Ain Shams University for his keen guidance,
kind supervision, valuable advice and continuous
encouragement, which made possible the completion of
this work.*

*I am also delighted to express my deepest
gratitude and thanks to **Prof. Ahmed Mohamed
Hamdy**, Professor of Pediatrics, Faculty of Medicine,
Ain Shams University, for his kind care, continuous
supervision, valuable instructions, constant help and
great assistance throughout this work.*

*I am deeply thankful to **Dr. Ragia Marei
Ali Said**, Assistant Professor of Pediatrics, Faculty of
Medicine, Ain Shams University, for her great help,
active participation and guidance.*

*I would like to express my hearty thanks to all my
family for their support till this work was completed.*

*Last but not least my sincere thanks and
appreciation to all patients participated in this study.*

Doha Ahmad Anwar

List of Contents

Title	Page No.
List of Abbreviations.....	5
List of Tables	6
List of Figures.....	7
Introduction.....	1
Aim of the Work.....	12
Review of Literature	
▪ Chronic Kidney Disease	13
▪ Celiac Disease	22
▪ The Gut- Kidney Axis	35
Subjects and Methods.....	46
Results.....	53
Discussion.....	70
Summary	81
References	82
Arabic Summary	

List of Abbreviations

Abb.	Full term
<i>APCs</i>	<i>Antigen-presenting cells.</i>
<i>CAKUT</i>	<i>Congenital anomalies of the kidney and urinary tract.</i>
<i>CD</i>	<i>Celiac disease.</i>
<i>CKD</i>	<i>Chronic kidney disease.</i>
<i>CRF</i>	<i>Chronic renal failure.</i>
<i>CVD</i>	<i>Cardiovascular disease.</i>
<i>DGPA</i>	<i>Deaminated gliadin peptides antibodies.</i>
<i>EATL</i>	<i>Enteropathy associated T-cell lymphoma.</i>
<i>eGFR</i>	<i>Estimated glomerular filtration rate.</i>
<i>EMA</i>	<i>Endomysial antibodies.</i>
<i>ESRD</i>	<i>End-stage renal disease.</i>
<i>GFD</i>	<i>Gluten-free diet.</i>
<i>GFR</i>	<i>Glomerular filtration rate.</i>
<i>GI</i>	<i>Gastrointestinal.</i>
<i>HLA</i>	<i>Human leukocyte antigen.</i>
<i>HTN</i>	<i>Hypertension.</i>
<i>IEL</i>	<i>Intraepithelial lymphocytes.</i>
<i>IgA</i>	<i>Immunoglobulin A.</i>
<i>NKF / KDOQI</i> ..	<i>National Kidney Foundation / Kidney Disease and Outcome Quality Initiative.</i>
<i>PD</i>	<i>Peritoneal dialysis.</i>
<i>RAAS</i>	<i>Renin angiotensin aldosterone system.</i>
<i>RCD</i>	<i>Refractory celiac disease.</i>
<i>ROD</i>	<i>Renal osteodystrophy.</i>
<i>tTG</i>	<i>Tissue transglutaminase.</i>

List of Tables

Table No.	Title	Page No.
Table (1):	Stages of chronic kidney disease in children	14
Table (2):	Marsh classification of histologic findings in celiac disease.....	31
Table (3):	Demographic data of cases & controls.....	53
Table (4):	Etiology of chronic renal disease among all included patients (n=90).	54
Table (5):	Anthropometric data of all included patients(n=90).	55
Table (6):	Comparisons of anthropometric measurements among ESRD& conservative patients.....	56
Table (7):	Comparisons of blood indices between ESRD & conservative cases.	58
Table (8):	Comparison between ESRD & conservative cases regarding bone profile.	59
Table (9):	GIT symptoms among all included patients (n=90).	60
Table (10):	Comparisons between cases & controls regarding GIT symptoms.....	61
Table (11):	Comparisons between ESRD & conservative patients regarding frequent GIT symptoms(n=90).	66
Table (12):	Distribution of cases on Bristol stool chart.	68
Table (13):	Comparison between the two studied groups regarding Bristol stool chart.	68
Table (14):	All cases had serum level of antitissue transglutaminas IgG & IgA <10 U/ml.	69

List of Figures

Fig. No.	Title	Page No.
Figure (1):	The “iceberg model” idealizing the interplay between celiac disease genetic makeup and exposure to gluten	26
Figure (2):	Duodeno-endoscopic finding (arrow): nodularity	29
Figure (3):	Duodeno-endoscopic finding (arrow): mosaic pattern	30
Figure (4):	Simplified schematic representation of research approaches to develop gluten-targeted therapies for celiac disease	34
Figure (5):	Effect of CKD on the colonic microbiome (dysbiosis) and mucosal structure and function	38
Figure (6):	Illustration of the vicious cycle of uremia in the colon	42
Figure (7):	The link between gastrointestinal and renal disorders.....	45
Figure (8):	Bristol stool chart.	47
Figure (9):	Weight centile for ESRD patients on dialysis and conservative.....	57
Figure (10):	Height centile for ESRD patients on dialysis and conservative.....	57
Figure (11):	GIT symptoms between patients and controls.....	62
Figure (12):	Incidence of waterry diarrhea between patients and controls.	62
Figure (13):	Incidence of constipation between patients and controls.	63

List of Figures cont...

Fig. No.	Title	Page No.
Figure (14):	Straining between controls and patients.	63
Figure (15):	Pain in defecation between controls and patients.	64
Figure (16):	Incontinence between controls and patients.	64
Figure (17):	GIT symptoms between controls and patients.	65
Figure (18):	Diarrhea between ESRD and conservatives	65
Figure (19):	GIT symptoms between ESRD and conservatives	67
Figure (20):	GIT symptoms between ESRD and conservatives	67

INTRODUCTION

The terms chronic renal failure (CRF) and chronic renal insufficiency have been replaced by the term chronic kidney disease (CKD) which was proposed by National Kidney Foundation/Kidney Disease and Outcome Quality Initiative (NKF /KDOQI) group in 2002 for any patient who has kidney damage lasting for at least 3 months with or without a decreased GFR or any patient who has a GFR of <60 mL/min/1.73 m² lasting for 3 months with or without kidney damage. CKD refers to a multi-systemic clinical condition characterized by an irreversible deterioration of renal function that can further progress to end-stage renal disease (ESRD) (*Oliveira and Mak, 2018*).

Celiac disease (CD) is one of the most common lifelong food-related disorders worldwide. CD is a permanent intolerance to ingested gluten present in wheat, rye and barley resulting in immune- mediated enteropathy in individuals who are genetically susceptible to the disease (*Lindfors et al., 2019*).

Until the mid-1970s, CD was described as a malabsorption syndrome during childhood. However, more studies have shown that the disease can arise at any age and affect any organ in the body (*Tersigni et al., 2014*).

CD is thought to be underdiagnosed owing to the fact that its extra intestinal manifestations can misdirect the diagnosis and in some cases they are the only clinical manifestations. Some of these manifestations are direct consequences of autoimmunity, whereas others are indirectly related to inflammation and/or malabsorption (*Leffler et al., 2015*).

The key to CD diagnosis is increased awareness of the wide spectrum of symptoms and screening in risk groups (*Lindfors et al., 2019*).

Although intestinal biopsy remains the gold standard for the definite diagnosis of CD, highly sensitive and specific serological tests, such as tissue transglutaminase (tTG), endomysial IgA (EMA) and deamidated gliadin peptide antibodies, have become more important in the screening of large populations. Serological tests are widely used to facilitate selection of patients for diagnostic endoscopy and small bowel biopsy (*Caio et al., 2019*).

CD is a lifelong disease and complete avoidance of gluten-containing food products is the only known effective treatment for it. There are challenges in maintaining a good compliance to gluten free diet (GFD), therefore it is essential that a reliable diagnosis of CD is made before instituting GFD in the patients (*Bascuñán et al., 2017*).

Mass screening of CD by serology in the general population has been suggested as it fulfills many of the WHO criteria for mass screening as it is an important health problem, common, simple to diagnose, and treatment is available. There is evidence that screening at-risk groups for CD could be beneficial, but more studies are needed before large scale population screening can be recommended (**Kivelä and Kurppa, 2018**).

Chronic kidney disease (CKD) and end-stage renal disease (ESRD) cause many organ complications including gastrointestinal (GI) tract (GIT). CKD affects whole GIT parts leading to multiple different lesions, GIT involvement in CKD manifests as uremic anorexia, gastroenteritis, nausea, vomiting, uremic fetor, idiopathic ascites, peptic ulcer disease, GIT bleeding, viral hepatitis, and peritonitis (**Chillon et al., 2016**).

AIM OF THE WORK

The aim of this study is to:

- 1- Screening for celiac disease among pediatric patients with chronic kidney diseases.