

بسم الله الرحمن الرحيم

 $\infty\infty\infty$

تم رفع هذه الرسالة بواسطة / حسام الدين محمد مغربي

بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى مسئولية عن محتوى هذه الرسالة.

AIN SHAMS UNIVERSITY

Since 1992

Propries 1992

ملاحظات: لا يوجد





Study of Serum Total Immunoglobulin E in Egyptian Patients with Newly Diagnosed Colorectal Carcinoma

Thesis

Submitted for Partial Fulfilment of Master Degree in Internal Medicine

 $\mathcal{B}y$

Wessam Reda Atta Eid

M.B.B.CH

Under Supervision of

Prof. Dr. / Fawzia Hassan Abo Ali

Professor of Internal Medicine, Allergy and Clinical Immunology Faculty of Medicine, Ain Shams University

Dr. / Manar Farouk Mohamed

Lecturer of Internal Medicine, Allergy and Clinical Immunology Faculty of Medicine, Ain Shams University

Dr. / Sara Essam Mohamed Zaki

Lecturer of Oncology Faculty of Medicine, Ain Shams University

Dr. / Sara Ibrahim Abdelfattah Taha

Lecturer of Clinical Pathology Faculty of Medicine, Ain Shams University

Faculty of Medicine
Ain Shams University
2022



سورة البقرة الآية: ٣٢

Acknowledgments

First and foremost, I feel always indebted to **Allah** the Most Beneficent and Merciful.

I wish to express my deepest thanks, gratitude and appreciation to **Prof. Dr. / Fawzia Wassan Abo Ali,**Professor of Internal Medicine, Allergy and Clinical Immunology, Faculty of Medicine, Ain Shams University, for her meticulous supervision, valuable instructions and generous help.

Special thanks are due to **Dr.** / **Manar Farouk Mohamed,** Lecturer of Internal Medicine, Allergy and

Clinical Immunology, Faculty of Medicine, Ain Shams

University, for her sincere efforts, fruitful encouragement.

I am deeply thankful to **Dr. / Sara Essam Mohamed Zaki,** Lecturer of Oncology, Faculty of Medicine, Ain Shams
University, for her help, outstanding support, active participation and guidance.

Last but not least my sincere thanks and appreciation to *Dr. / Sara Ibrahim Abdelfattah Taha, Lecturer of Clinical Pathology, Faculty of Medicine, Ain Shams University, for her meticulous supervision, kind guidance,

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

Wessam Reda Atta Eid

Tist of Contents

Title	Page No.
List of Abbreviations	i
List of Tables.	v
List of Figures	vi
Introduction	1
Aim of the Work	4
Review of Literature	
Chapter 1: Immunoglobulin E	5
Chapter 2: Role of the Immune System in Malign	nancy 29
Chapter 3: Colorectal Carcinoma	42
Subjects and Methods	82
Results	89
Discussion	102
Summary and Conclusion	109
Conclusion	112
Recommendations	113
References	114
Arabic Summary	

Tist of Abbreviations

Abb.	Full term
AD	Atopic dermatitis
	Antibody-dependent cell-mediated cytotoxicity
ADCP	Antibody-dependent cell-mediated phagocytosis
AFP	Alpha Fetoprotein
AIO	Arbeitsgemeinschaft Internistische Onkologie
APCs	Antigen-presenting cells
ASC	Adenosquamous Carcinoma
ASRs	Age-standardized incidence rates
bid	Twice a day
CBC	Complete blood count
CCC	Clear Cell Carcinoma
CCE	Colon capsule endoscopy
CC-Type	Cribriform Comedo-Type Carcinoma
CD	Crohn's disease
CI	Confidence interval
CIN	Chromosomal instability
CIRs	Cecal intubation rates
CNVs	Copy number variations
COM	Carcinoma with Osseous Metaplasia
CpG	Cytosine-phospho-guanine
CRC	Colorectal cancer
CRC	Colorectal carcinoma
CS	Colonoscopy
CSU	Chronic spontaneous urticarial
CTC	Computed tomographic colonography
CTLs	Cytotoxic lymphocytes

Tist of Abbreviations cont...

Abb.	Full term
CVID	Common variable immunodeficiency
DC	
	Oouble-contrast barium enema
DFS	
DN	
	Dedicator of cytokinesis 8
	Disseminated tumor cell
EBVE	
	Enzyme linked immunosorbent assay Familial adenomatous polyposis
	1 01
FŒRsF	
FSF	_ ·
5-FUF	
	Hobal Cancer Observatory
	Iepatoid Adenocarcinoma
	Iuman hyper-IgE syndrome
	Iuman immunodeficiency virus
HNPCC	Iereditary non-polyposis colon cancer
	Iormone replacement therapy
IBDI	nflammatory bowel disease
iCCCI	ntestinal CCC
IgEI	mmunoglobin E
IgGSDIg	gG subclass deficiency
	mmune dysregulation, polyendocrinopathy, nteropathy, X-linked syndrome
IQRI	nterquartile range
ITAMI	mmuno-tyrosine activation motif
IVI	ntravenous

Tist of Abbreviations cont...

Abb.	Full term
KARs	Killer activation receptors
	Killer inhibitory receptors
	Lymphoepitelioma-Like Carcinoma
	Low Grade Tubuloglandular Adenocarcinoma
LOF	_
	Loss of heterozygosity
	Lipopolysaccharide
LV	
MA	Mucinous (Colloid) Adenocarcinoma
mAbs	Monoclonal antibodies
MAP	MUTYH-associated polyposis
MC	Medullary Carcinoma
MDSCs	Myeloid-derived suppressor cells
MM	IgE Mutliple Myeloma
MMR	Mismatch repair
MPA	Micropapillary Adenocarcinoma
MSI	Microsatellite instability
NK	Natural killer
OS	Overall survival
pChC	Primary Colorectal Choriocarcinoma
PgD2	Prostaglandin D2
RhC	Rhabdoid Colorectal Carcinoma
RNS	Reactive nitrogen species
ROS	Reactive oxygen
RV	Rhinovirus
SA	Serrated Adenocarcinoma
SCC	Squamous
SCC	Squamous cell carcinoma

Tist of Abbreviations cont...

Abb.	Full term
SD	Standard deviation
SIgAD	Selective IgA deficiency
SIgED	Selective IgE deficiency
SIgGD	Selective IgG deficiency
SIgMD	Selective IgM deficiency
SIR	Standardized incidence ratio
SPSS	Statistical package for Social Science
SRC	Signet Ring Cell Carcinoma
STAT3	Signal transducer and activator of
	transcription 3
TAA	Tumor-associated antigens
TAMPs	Tumor-associated molecular patterns
TLS	Tertiary lymphoid structures
TME	Tumour microenvironment
TNF	Tumour necrosis factor
TPO	Thyroperoxidase
Tregs	Regulatory T cells
TSA	Tumor-specific
UC	Ulcerative colitis
Ucs	Undifferentiated carcinomas
VC	Villous Carcinoma

Tist of Tables

Table No.	. Title Po	age No.
Table 1:	Conditions associated with elevated seru	m IgE24
Table 2:	Prognostic Groups	69
Table 3:	Demographic data	89
Table 4:	Histopathological data	90
Table 5:	Lab investigations	92
Table 6:	Distribution of patients according to IgE	level93
Table 7:	Relation between IgE level and tumor cri	teria94
Table 8:	Comparison between cases and coregarding IgE level	ontrols 97
Table 9:	Relation between sex and IgE level	98
Table 10:	Correlation between age and IgE level	98
Table 11:	Correlation between IgE level and TLC	99

List of Figures

Fig. No.	Title	Page No.
Figure 1:	Immunoglobulin E (IgE)	6
Figure 2:	IgE-Receptor Interactions	8
Figure 3:	Overview of potential roles of pathology	-
Figure 4:	Mechanism of action and thera omalizumab	
Figure 5:	Molecular mimicry in AD	18
Figure 6:	Hypothetic cellular pathways autoreactivity in atopic dermatit	<u> </u>
Figure 7:	Mechanisms of mast cell active spontaneous urticaria. Type I	
Figure 8:	Immune response against helmin	nthes23
Figure 9:	Demonstration of major B-cell fi	
Figure 10:	Roles of innate immune cells cancers	
Figure 11:	Nature killer (NK) cells	34
Figure 12:	The IgE isotype uniquely encorfunction in the pathophysiologreactions, parasitosis, and tumou	gies of allergic
Figure 13:	IgE and IgE therapy-mediated of surveillance against cancer	
Figure 14:	IgE functions against cancer cell	s41
Figure 15:	World and colorectal cancer in 20	02044
Figure 16:	Gut microbiota-related mecha which obesity may increase ri cancer	sk of colorectal

Tist of Figures cont...

Fig. No.	Title	Page No.
Figure 17:	Potential benefits of short-chain may contribute to the anticancer	•
Figure 18:	Potential role of the gut microbio the effect of carcinogenic factors is	•
Figure 19:	The pathogenesis of colitis involute microenvironment, co-opprogression to dysplasia and can	pted in the
Figure 20:	Pathways implicated in pathog traditional, alternatic and serrat	
Figure 21:	Distribution percentage of CRC b	oy site61
Figure 22:	Pie chart showing the frequence carcinomas by histologic type	· •
Figure 23:	Colonoscopy	71
Figure 24:	Colorectal polyps	74
Figure 25:	IgE cross-linking on the surface triggers upregulation of pro-inf surface marker expression and of regulatory cell surface marker	flammatory cell downregulation
Figure 26:	Percentages of colorectal car according to stages	
Figure 27:	Percentage of different types of C	CRC91
Figure 28:	Percentage of colorectal car according to anatomical sites	
Figure 29:	Distribution of patients according	g to IgE level93
Figure 30:	Relation between total IgE le staging.	
Figure 31:	Relation between IgE level and to	umor site95

Tist of Figures cont...

Fig. No.	Title	Page No.
Figure 32:	Relation between IgE level Pathology	
Figure 33:	Comparison between cases a regarding IgE level.	
Figure 34:	ROC curve analysis for ability of differentiate between cases and con	•
Figure 35:	ROC curve for ability of IgE level to between stages (II & III) and stage	

ABSTRACT

Colorectal carcinoma (CRC) is the third most common non-skin cancer in the United States after lung cancer in both men and women, with an annual incidence of 42.9 per 100,000 people. It accounts for 8% of cancer-related deaths in the US alone (*Bibbins-Domingo et al.*, 2016).

Colorectal cancer is the 7th commonest cancer in Egypt, representing 3.47% of male cancers and 3% of female cancers (*Metwally et al.*, 2018).

Links between IgE or IgE-mediated diseases and malignancy have been reported with early studies finding decreased cancer risk associated with the presence of allergy and decreased prevalence of atopy in cancer patients (McCraw et al., 2021). In cancer patients themselves, there is evidence to suggest that higher IgE levels may correlate to a prolonged survival compared to those with low or even average levels (Bankova & Barrett, 2019).

In the current study, that the Best cut off value of total IgE to differentiae between CRC cases and healthy controls was > 42.50 IU\mLwith sensitivity=57.1% and Specificity = 53.8%.

In the current study, there was a statistical significance regarding the level of total IgE between CRC cases and controls p value =0.05. Twelve (20%) CRC patients had total IgE level between 5-10 (IU\ml), 37 patients had total IgE level 10-100 (IU\mL), 11 patients with total IgE level>100 (IU\mL). 20 CRC patients were stage II, 19 patients were stage III, 21 patients were stage IV. 54 patients were diagnosed with adenocarcinoma, two patients with Mucinous adenocarcinoma, two patients had Tubulovillous adenocarcinoma, one patient had Villous adenocarcinoma, and one patient had squamous cell carcinoma (SCC). 18 patients had rectal carcinoma, 40 patients had only the Colonic carcinoma, and only two patients had both colorectal carcinoma.

In the current study, that the Best cut off value of total IgE to differentiae between CRC cases and healthy controls was >42.50 IU\mLwith sensitivity=57.1% and Specificity = 53.8%.

In the current study, 20 CRC patients were stage II, 19 patients were stage III, 21 patients were stage IV.

Keywords: Serum Total Immunoglobulin E, Colorectal Carcinoma

Introduction

olorectal carcinoma (CRC) is the third most common non-skin cancer in the United States after lung cancer and breast cancer in both men and women, with an annual incidence of 42.9 per 100,000 people. It accounts for 8% of cancer-related deaths in the US alone (*Kumar and Lewis*, 2021).

Colorectal cancer is the 7th most common cancer in Egypt, representing 3.47% of male cancers and 3% of female cancers (*Hassan et al.*, 2021).

Intriguingly, recent studies reveal a correlation between IgE deficiency and increased malignancy risk (*Ferastraoaru et al.*, 2020).

CRC incidence is attributed to dietary factors along with genetic and environmental factors. It also displays a strong correlation with increased age, the maximum rate at the age above 75 years, and lowest below 40 years. Males are affected more than females. African Americans have the highest incidence, and Asian Pacific Islanders have the lowest (*Rahul and Catherine*, 2020).

With the advent of newer and better screening tools, CRC related mortality rate has decreased, on average, about 2.7% between 2004 and 2013. It is expected to decrease further to about 38% for 50 to 74-year-olds and about 45% for those older than 75-years-old by 2030 (*Rahul and Catherine*, 2020).