

شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلو

# بسم الله الرحمن الرحيم





HANAA ALY



شبكة المعلومات الجامعية التوثيق الإلكتروني والميكرونيله



شبكة المعلومات الجامعية التوثيق الالكتروني والميكروفيلم



HANAA ALY



شبكة المعلومات الجامعية التوثيق الإلكترونى والميكروفيلم

# جامعة عين شمس التوثيق الإلكتروني والميكروفيلم قسم

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



يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار



HANAA ALY





# Serum Selenium Levels among Ain Shams University Medical Students with Family History of Cancer, A pilot study

Chesis

Submitted for Partial Fulfillment of Master Degree in Clinical Nutrition

By

#### Heba Mohamed Essam El Banna

M.B.B. Ch – Bachelor of Medicine and Surgery (2014) Diploma of Clinical Nutrition the American university in Cairo

## Under Supervision

#### Prof. Zeinab Abdel Hafeez Elsayed

Professor of Clinical Oncology and Nuclear Medicine Faculty of medicine Ain shams University

#### Assist. Prof. Amira Ibrahim Hamed

Assistant Professor of Clinical Pathology and Immunology Faculty of medicine Ain shams University

#### Dr. Reham Mohamed Faheim

Lecturer of Clinical Oncology and Nuclear Medicine Faculty of medicine Ain shams University



First I would like to express my sincerest gratitude and gratefulness to Allah who continues to bless and fill me the hope, faith and patience that enable me to carry out all my daily work.

I am greatly honored to express my thanks and gratitude to **Prof. Dr. Zeinab Abdel Hafeez Elsayed**, Professor of Clinical Oncology and Nuclear Medicine, Faculty of medicine Ain shams University, for guidance, great help, encouragement and her creative support throughout the whole up of this thesis.

I would like to express my thanks and gratitude to Assist. Prof. Dr. Amira Ibrahim Hamed, Assistant Professor of Clinical Pathology and Immunology, Faculty of medicine Ain shams University, for her valuable help, advice and her creative support for me to accomplish this work.

It is with great pleasure, deep satisfaction and gratitude that I acknowledge the help of **Dr. Reham**Mohamed Faheim, Lecturer of Clinical Oncology and Nuclear Medicine, Faculty of medicine Ain shams University, for her unlimited help, effort, support, guidance and for the time she devoted to me in this work. I would not have been able to start and continue this work without her help.

I am extremely sincere to my family who stood beside me throughout this work giving me their support.



Thank you all Heba Mohamed Essam El Banna

# **List of Content**

List of Abbreviations			
List of Figures			
List of Tables			
Introduction			
Aim of the work	3		
Review of literature			
Chapter I. Selenium and Human Health	4		
Chapter II. Selenium in relation to Cancer	40		
Chapter III. Mental Health with Cancer and	51		
Selenium			
Subjects and methods	58		
Results			
Discussion			
Conclusion and Recommendation			
Summary			
References			
Arabic Summary			

# **List of Abbreviations**

AIDS	Acquired Immunodeficiency Syndrome
Ca	Calcium
CATs	Catecholamines
CD	Crohn's Disease
CI	Confidence Interval
CVB	Coxsackie Virus B
CVD	Cardiovascular Disease
DM	Diabetes Mellitus
FBS	Food Balance Sheet
Fe	Iron
GDF-5	Growth Differentiation Factor-5
GPx1	Cytosolic Glutathione Peroxidase
GPx2	Gastrointestinal-Specifific Glutathione
	Peroxidase
GPx3	Plasma Glutathione Peroxidase
GPx4	Phospholipid Hydroperoxide Glutathione
	Peroxidase
GPxs	Glutathione Peroxidases
H2O2	Hydroxyl Peroxide
H2Se	Selenide
HBV	Hepatits B Virus
HCC	Hepatocellular Carcinoma
HCV	Hepatits C Virus
HIV/AIDS	Human Immunodeficiency Virus
НО	Hydroxyl Radical
<b>HPA</b> axis	Hypothalamic Pituitary Adrenal Axis
I	Iodine
IBD	Inflammatory Bowel Disease
ICU	Intensive Care Unit
IL-6	Interleukin-6
KBD	Kashin-Beck Disease
KD	Keshan Disease
MNDs	Micro-Nutrient Deficiencies

NHANES	National Health And Nutrition Examination
	Survey
NK	Natural Killer cell
NO	Nitric Oxide
<b>O2</b>	Singlet Oxygen
O2-	Superoxide Anion Radical
ONOO -	Peroxynitrite
OP	Osteoporosis
OR	Odds Ratio
PS	Psychological Stress
PSA	Prostate Specific Antigen
RCTs	Randomized Controlled Trials
RDA	Recommended Daily Allowance
RNI	Recommended Nutrient Intake
ROS	Reactive Oxygen Species
Se	Selenium
SELENOP	Selenoprotiens
SePP	Selenoprotien P
SetMet	Seleniomethionine
SIRS	Systemic Inflammatory Response Syndrome
SNPs	Single Nucleotide Polymorphisms
SNS	Sympathetic Nervous System
T-2	Trichothecene Mycotoxin
TB	Tuberculosis
Trx	Thioredoxin
<b>TXNRDs</b>	Thioredoxin Reductases
UC	Ulcerative Colitis
WHO	World Health Organization
Zn	Zinc

# **List of Figures**

Fig.	Title	Page
1	Contribution of each food group to total population dietary exposure in the UK.Adapted from data presented in the UK Food Standards Agency document	7
2	A scheme for selenium absorption, metabolism, and distribution	11
3	Purported mechanisms of action of selenium against cancer and key factors modulating the effect of selenium	25
4	Dose-response relationship between dietary selenium intake and the odds ratio for osteoporosis	32
5	U-shaped relationship between Se status and disease risk	35
6	Odds ratios of prostate cancer by quartile of serum selenium	47
7	Simplified hypothetical scheme for the role of psychological stress in carcinogenesis and aging	54
8	Comparison between control group and subject group according to age	77
9	Comparison between control group and subject group according to BMI	77
10	Comparison between control group and subject group according to systolic blood pressure	78
11	Comparison between control group and subject group according to diastolic blood pressure	78
12	Co-Relation between Age and Serum Se	79
13	Comparison between Control (C) and subjects (P) in terms of stress levels	80

## **List of Tables**

Table	Title	Page
1	Pharmacodynamic mechanisms of selenium supplementation in normal and malignant cells.	43
2	Combination of selenium with systemic therapies and radiation.	45
3	Descriptive statistics of subjects and controls as regards systolic and diastolic BP, BMI and Age	74
4	Comparison between subjects and controls as regards systolic and diastolic BP, BMI and age using ANOVA (Analysis of Variance) test	75
5	Comparison between males and females in sample population using Chi-Squared Test	76
6	Means of stress between control group (C) and subject group (P).	80
7	ANOVA (Analysis of Variance) with the variables selenium intake (mcg/l) and serum selenium (mcg/l)	81
8	Comparison between the studied groups as regards selenium intake and serum selenium using ANOVA Test	82
9	Regression Analysis of Serum Se (mcg/l) versus Stress and Se intake (mcg/l)	83



## Introduction

According to the WHO, the global cancer burden raised up to 18.1 million new cases and 9.6 million deaths in 2018. The crude incidence rates on the national level for all sites excluding nonmelanoma skin cancer in Egypt is 113.1/100,000 (both sexes), 115.7/100,000 (males), and 110.3/100,000 (females) (**Ibrahim et al., 2014**).

A study estimated that 50 percent of certain types cancer can be preventable (Wolin et al., 2010). In addition, the World Cancer Research Fund estimates that about 20% of all cancers diagnosed in the US are related to several preventable measures such as body fatness, physical inactivity, excess alcohol consumption as well as poor nutrition (WCRF, 2014).

The psychological burden on family members of cancer patients especially first-degree relatives have been extensively studied in international literature. In fact, previous researches showed that the level of distress experienced by family members is higher than the one experienced by the patient himself (Edwards et al., 2004, **Segrin et al., 2007).** 

Studies have shown that psychological increases circulating cytokines which in turn increases reactive oxygen species (ROS) that leads to increase in oxidative stress (Teruo Havashi, 2014).



It has been estimated that around 1 billion people worldwide have inadequate selenium intake (Gerrad et al., 2017).

Selenium is present in many enzymes and proteins in their active centers, it has many roles such as activating anticancer agents, preventing heart and vascular diseases, exhibiting anti-proliferative and anti-inflammatory properties, and stimulating the immune system (Duntas et al., 2015). It also forms the main part of seleniumcontaining proteins and several antioxidant enzymes, such as glutathione peroxidase (GPx), thioredoxin reductase (TRxR), and iodothyronine deiodinase (DIO) (Kieliszek et al., 2015). The studies have shown that selenium may have anti carcinogenic effects, especially against cancers of the lung, prostate, skin, and GIT system (Lee et al., 2000, Rayman, 2005). Selenium resembles butyrate which induces DNA methylation and acts as an inhibitor of histone deactylase (Lee et al., 2009, Supic et al., 2013).

## Aim of the Work

The aim of this work is to compare serum levels of selenium in medical students who are first degree relatives of cancer patients to those with no family history of cancer.

### **Selenium and Human Health**

#### A. **Introduction:**

Selenium (Se) in blood is found in plasma as well as within the cellular compartment where concentrations are higher and the concentrations are most elevated in tissues such as liver, kidneys, and spleen. Se is from the bunch of six components, which has been examined for antioxidant and anticancer properties (Hashemi et al., 2017).

More than 800 million individuals have inadequate dietary energy intake universally, with >2 billion individuals at chance of one or more micro-nutrient insufficiencies (MNDs), or Hidden Hunger. Worldwide disease burdens ascribed to MNDs are based on iron (Fe), zinc (Zn), iodine (I) and vitamin A, which are considered to be the MNDs of most noteworthy open wellbeing concern by the World Health Organization (WHO). Be that as it may, later estimates of dietary mineral supplies, determined from Food Balance Sheets (FBS) combined with food composition tables, demonstrate that other MNDs, such as calcium (Ca) and selenium (Se) may moreover have impressive public health importance at a regional level (**Phiri et al., 2019**).

Micronutrient deficiencies, including essential trace elements, affect as many as 3 billion people worldwide. The availability of trace elements in foods largely depends on their soil concentration. Micronutrients

are essential for maintaining human health. Although only micronutrients are needed, it is reported that 3 billion people in the world lack them. One such micronutrient is selenium. Insufficient intake of selenium from food affects up to one in seven people and is known to have a negative impact on the health of farm animals. Since dietary selenium intake largely depends on soil selenium content and plant bioavailability, understanding the mechanisms driving soil concentration and predicting global distribution can help prevent selenium deficiency. However, the global selenium concentration in the soil and the factors affecting selenium distribution are largely unknown. Except for soil, Se is present in all other environmental divisions [that is, coupled with the depletion of micronutrients in farmland, the predicted loss of total selenium in soil indicates that the nutritional quality of food may decline, thereby increasing the risk of global micronutrient deficiencies. It is estimated that about 1 billion people in the world have insufficient selenium intake (Jones et al., 2017).

In the past century, interest in selenium and health has focused on the potential toxic effects of high human intake due to reports of alkaline diseases in livestock in selenium areas (Smith et al., 1936). The essence of selenium was established in the mid-1950s, when mice fed high-purity casein suffered from fatal liver disease. Certain foods (including brewer's yeast) can prevent this disease. Selenium has been identified as the active ingredient (Schrauzer and Surai, 2009).