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Impact of Some heavy metals on thyroid gland functions

A Thesis

Submitted to the College of Science Al-Nahrain University as partial Fulfillment of the Requirements for the Degree of Master of Science in Chemistry/ (Biochemistry).

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بسم الله الرحمن الرحيم

(قُل لَّوْ كَانَ الْبَحْرُ مِدَادًا لِّكَلِمَاتِ رَبِّي لَنَفِدَ الْبَحْرُ قَبْلَ أَن تَنفَدَ كَلِمَات رَبِّي وَلَوْ جِئْنَا بِمِثْلِهِ مَدَدًا)

صدق الله العظيم

سورة الكهف (108 – 109)

Committee Certfication

We, the examining committee certify that we have read this thesis entitled " Impact of Some heavy metals on thyroid gland functions " and examined the student " **Sara Jawad Kadhim** " in its contents and that in our opinion, it is accepted for the Degree of Master of Science in Biochemistry

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Dedication

To The Realest And Purest Love In The World

Mother

And To All My Family
And to my country Iraq

Sara Jawad

Acknowledgment

First of all I would like to thank our God for his merciful and continuous help through my life. and praise upon Mohammad his Prophet and upon his Family.

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Abbreviations

Symbol	Terms
*	*significant*
**	*Highly significant*
AAS	*Atomic absorption spectrophotometer*
BMI	*Body mass index*
BPA	*Bisphenol A*
Cd	*Cadmium*
ECD	*Electron Capture Detector*
GC	*Gas chromatography*
GFAAS	*Graphite furnace Atomic absorption spectrophotometer*
HDL	*High density lipoprotein*
Hg	*Mercury*
HPLC	*High-performance liquid chromatography*
LDL	*low density lipoprotein*
LSD	*Least significant differences*
Max.	*Maximum*
Min.	*Minimum*
Pb	*Lead*
PCBs	*Polychlorinated biphenyls*
POPs	*Persistent Organic Pollutants*
PPb	*Part per billion*
PPM	*Part per million*
STD	*Standard division*
T3	*3,5,3´-triiodothyronine*
T4	*Thyroxine or 3,3´,5,5´-tetraiodothyronine*
TC	*Total cholesterol*
TG	*Triglyceride*
Tg-Ab	*Thyroglobulin antibodies*
TH	*Thyroid hormones*
TSH	*Thyroid stimulating hormone*
U.S	*United state*
VLDL	*Very low density lipoprotein*

Summary

Heavy metals, such as mercury (Hg), lead (Pb) and cadmium (Cd) are, widely known of being toxicants, also persistent organic pollutants, such as polychlorinated biphenyls (PCBs) and bisphenol-A (BPA), exposure have been attached to a variety of toxic effects in human. Therefore, the aim of the present work is to study the effect of persistent organic pollutants and toxic heavy metals and their contamination in any type of environmental pollution resulting from terrorist and military operations in three regions of Baghdad on thyroid gland and lipid profile in a sample of Iraqi individual from (AL-karradah and Abo-Gharib) groups compared with (AL-jadria) (control groups). The correlation between the thyroid hormones thyroxine T4 , triiodothyronine T3, thyroid stimulating hormone (TSH), and thyroglobulin-antibodies(Tg-Ab) and the levels of Pb, Cd, Hg , (PCBs) and (BPA) have been studied in the sera of the three studied groups. Seventy Five volunteers from three Iraqi areas were included in this study. Their ages ranged between (15-65) years, and patients with any endocrine disease and thyroid disease were excluded. Our analysis suggests an inverse association between Hg exposure and thyroid hormones (TH) and an inverse association between Pb exposure and thyroid hormones, and (Tg-Ab) ,and a positive association between Hg exposure and thyroglobulin- Ab , and a positive correlation between cadmium exposure and thyroid hormones and Tg-Ab. T4 and T3 were negatively correlated with (Tg-Ab) so, there were significant positive correlation between the heavy metals themselves. Therefore, increased heavy metal and POPs exposure may be a factor in the etiology of hypothyroidism diseases and disruption thyroid gland function. The results of this study revealed that there is a direct effects of blood serum Hg, blood Serum Pb, blood serum Cd, blood serum

PCBs and blood serum BPA on thyroid hormones, and also revealed the effect of military and terrorist operations on the thyroid gland, (Tg-Ab) and lipid profile. In the end we concluded that the heavy metals such as mercury, cadmium and lead as well as persistent organic pollutants such as (PCBs) and (BPA) resulting from the explosions and terrorist operations in the area of (Al-karadah , Abo-Gharib) are higher compared with the control (Al-jadria) . This leads to many health problems to the human body especially on the thyroid gland which in turn causes a negative effect on thyroid hormones and then thyroid disease.

Chapter One

Introduction and Literature Review

1.1 Pollution

The study of pollution is very important to keep human in health, pollution as any substance affecting the environment by human activities that could have hazardous effects on human body health, hormonal changes, ecosystems and damage living resources. [1]

Studies of the effects of metal and persistent organic pollutants (POPs) Contamination in any type of environmental pollution might alter thyroid hormones levels via several mechanisms, including disruption of thyroid peroxidase, thyroid hormone -binding proteins, hepatic catabolism, receptor binding deiodinases , and the impacts of heavy metal contamination on thyroid function. [2]

Bioaccumulation means an increase in the degree of a chemical content in a living organism over time, a high level exposure to these pollutants at the long term and short term can lead to some adverse health effects compared with chemical’s level in the environment. Heavy metals can be the reason of serious health effects with different signs depending on the nature and the amount of the metal consumed. [3]

Iraq is also facing very serious environmental problems, including poor water quality, air pollution, waste management, contaminated sites and the deterioration of key ecosystems, with environmental problems neglected to a large extent prior to the war as well, the decades of war, conflicts and economic sanctions have further worsened the environmental conditions, the problems are aggravated by the country’s weak environmental governance structure. [4]

Al-Hilla river has been studied by many authors especially in the sense of water quality such as heavy metals. [5]

Air pollution studies and researches in Iraq are very limited particularly those on the air pollution from oil industries activities, some study had been carried out by Iraqi scientists and researchers on environmental air pollution in Iraqi governorates especially in some industrial areas. (6)

Recently, the general quality of ambient air in Basra city (southern Iraq) has been decreasing because of an increase in the city's population and high traffic levels, as well as the expansion and establishment of several industrial plants, including petrochemical plants, oil fields, burned natural gas flames, fertilizer plants, paper and pulp mills, power generation stations, and industrial workshops, these have put the local population in direct daily contact with the different gaseous pollutants that are caused by daily urban activities, mostly by increasing the use of fossil fuel combustion from electrical generators and motors vehicle, as well as exposing the population to industrial activities.

Previous studies have indicated high concentrations of CO, NO2 and SO2 within the industrial area in Basra city, and given that concentrations from these emissions are constantly increasing, these high levels have become hazardous to human health, the lack of management and control of the gaseous discharges and residues in urban and industrial areas has increased the possibility that the air quality has become worse. (7)

Drinking water in Iraq comes from rivers, lakes, wells and springs, these sources are exposed to a variety of pollutants caused by the diffusion from nonpoint and point sources which are difficult to control, monitor, and evaluate, such as sewage, agricultural and industrial wastes, the water pollution of rivers requires great efforts, and water quality is an important issue in the field of water resources planning and management and requires data gathering, analysis, and interpretation, al-Gharraf river is the primary source of water in the south of Iraq, it branches from the Tigris close to Al-Kut city and runs through the wasit and dhi-qar regions, the through the wasit and dhi-qar regions, the water from it is utilized for essential uses such as; drinking, raising live stock, irrigation and fishing . [(8)]

Heavy metal pollution is a real environmental problem in the world. They are a unique class of toxicants since they cannot be broken down to non-toxic forms easily, soil pollution by heavy metals has reasonably increased in last few decades due to discharge of waste water, and waste from anthropogenic sources , metals like Pb, Hg and Cd have no biological function and are toxic to life even at very low concentration. [(9)]

1.2. Terrorism

A central factor distinguishing terrorism from other major types of violence or intimidation is that it is usually focused by the perpetrators on specific high value targets , by its very nature, the damages from terrorism go beyond the immediate loss of life human health ,air pollution and property , accordingly an analysis of the effects of terrorism on environmental disease , even if people are exposed to direct dangers , direct exposure to radiation, they may face or ignorance increase the risk of certain cancers, such as leukemia and thyroid cancer. It has been destroyed the lives of a number of people much greater than justified time. [(10)]

Fallujah and Basrah, two heavily bombarded cities, are both contaminated with extremely toxic heavy metals such as lead and mercury. The resulting contamination is suspected of causing a high number of serious diseases throughout Iraq, including rises in congenital birth defects, miscarriages, premature births, infertility, sterility, leukemia, cancer and other illnesses. [11]

1.3 Pollute metals

1.3.1 Pollution of lead (Pb)

Lead, at definite levels, is a poisonous substance to all living subjects. Different communities are exposed to lead from air and food in roughly equal proportions. Lead can reach humans via the food chain because airborne lead can be deposited on soil and water. Lead is considered as a neurotoxin that damages the nervous system causing brain disorders; it also has cumulative effects through deposition in both soft tissues and bones. [12]

In Iraq, most studies on lead exposure have been conducted in exposure risk groups. However, considering that there are still many gasoline power generators and vehicles using leaded petrol in the country, it is possible that high lead levels exist in the general population living in areas of heavy traffic and high emission of lead into the atmosphere. [13]

Several researchers had been carried out studies on environmental soil pollution, but there are very limited studies particularly of the soil pollution from oil industrial activities in Iraq. The climatic parameters such as rainfall, speed and direction of wind have an important effect on the concentration of pollutants in the soil in which lead is a key role in controlling the spread of various soil pollutants. [14]

Researchers had studied the biological effects of Pb poisoning in Baghdad, it that the children are at greater risk than adults due to lower body weight and increasing incidence of cancer and blood poisoning, through the study of atmospheric pollution of Baghdad city it was found that the anthropogenic activities were main responsible sources of pollution. [15]

Heavy metals may be transferred to human bodies by way of ingestion, inhalation and dermal contact, or through the food chain, heavy metal contamination in urban soil within Baghdad city was analyzed in soil adjacent to ishaqi river, north of Baghdad city. [16]

Lead in the environment is poisonous to humans, and the lead antiknocks in gasoline are by far the largest source of lead aerosol among the most toxic air pollutants in many developing countries, including Iraq. [17]

Investigated the lead concentration in the atmosphere of al-Najaf city found that its concentration was greater than the allowable limits. [18]

Lead contamination also threatens the ecosystem of the planet reducing the availability of safe food and water. Thus, the continuous environmental lead pollution could be qualified as an act of terrorism. Currently, the world population is still exposed to a dangerous level of environmental lead. [19]

The effect of war on the environment in Iraq has been investigated by study of residents in Basrah city .It was found that lead levels were higher in parents of children with birth defects than those without defects, the tooth of a child with birth defects was also found to contain lead (pb) levels three times higher than those of children living in “unimpacted areas” . [11]

1.3.2 Pollution of cadmium (Cd)

Cadmium (Cd) is a standout amongst the most deleterious heavy metals both to plants and animals, industrialization and culture cause cadmium the most harmful and widespread pollutants in agricultural soils and soil plant environment system . [20]

Cadmium is of major concern, mainly due to their presence at relatively high concentrations in drinking water .Among the heavy metal, cadmium has extensively been studied for their public health effects. [21]

Cadmium in the road side soil in right Khasa of Kirkuk city was the highest; it ranges between 0.32 - 0.64 ppm with an average of 0.599 ppm , the lowest value Cd was recorded in the left Khasa in Kirkuk city, it ranges between 0.21 - 0.62 ppm with an average of 0.4 ppm, the high rate of Cd in right Khasa due to anthropogenic and industrial activities, the high concentricity of Cd in road soil in the right Khasa of studied area 0.599 ppm could reflect the effect of human activity. As a result of urban industrial and agricultural practice, human activity can contribute to increased Cd levels, atmospheric deposition and phosphate fertilizer use had resulted in the emission of significant amounts of Cd to the environment. [22]

Human activity has significantly increased Cd concentration in the aquatic ecosystem. The Cd concentration in the Mahrut river water varies from 8.0 to 12.0 µg/L in the summer season and from 13.9 to 23.5 µg/L in the winter season. However, the results indicated that the mean concentration of dissolved cadmium well above the recommended value for rivers maintaining system pollution and the acceptable guidelines values for protection of aquatic life. The reason of increasing Cd concentration in these study sites may be related to the sewage, industrial and the agricultural activities. [23]

Iraqi fuel also contains significant quantity of Cd the composition and quantity of chemical matrix of road dust are indicators of environmental pollution.

Some study has focused on the concentration distribution and source identification of heavy metals in roadside dust. Some researchers have studied soil, water and plants have detected high heavy metals concentration in different sampling media. They suggested that the high concentration of Pb, Cd and Hg may be attributed to the car exhausts. They found high concentrations of heavy metals in Basra soil which were mainly attributed to the drilling and oil production. Atmospheric pollution study of Baghdad city found that the anthropogenic activities are the main responsible sources of pollution. (24)

1.3.3 Pollution of mercury (Hg)

Mercury is a highly toxic element and there is no known safe level of exposure to which there is no adverse effects. Ideally, neither children nor adults should have mercury in their bodies because it does not provide any physiological function. However, almost all people in the world have at least trace amounts of the organic form of mercury in their bodies, reflecting its persistence in the environment. (25)

During the early months of 1972, cases of mercury poisoning were reported among farming communities in various parts of Iraq. This was caused by ingestion of grain treated with methylmercuric fungicide. There were 6,530 cases admitted to hospitals throughout the country and 450 hospital deaths attributed to mercury poisoning were reported. This was the most devastating outbreak of mercury poisoning to be recorded. This study concerns the psychiatric manifestations exhibited by the poisoned patients. [26]

Metals such as mercury enter the aquatic environment of southern Iraq from both natural and anthropogenic sources. Natural sources include dust storms, erosion or crustal weathering and decomposition of the biota in the water. Accumulation and distribution of heavy metals in shell of mollusks depend on many factors such as concentrations of metals, exposure time, temperature and salinity, food habits, physical conditions, growth, age, sex, and pollutants interactions. Mercury considered as a nonessential element, highly visual path spectrophotometer provide low detection toxic heavy metal and it has been a global contaminated due limits. [27]

1.3.4 Pollution of polychlorinated biphenyls (PCBs)

Soil pollution is increasingly becoming a large problem, which confronts humans since the industrial revolution. Before soil pollution can be stopped, the sources of pollution must be identified. The major sources of soil pollution are persistent organic pollutants (POPs) like polychlorinated biphenyls. Levels of Polychlorinated biphenyls were studied in soil samples collected from the vicinity of the Ahdab oil field in Kut area/Iraq that found much higher compared with those from the more industrialized city of Moscow/Russia , this is obviously because of its proximity to the Ahdab Iraqi oil field. [28]

1.3.5 Pollution of bisphenol-A (BPA)

Bisphenol -A is a pseudo-persistent chemical, which despite its short half-life is universal in the environment because of continuous release. So, it has been reported that BPA is an infamous environmental contaminant which pollutes atmosphere, hydrosphere and lithosphere in circular modus. Furthermore, it also creates menace to human health. Therefore, it had unwrapped a different area of exploration with a great prerequisite to have continuous monitoring and elimination of malicious effects of BPA and its exchange between in environment. This will help in formulation of strategies which will monitor the levels of BPA in environment and decrease the level of BPA pollution. (29)

1.4 Environmental sources of pollution metals

1.4.1 Source of Lead

Lead is a naturally occurring metal found in the earth's crust. Lead can be found everywhere, so lead is a toxic metal whose widespread use has caused extensive environmental contamination and health problems in many parts of the world. (30)

Pollutant arising from increasing industrialization, coal combustion, manufacturing of batteries, and water. (31)

Pb, like Hg, occurs naturally in the environment. However, most of the Pb that people are exposed to is the result of human activity, particularly leaded gasoline exhaust, mining, factories, and pesticides. This human activity leads to lead in the air, water, food, and soil. The environmental lead rose dramatically between 1950 and 2000 primarily as a result of vehicle exhaust from leaded gasoline, inhalation is often the greatest cause of Pb in the body, and burning leaded gasoline was at one point the primary source of Pb emissions. Nevertheless, the inhalation of Pb, specifically by people working in metal (iron and steel) production factories, lead-acid-battery manufacturing, paint, and nonferrous (brass and bronze) foundries, can cause harmful amounts of Pb to enter the body. Several other industrial workers are exposed to Pb regularly., past uses of Pb have caused increases Pb levels in air, water and soil, which have also increased the levels of Pb in plants and animals from contaminated areas. Often the causes of Pb exposure for humans is exposure to hazardous waste sites, contaminated food or water, old houses that contain lead-based paint and pesticides that involve close-contact with lead products. Drinking water supplies are also typically safe, but some can have acidic water, which makes it easy to increase Pb levels in the water from the lead piping. (32)

1.4.2 Source of Cadmium

Cadmium is non essential and harmful heavy metal pollutant which is usually released in soil. (33)

Environmental sources of cadmium toxicity include foods such as sea food, vegetables and cereals, residence in cadmium polluted areas and Indian medicinal herbs .Main source of Cd exposure include smoking, foods and water polluted with this metal herbs. (34)

Cd occurs naturally in the environment from the gradual process of erosion and abrasion of rocks and soils, in the environment, Cd is dangerous because humans consume both plants and animals that absorb Cd efficiently and concentrate it within their tissues, depending on the dose, route and duration of exposure, Cd can damage various organs including lung, liver, kidney, bones, testes and placenta, Cd is implicated in the pathogenesis of several diseases, including thyroid disease. (35)

1.4.3 Source of Mercury

Mercury (Hg) is a toxic element from natural and anthropogenic sources. [36]

Environmental sources of mercury include contaminated fresh water fish Industries like paints, pulp, paper, oil refining, rubber processing, fertilizer, batteries, dental fillings adhesive, fabric softeners, drugs, electroplating, steel industries, agriculture, and thermometers other sources of Hg exposure include dental enamel fillings, certain household products and industrial items (thermostats, fluorescent light bulbs, barometers, glass thermometers, and some blood pressure devices), waste sites, certain medicinal products that contain mercurous chloride (laxatives, worming medications, and teething powders), and various working environments (manufacturing, electrical, construction, medical).[37]

Because Hg occurs naturally in the environment, very low levels of Hg in air, water, and food are the primary sources of human exposure. Nevertheless, the amount of Hg that exists in the air, surface water, and soil are far below the levels considered unsafe to breath, drink, and be exposed to. One of the most common sources of exposure is diet, specifically certain fish, shellfish, or marine mammals that are from Hg-contaminated waters. Such foods contain methyl mercury, which accumulates in the food chain, causing some fish to contain higher levels than others. Particularly, fish from local waters are the most likely to have high levels of Hg. Also, some mushrooms that grow in Hg-contaminated soil have been found to be harmful if eaten in large quantities. [38]

The body removes Hg from itself in different ways and with different efficiency based on the type of exposure. Thus, workers exposed to Hg in working environments where Hg vapors are prevalent can hold onto that Hg in their bodies from long periods of time. [38]

1.4.4 Source of Polychlorinated Biphenyls

Polychlorinated biphenyls are persistent and toxic pollutants which have been widely dispersed into the environment. [39] Polychlorinated biphenyls are a category of industrial chemicals historically used as coolants or heat transfer agents in electrical transformers. They have also been used in microscope immersion oils, carbonless copy paper, capacitor, spills, dredge spoils, cutting oils, or as electrical insulators and as an inert ingredient in pesticides and PCBs may be found as intermediates and by products of other chemical .[40]

1.4.5 Source of Bisphenol-A

Bisphenol -A (BPA, 4,4'- isopropylidine diphenol) is an estrogenic endocrine disrupting chemical. It is a commercially used chemical, an additive in the production of polycarbonate plastics as a developing agent in manufacturing of thermal paper and epoxy resins. Bisphenol-A is also present in dental sealants, water bottles and baby bottles, paper coatings, adhesives, flame retardants, food, building materials, electronic components and beverage packaging. [41] Chemicals implicated in endocrine disruption include biocides, industrial compounds, surfactants, and plasticizers including bisphenol-A . [42]

1.5 Graphite furnace Atomic absorption spectrophotometer (GFAA) [43]

GFAA has been the most common instrument used for Pb, Hg and Cd analysis, and in countries where this element is a criterion for pollution standards. GFAAS is generally the technique used in the reference methods to quantify Pb , Hg and Cd in total suspended particles, using a nitric acid digestion–based GFAAS method. A GFAAS method was used in conjunction with voltammetry for Pb, Hg and Cd analysis to evaluate a rapid digestion technique using a microwave oven, comparing this with traditional methods after establishing the optimal efficiency of digestion in terms of power setting, time and the use of different acids for low level determination of volatile elements such as As, Ge, Hg, Sb, and Se, hydride generation coupled with AAS provides lower detection limits (milligram–microgram range).

The three-step sample preparation for graphite furnaces is as follows

1_ Dry - evaporation of solvents (10–100 s) .

2_ Ash - removal of volatile hydroxides, sulfates, carbonates (10–100s) .

3_ Fire/Atomize - atomization of remaining analyte (1 s) .

Atomic Absorption components

1-Radiation source

2-Atomizer

3-Monochromator

4-Detectometer

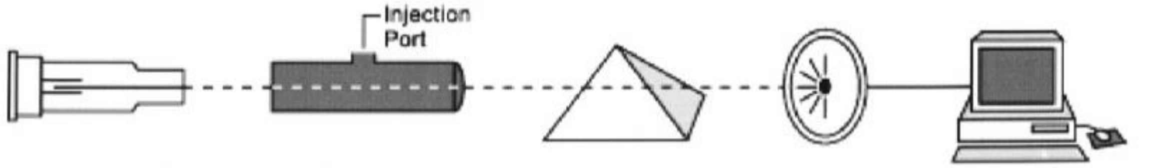

Figure (1.1) Diagram of the basic components of a GFAAS

1.6 high performance liquid chromatography (HPLC)

HPLC, also called high pressure or high speed liquid chromatography, is essentially an instrumental version of the common open-column chromatographic techniques used for sample cleanup. The instrumentation consists of a pumping system, injector, separation column, and a detector. All components are linked by tubing, so the separation and detection are done in one continuous operation. The separation may be based on liquid-solid partitioning (e.g., hexane on silica gel), liquid-liquid partitioning (e.g. bonded alkane columns such as C_{18}),size exclusion (gel permeation),or chemical functionality interactions (e.g., amine columns). Liquid-solid and liquid-liquid chromatography are collectively know as adsorption chromatography, since the interaction with the stationary phase occurs at the surface. Separation of analytes by adsorption chromatography may be effected using either of two modes of operation controlled by the nature of the mobile phase: normal or reverse phase. In normal-phase adsorption chromatography, the mobile phase or solvent (e.g.,hexane, methylene chloride, benzene) is less polar than the stationary phase (e,g.,silica or alumina) reverse phase chromatography utilizes a more polar solvent (e.g.,water, acetonitrile, methanol) relative to the stationary phase (e.g.,chemically bonded C_8 or C_{18} silica gel).

Common detectors include UV (not very selective), fluorescence (somewhat selective), and electrochemical (selective, depending on compounds are classes).Several other detectors are employed less commonly including MS. The intensity (height or area) of the peak is used for quantitation by comparison to the response obtained from a standard. [44]

HPLC is just one type of liquid chromatography (LC), defying the mobile phase is a liquid. The reversed phase HPLC is the most common type of HPLC, where the mobile phase is relatively polar and the stationary phase is relatively non-polar, thus non-polar compounds are more retained (i.e., have longer retention times t_R) than a polar compound. Other more general types of HPLC include partition, size exclusion, ion-exchange, adsorption and thin layer chromatography. Common specific applications of HPLC include quantitative and/or qualitative analyses. [45]

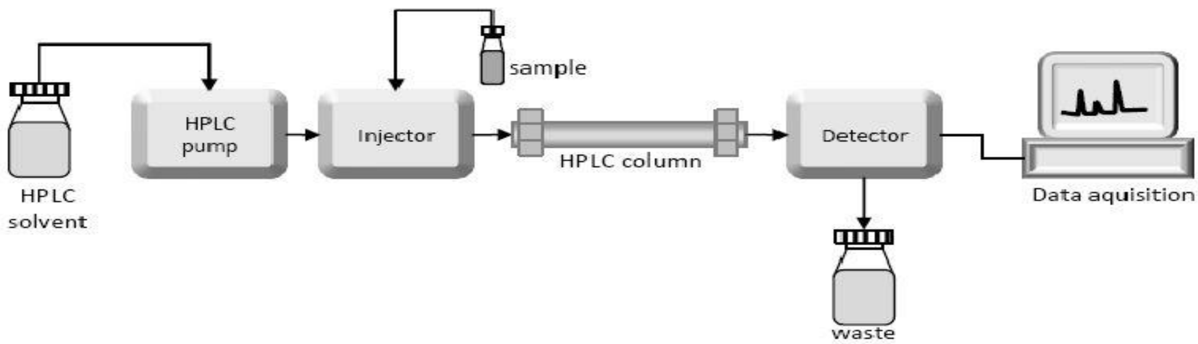

Figure (1-2) Instrumentation of HPLC

1.7 Thyroid Gland

The thyroid gland in human consists of 2 lobes that are lateral and inferior to the anterior side of the larynx and are connected across the larynx by an isthmus to produce a U – shaped structure averaging 30 gm in weight in adults. (46)

Thyroid gland mobilizes dietary iodine, converting it to an organic compound that can accelerate metabolic processes. It is necessary to the development and function of all body cells, the iodine containing levorotatory amino acids, thyroxine T4 and triiodothyronine T3, occur in the gland and are physiologically active upon oral administration. These metabolites also occur in the gland bound with globulin (thyroglobulins), and the exogenously administered amino acids could conceivably bind with serum protein to form physiologically active molecules that are responsible for the ultimate hormonal action .the thyroid gland can store thyroglobulins and other iodometabolites. The release of these thyroid hormones appears to be controlled by thyrotropin, a hormone of the anterior pituitary . (47)

Thyroid gland is one of the largest endocrine glands in the body of human. Thyroid gland is found in the neck of human inferior to the thyroid cartilage (also known as the Adam's apple in men) and at approximately equal the same level as the cricoid cartilage . (48)

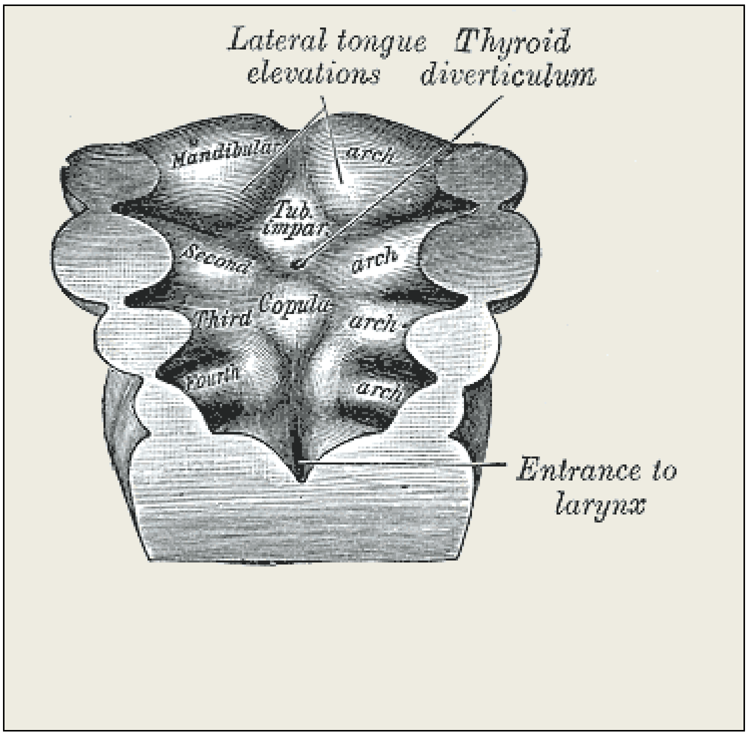

Figure (1.3) Anatomy of thyroid gland. [49]

1.7.1 Thyroid Physiology

The essential function of the thyroid gland is production of the hormones thyroxin (T4), triiodothyronine (T3), and calcitonin. Up to 80% of the T4 is converted to T3 by peripheral organs such as the liver, spleen and kidney . T3 is about ten times more active than T4. Thyroxin (T4) is synthesised by the follicular cells from free tyrosine and on the tyrosine residues of the protein called thyroglobulin (TG). Iodine is captured with the "iodine trap" by hydrogen peroxide H2O2 created by the enzyme thyroid peroxidase (TPO) and linked to the 3' and 5' sites of the benzene ring of the tyrosine residues on TG, and on free tyrosine. Upon stimulation by the thyroid-stimulating hormone , the follicular cells reabsorb TG and proteolytically cleave the iodinated tyrosine from TG, forming T4 and T3 (in triiodothyronine T3, one iodine is absent compared to Thyroxin T4), and releasing them into the blood.

Deiodinase enzymes convert Thyroxin T4 to T3. Thyroid hormone (TH) that is secreted from the gland is about90% T4 and about 10% T3. [50]

1.7.2 Thyroid Hormones

Thyroid hormones assist the function of all tissues and affect essentially every major pathway, including growth, carbohydrate metabolism, lipid homeostasis, development as well as regulation of metabolism and thermogenesis. [51] Thyroid gland produces three important metabolic hormones, thyroxine, tri-iodothyronine, and calcitonin, thyroid stimulating hormone (TSH) produced by the anterior pituitary gland controls the production of these hormones, thyroxine (T4) the major form of thyroid hormone, and triiodothyronine (T3) the active take shape, are controlled by thyroid-stimulating hormone (TSH) and released by the thyroid gland, as shown in figure (1.6), tied to plasma proteins, these thyroid hormones are transported throughout the body and diffuse from maternal blood across the placenta to reach the fetus. [52]

Most research's on endocrine disruptors and thyroid metabolism have only focused on measuring TSH, T4, and the presence of the most common thyroid antibodies: thyroperoxidase antibodies (TPOAb) and thyroglobulin antibodies (Tg-Ab). In other studies, PCB, and heavy metal exposures have also been associated with increased levels of both TPOAb and Tg-Ab in residents living near waste sites. [53]

Thyroglobulin antibodies: these are antibodies that attack the thyroid instead of bacteria and viruses; they are a marker for autoimmune thyroid disease, which is the major underlying cause for hyperthyroidism and hypothyroidism in the United States, these antibodies usually disappear once all thyroid tissue is removed successfully. [54]

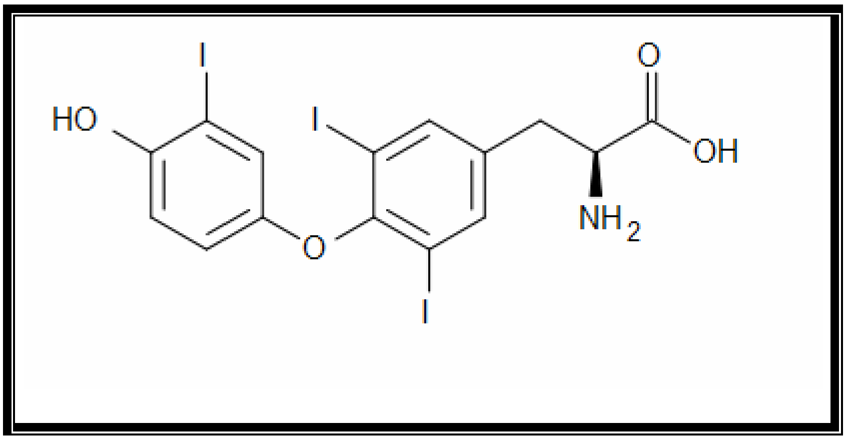

Figure (1.4) Triiodothyronine (T3) structure (55)

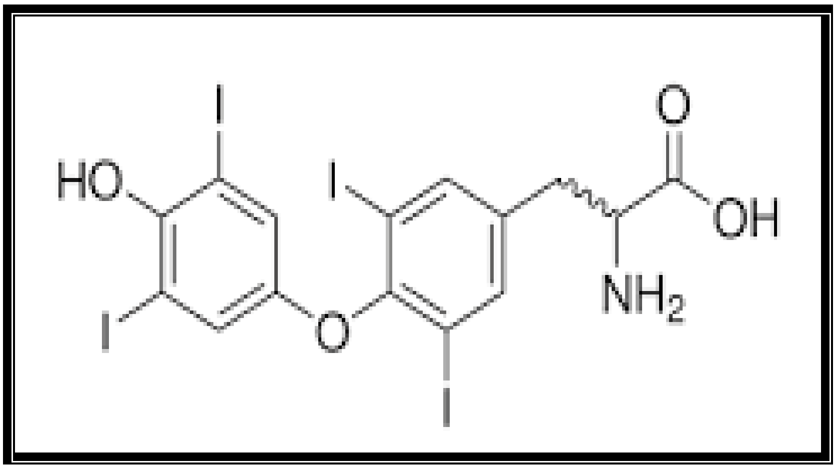

Figure (1.5) Thyroxin (T4) structure (55)

1.7.3 Thyroid Disease

Thyroid disorders are obviously more frequent in reproductive age with preponderance in females, both hyperthyroidism and hypothyroidism may be associated with menstrual disorders, increased hazard of abortion and ulterior effects in children born by these women mainly in neurodevelopment, apparently, thyroid disorders are implicated with reproductive health and given their prevalence in women of childbearing age, they are deemed of utmost importance. Studies on the effect of thyroid hormones, namely (T3) and (T4) as well as thyrotropin or thyroid stimulating hormone (TSH) on in both mammalians and human, have yielded conflicting results. In particular, a favorable. (56)

Thyroid disease is widespread and may present to a wide range of health professionals in clinical practice. With the advent of TSH radioimmunoassay, the entity of mildly elevated TSH and normal serum thyroid hormones levels were increasingly recognized, sensitive TSH identified the entity of subclinical hyperthyroidism in which serum TSH is suppressed and serum T4 and T3 levels are normal. (57)

1.7.4 Thyroid Problems

There are two primary types of thyroid disease: hypothyroidism and hyperthyroidism, which both have different symptoms and causes. Hypothyroidism can have many causes, including autoimmune disease, surgical removal of thyroid gland, damage to the thyroid gland, too little iodine or too much, and radiation treatment left untreated, the symptoms of hypothyroidism will commonly progress, and can reason more serious complications. (58)

Hyperthyroidism or an overactive thyroid gland occurs when the thyroid gland releases too much thyroid hormone in the bloodstream, speeding up the body's metabolism. Hyperthyroidism tends to run in families, occurring most usually in young women. The majority of cases of hyperthyroidism are caused by a condition called Graves' disease. In this condition, antibodies in the blood activate the thyroid gland, causing it secrete too much thyroid hormone and to grow in size. Another type of hyperthyroidism is characterized by nodules or lumps in the thyroid gland that increases the levels of thyroid hormone in the blood. It is important that the symptoms of hyperthyroidism are not left untreated as serious complications can occur. (59)

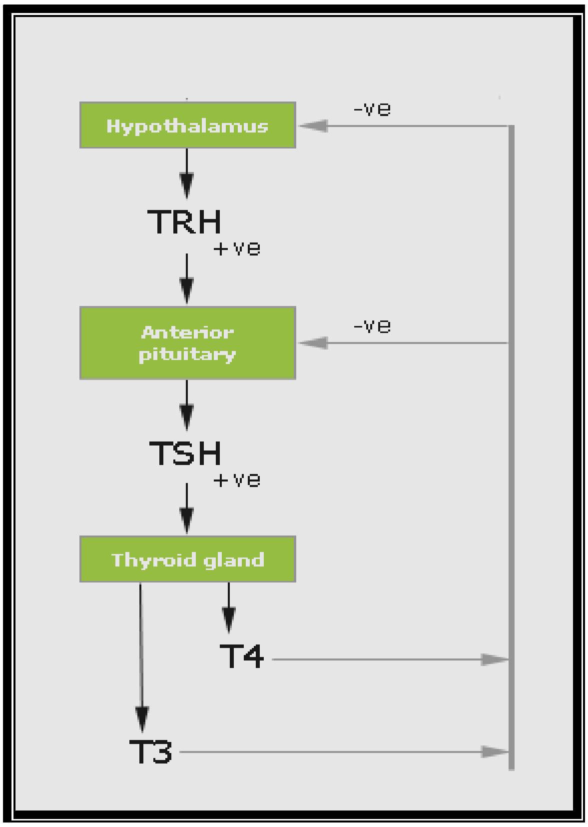

Figure (1.6) Thyroid hormones feedback. (139)

1.8 Pollution and Thyroid Disease

Thyroid diseases are endocrine disorders of the body, in addition to genetic factors; increasing evidence indicates that environmental pollutants factors, such as endocrine disrupting chemical pollutants affect thyroid hormone levels, autoimmune thyroid disease, causing changes of thyroid morphology, and thyroid tumor, etc. (60)

A significant focus in clinical thyroid disease is to detect and evaluate thyroid function. At the earliest stages of abnormal thyroid function detected in association with an environmental exposure is usually thought to be a direct effect of the agent dysfunction. However, could be due to the agent triggering autoimmune thyroid disease. [61]

Primary hypothyroidism was present if thyroid stimulating hormones TSH was elevated concomitant with normal or low T4. Hyperthyroidism was defined as low or normal TSH and elevated T4, central hypothyroidism was considered When TSH was normal and T4 was low. [62]

1.8.1 Lead and Thyroid Disease

Lead is another heavy metal that we are exposed to on a daily basis through our food, air, Coal combustion, manufacturing of batteries, and water. Which adversely affects thyroid gland function and structure; it is linked to thyroid disorders in many studies. One of note shows how sensitive a woman's hormonal system compared to men. Women's hormones appear to be more interconnected than men's hormones. For example many women increase thyroid disease during pregnancy due to increases in estrogen and progesterone. One study compared men and women's blood levels of lead and mercury to alterations in thyroid hormones and found women were more affected by the heavy metals. [63]

Lead adversely affects the secretion, production, and biological activities of thyroid and stress hormones and of hormone-related metabolism. Pb poisoning partially affected the thyroid hormones, which may be related to the duration and level of Pb ingestion. [64] TSH level increased among workers exposed to lead. [65]

Lead can have adverse effects on many organ systems, and various effects of lead on thyroid function have been reported in the past 50 years. [66]

Human serum Pb levels have also revealed relationships with thyroid hormones. Changes in levels of thyroid hormones, particularly T4 and TSH, have been shown to occur in exposed workers with human serum Pb levels greater than 40-60 ug/dL. [32]

However, several factors from previous studies such as subject age subject exposure, subject tobacco use, and small sample sizes in those studies often caused inconsistent and inaccurate findings. In previous study, T4 levels were suggested to decrease in workers with very high Pb. [67] Another study suggests that T4 along with T3 were decreased when workers were exposed to occupational lead poisoning. [68]

1.8.2 Cadmium and Thyroid Disease

Autoimmune thyroid diseases commonly affect more frequently females than males, like in many other autoimmune diseases. The metal concentration in tissues has been rarely measured in the thyroid. Cadmium is considered a category I carcinogen (on lungs, testicles, and prostate). Cadmium accumulates in pancreas, liver, kidneys, and also in the thyroid. In chronic Cd toxicity, multinodular goiter and thyroglobulin hypo secretion, we are exposed through cigarette smoke, food grown in contaminated soil, water pollution and air contamination. There are some studies linking thyroid disease to cadmium exposure. It has been concluded that cadmium has the affinity to concentrate in the thyroid gland in addition to the liver, kidneys, and pancreas. Human serum cadmium levels have a positive correlation with thyroid gland accumulation. Also, the thyroid-disrupting effect of cadmium has been reported as structurally degrading the rough endoplasmic reticulum of this tissue. [69]

Cadmium is a toxic metal with negative effects on health. Occupational exposure is mainly from industrial processes. Contaminated food and food Smoking tobacco contaminated food such as vegetables and rice are the main sources of general cadmium exposure, human serum cadmium levels vary by region, age and ethnicity. Recent research has focused on the role of cadmium as an important environmental endocrine disruptor. Epidemiological studies have linked cadmium exposure to metabolic diseases such as thyroid disease. (70)

1.8.3 Mercury and Thyroid Disease

Mercury is also linked to thyroid disease in adult and children. Mercury is one of the most toxic metals in the environment and represents a significant threat to human and environmental health, excessive exposure can cause neurological problems, with symptoms including tremors, memory loss, neuromuscular effects, headaches, cognitive, dizziness, and motor dysfunction, mercury exists in three basic forms elemental, inorganic and organic. (71)

There are numerous factors which can trigger an autoimmune response and it show as if exposure to some of the heavy metals can cause this to happen as fully. Studies have shown evidence of a link between mercury exposure and increased levels of thyroid antibodies. (72) There are also studies that indicate a relationship between Hg exposure and thyroid-related autoimmune responses. A study, in which a 13-year-old boy was exposed to Hg vapor, resulted in the child's triiodothyronine (T3) and thyroxine (T4) levels increasing drastically, while having a decrease in thyroid stimulating hormone (TSH). (73) Another study showed slight, but significant, increase in triiodothyronine and thyroxine in industrial workers exposed to mercury vapor during their work over a 10 year period. (74) One explanation is the possibility of Hg increasing T4 and promoting the conversion of T4 into active T3. However, two other occupational studies suggested no relationship between Hg exposure and endocrine function. (75)

1.8.4 Polychlorinated Biphenyls and Thyroid Disease

Large amount of PCBs can affect thyroid gland and may also affect the reproductive development of children of exposed mothers, studies showed that an exposure of PCBs to pregnant women affects the birth weight of the newborn children, according to previous research; PCBs decreases the level of T4 concentration in human serum but not T3 and TSH concentration. [76]

Long-term human studies on the effects of environmental chemicals on thyroid-related outcomes such as growth and development are still lacking. An increased incidence of autoimmune thyroid disease has been associated with exposure to a number of environmental pollution. Polychlorinated biphenyls have thyroid disrupting effects, as well as it is suggested that, bisphenol-A, brominated flame retardants, and perfluorinated chemicals pollutants show thyroid disrupting characteristics. PCBs disrupt thyroid hormone homeostasis, or other persistent organochlorine compounds, as shown by animal studies, while dietary exposure to PCBs affects serum thyroid hormones and TSH in human subjects. Among the considered studies by a systematic analysis of associations between PCBs exposure and thyroid hormones or TSH in newborns and pregnant women, only one study showed a significant association between PCBs and T3 levels, but no association was evidenced assessing thyroid function by serum TSH and T4. [77]

Exposure to polychlorinated biphenyl has been associated with disarrangement of thyroid hormones in various human epidemiological studies. [78] The potential effects of persistent organic pollutants (POPs) such as polychlorinated biphenyl on thyroid homeostasis can mimic or prevent the response of natural hormones even at low doses, therefore accumulating some POPs might be more potent endocrine disruptors and affect to the thyroid function at low concentrations. [79]

PCBs each consist of a total of 209 congeners with varying degrees of chlorination and various degrees of bromination, respectively, and the effects of individual congeners , toxic activities and their metabolites on Thyroid hormones signaling and regulation are not well understood. While these compounds such as PCBs may derive some of their toxicity from their structural similarity to thyroid hormones thyroxine and triiodothyronine. (80)

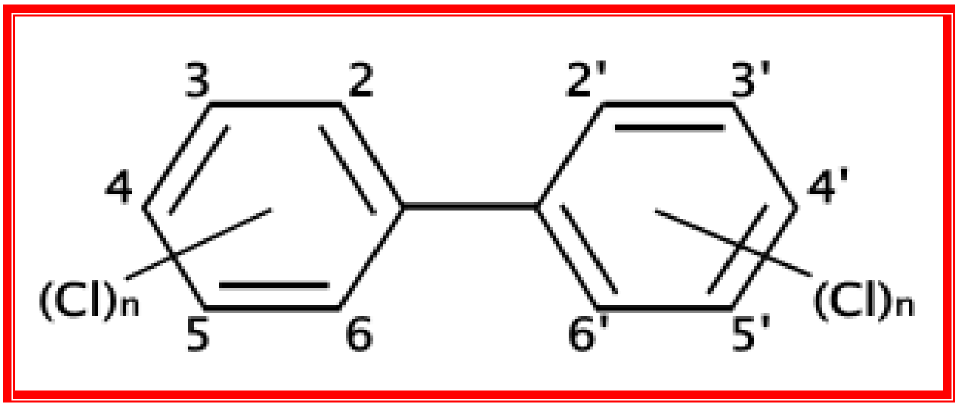

Figure (1.7) Polychlorinated Biphenyls (PCBs) structure (140)

1.8.5 Bisphenol-A (BPA) and Thyroid Disease

BPA interferes with the thyroid system by binding to the thyroid hormone receptor. It causes a number of adverse health effects such as hypothyroid effect because it decreases the level of thyroid hormone. (81)

Most realizations have focused on reproductive functions based on the estrogen-mimetic properties of this compound, leading to changes in thyroid hormones. However, guide has accumulated that BPA might have negative effects on other endocrine systems including thyroid function, suggests that BPA exposure might be associated with thyroid disruption characterized by a suggestive inverse relationship between human serum BPA concentrations and T4 concentrations.(82) BPA, which is used in polycarbonate plastic products is widespread, epoxy resins, manufacturing of thermal paper, and other products, has also been reported to exert effects on the thyroid receptor in experimental studies, human studies of BPA and thyroid hormones are lacking, suggests although a suggestive inverse relationship was observed between human serum BPA concentrations and thyroid-stimulating hormone (TSH). [83] We previously reported a negative association between human serum BPA and human serum thyroxine with positive human serum thyroid antibodies. [84]

A few studies have focused on whether BPA exerts its action through nuclear receptors such as thyroid receptors. [85]

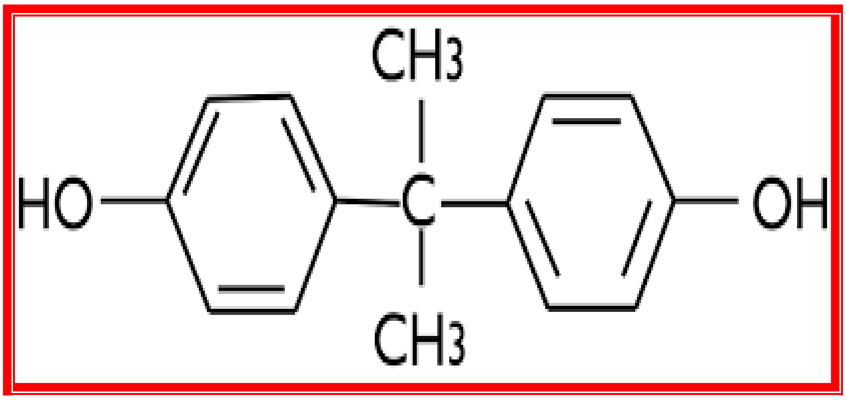

Figure (1.8) Bisphenol-A (BPA) structure [141]

1.9 Lipid Profile

Lipids are a group of fats and fat-like substances that are important constituents of cells and sources of energy. Different plasma lipids vary greatly in various populations due to differences in geographical; cultural a lipid profile measures the level of specific lipids in the blood serum. A typical lipid profile includes total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL), high density lipoprotein (HDL) and very low density lipoprotein (VLDL). [86]

Interest has focused chiefly on the very low density and low density lipoproteins (VLDL and LDL); there has been relatively little interest in the role of the high density lipoproteins (HDL), which ordinarily carry about 20% of the total human serum cholesterol. [87]

1.10 Pollution on Lipid Profile

Study of lipid profile in the general population is important the society. From study the serum total cholesterol levels in the urban compared with the rural population, it is clear that deficiencies of some trace elements cause marked alterations in lipid and lipoprotein metabolism. [88]

The increase in total cholesterol may have resulted from the damage to the hepatic cells by the toxic pollutants. The observed decrease in high density lipoprotein in the test group population may have resulted from the accumulation of cholesterol released into the human serum from the dying cells and from membranes undergoing turnover. [89]

1.10.1 Lead on Lipid Profile

Lipid profile can also be used to assess the effects of environmental contaminants on the health and well being of persons exposed to such pollutants. Extensive studies in human has established increment in serum lipids following lead exposure which associated with increased serum values of TC and HDL in occupationally exposed workers. They speculated that the increase in human serum triglycerides could be caused by lead-induced inhibition of lipoprotein lipase activity or decreased activity of hepatic lipase. The observed increase in the lipid profile of the subjects exposed to prolonged gas flares may be due to the various harmful constituents of flared gas. [90]

1.10.2 Cadmium on Lipid Profile

The lipid profile gets altered by cadmium exposure as lipoprotein and the lipid abnormalities play significant role in the pathogenesis and cardiovascular diseases and progression of atherosclerosis.

Administration of cadmium causes a dose dependent increase in the human serum triglyceride levels with increased concentrations of very low density Lipoprotein and low density lipoproteins cholesterol fractions along with increase in human serum total cholesterol levels and a marked reduction in the high density lipoprotein cholesterol level. These findings that lipid profile was affected by cadmium exposure. Studies have demonstrated that the toxicity of cadmium may partly be due to its disruption of lipid metabolism as there is modulation of cholesterol homeostasis as well as interference with lipid transport.it has been found that pretreatment with Moringa oleifera leaf extract presented a decrease in the total cholesterol level, LDL, triglyceride and VLDL cholesterol fractions with an increase in the HDL cholesterol levels thereby having beneficial effect on lipid profile in cadmium exposed rats. (91)

1.10.3 Mercury on Lipid Profile

Smoking not only affects blood lipids but also helps heavy metals be absorbed and bound to the tissues with minimal disposal, causing health problems with ages. (92)

1.10.4 Polychlorinated Biphenyls on Lipid Profile

There are a number of reports connecting lipid levels, and the metabolic syndrome with specific persistent pollutants, such as organochlorinated pesticides, and polychlorinated biphenyls, other less tangible environmental factors, such as air pollution may also have an adverse relationship with lipid levels. We conduct a more systematic approach to associating multiple environmental chemical factors with serum lipid levels, environmental chemical factors correlated with HDL, LDL and triglycerides respectively, including a spectrum of persistent organic pollutants. (93)

1.10.5 Bisphenol-A on Lipid Profile

Evaluation of the relationship of BPA levels with each of the outcomes TC, HDL, LDL, and TG has been previously studied. (94)

BPA can induce estrogenic activity where estrogens reduction of HDL cholesterol with BPA a significant effect on human serum cholesterol. The effect on cholesterol is probably due to an action of the hormone on the lipoproteins associated with cholesterol in the circulation. The effect of BPA may be the reason for the incidence thyroid diseases also. It was found that treatment of bisphenol-A increased serum total lipid in rabbits after 12 weeks of intravenous injection, triglycerides and total cholesterol were also increased. The increase in human serum cholesterol caused by bisphenol-A was apparent for the lipoproteins VLDL and LDL, but not for HDL. Bisphenol-A is associated with early sexual maturation, altered behavior, and density lipoprotein and high density lipoprotein. (95)

Aim of Study

This study aimed to determine of heavy metal Pb, Hg and Cd and persistent organic pollutants (POPs) in human serum of population, as a result of military and terrorist operation in two areas in Baghdad (Al-Karradah, Abo-Gharib) compared with Al-Jadriah areas as control group. Also, study the effect of military and terrorist operations on the thyroid gland by study the effect of lead, mercury, cadmium, polychlorinated biphenyls, and bisphenol-A on thyroid hormones T3,T4,TSH and Tg-Ab and then on lipid profile.

Chapter Two

Materials and Methods

2.1 Subjects

The present study comprised of 75 individual (40 Female and 35 Male), with no symptoms of thyroid disease or any endocrine disease as well as nonsmoker and pregnant women. The studied group was divided into three subgroups [namely control Al-jadriah group (n=25), Al-karradah group (n=25) and Abo-Gharib(n=25), individual aged between 15–65 years , blood samples were collected from each individual at three hospitals, 1) Abdul mageed private hospital 2) Abu Ghraib General Hospital 3) Jadria Health Center. The samples were hospitalized at laboratories in the Abdul mageed private hospital; the samples were collected from October 2016 to February 2017.

2.2 Materials & Instruments

2.2.1 Kits

Kits that used in this study and their supplied company are listed in table 2-1:

Table (2-1): Kits that used in the study along with supplied company

Kits	**Suppliers**
Thyroglobuline-Ab kit	(Human- from Germany)
Thyrotropin Kit	(Human –from Germany)
Thyroxine kit	(Human –from Germany)
Triiodothyronine kit	(Human –from Germany)

2.2.2 Instruments

Instruments that used in the study along with supplied company are listed in table 2-2:

Table (2-2) Apparatus and equipment used in this study

Instrument	Company
Centrifuge	Hettich (Germany)
Cobas c111	Roche (Germany)
Deep freeze	Froilabo (France)
Furnace atomic absorption spectrophotometer	Analytica Jena (Germany)
Gas chromatography	Shimadzu (Japan)
high-performance liquid chromatography	Sykam (Germany)
Microcenterifuge	Eppendrof (Germany)
Micropipette (Automatic)	Dragon (China)
Refrigerator	Samsung (Thailand)

2.3 Methods

2.3.1 Blood sampling

Blood sampling was performed at 8.30 - 12.30 a.m. A 5mL of venous blood were obtained, and allowed to clot for at least 10-15 min. at room temperature 25°C, centrifuged for (10) min. at (4000 rpm). Serum was divided into several parts by using sterilized eppendrof tubes, 1ml of serum used for measuring the biochemical parameters Pb, Hg, Cd, PCBs, and BPA and the other part was stored at -20 °C

2.3.2 Body Mass Index (BMI):

BMI has been proposed as an alternative to the traditionally used height-weight tables in assessing obesity. BMI measures weight corrected for height and is significantly correlated with total body fat content. BMI was calculated as weight (in kilograms) divided by height (in meters) squared.

BMI= Weight (kg) / Height (m^2)

BMI was classified into:

-Underweight when BMI < 18.5 kg/m^2.

-Normal when BMI between 18.5-24.9 kg/m^2

-Overweight when BMI between 25.01-29.9 kg/m2 .

-Obesity when BMI between 30.01-39.9 kg/m2 .

-Extreme obesity when BMI ≥ 40.0 kg/m2.

2.3.3 Measurement of lead, Mercury and Cadmium in the sera of three studied groups

Basic principle of GFAAS:

The selectivity in GFAAS is very important, since each element such as Pb, Hg and Cd has a different set of energy levels and gives rise to very narrow absorption lines. However, the selection of the monochromator is vital to obtain a linear calibration curve (Beers' Law), the bandwidth of the absorbing species must be broader than that of the light source; which is difficult to achieve with ordinary monochromators. The monochromator is a very important part of a GFAA spectrometer because it is used to separate the thousands of lines generated by all of the elements in a sample. without a good monochromator part of GFAA, detection limits are severely compromised . A monochromator of GFAA is used to select the specific wavelength of light that is absorbed by the sample and to exclude other wavelengths. The selection GFAA of the specific wavelength of light allows for the determination of the specific element of interest when it is in the presence of other elements. The light chosen of GFAA by the monochromator is directed onto a detect or typically a photomultiplier tube of GFAA, whose function is to convert the light signal into an electrical signal proportional to the light intensity. The challenge GFAA of requiring the bandwidth of the absorbing species to be broader than that of the light source is solved with radiation sources with very narrow lines. The study of trace metals Pb, Hg and Cd in wet and dry precipitation has increased in recent decades because trace metals have adverse environmental and human health effects. Some metals like Pb, Cd and Hg, accumulate in the biosphere of air and can be toxic to living systems Anthropogenic activities have substantially increased trace metal concentrations in the atmosphere . In addition to that, acid precipitation promotes the dissolution of many trace metals which enhances their bioavailability. In recent decades, trace metal concentrations have increased not only in the atmosphere but also in pluvial precipitation. Metals, such as Pb, Cd and Hg, are known to accumulate in the biosphere and to be dangerous for living organisms, even exposure at very low levels of metals. Many human activities play a major part in global and regional trace element budgets.In addition, when present above certain element concentration levels, heavy metals are potentially very toxic to marine and terrestrial life.so, biogeochemical perturbations of metals are a matter of crucial interest in science, the atmospheric input of heavy metals exhibits strong temporal and spatial variability due to short atmospheric residence times and meteorological factors. (96)

Lead, mercury and cadmium were determined using graphite furnace atomic absorption spectrometer. It is the analytical methods based on absorbing the ultraviolet and visible by atoms of material in the gas state. The sample is converting to atoms by pass the sample solution to furnace as the form of spray.

Digestion of samples:

All samples were digested using the following solutions

1-Triton X-100(10%):added 5ml from triton X-100 in 50 ml of distilled water

2- Nitric acid HNO_3 (conc.)

3-Ammonium dihydrogen phosphate (20%): 20gms. of ammonium dihydrogen phosphate were dissolved in 100ml of distilled water

Procedure:

1-A volume of 25ml of triton X-100(10%), 5ml of ammonium di hydrogen phosphate (20%) and drops of HNO3 conc. were mixed in 1000ml a volumetric flask then the volume completed to the sign with distilled water

2-Nine ml of digestion of samples were add to one ml of each serum sample then lead, mercury and cadmium were determined using graphite furnace atomic absorption. (43)

Steps of furnace atomic absorpation spectroscopy (97)

1-Evaporation: It happens drying (dehydration) to the samples of the three groups containing the metal because of the flame temperature and the solvent evaporates.

2-Dissociation: molecules convert to atoms.

3-Atomization: the reduction of the metal ions which was dissolved in a sample solvent to the metal atom.

4-Excitation: absorbs metal electrons energy from the flame temperature and thus moves to a higher energy level, which happens to its excitement.

2.3.4 Measurement of Bisphenol-A in the sera of three studied groups

Sample Preparation [98]

Bisphenol-A 0.01gm mixture was dissolved in 200 mL of acetonitrile. Human serum and 50 ppm bisphenol-A was measured by high performance liquid chromatography (HPLC) with UV detector, the analytical conditions of the HPLC system were as follows:

Table (2-3) Separation Conditions of HPLC

Column:	C_{18}_ODS
Flow Rate:	1ml/min
Injection details:	50 µL
Mobile phase A:	Methanol
Mobile phase B:	Water
UV detector wavelength:	280 nm

2.3.5 Measurement of Polychlorinated biphenyls in the sera of three studied groups [99]

Sera Seventy five of the three studied groups were performed using gas chromatography (GC) with electron capture detection (ECD) (Shimadzu /Japan). Chromatographic separations of GC were completed using column (OPTIMA® MS, 50 m × 0.20 mm ID, 0.2 µm film thickness). The instrumental operating conditions are shown in Table 2-4.

Table (2-4) Gas chromatograph operating conditions

Parameter	Conditions of GC
Carrier Gas	2.6 ml/min He
Column	OPTIMA® δ-3,60 m × 0.25 mm ID,0.25 µmfilm,REF 726420.60,max.temperature 340/360 °C
Detector	Electron Capture Detector
Detector temperature	3oo °C
Injection	1 µl PCBs ,splitless,36 pg/45 pg
Oven program (Temperature)	60 °C for 1 min, then 20 °C/min to 200 °C held for 1.5 °C/min to 290 °C(3 min)

Sample Preparation

Polychlorinated biphenyls 10 mg/L mixture was dissolved in 200 mL of hexane. Human serum of Polychlorinated biphenyls was measured by gas chromatography (GC) with electron capture detector, these solutions were stored at 4°C in the absence of light, and the analytical conditions of PCBs were as follows:

Table (2-5) The analytical conditions of PCBs

Parameter	Conditions of GC
Column Oven (SE-30)	110 °C-230 (3 °C /MIN)
Detector	Electron Capture Detector
Injection Volume	1 µl
Pressure	100 KPa
Temperature Detector	320 °C
Temperature injector	280 °C

Procedure:

The serum samples (1 ml) for the three groups were denatured with 1 mL of Methanol. The target compounds of it were extracted twice with 500 µL of n-hexane, after adding the surrogates, the extracts were combined and washed with very ultrapure water. The solvent of it evaporated residue was dissolved in 3 mL of n-hexane, passed through a glass column packed, and appears chart on the device. [100]

2.3.6 Determination of Triiodothyronine (T3) in the sera of the three studied groups

A-Principle:

The T3 ELISA technique is based on the principle of competitive binding between T3 in serum and T3-peroxidase conjugate for a limited number of binding sites on the anti-T3 coated well. Thus the amount of T3-peroxidase conjugate bound to the well is inversely proportional to the concentration of T3 in the specimen.

After incubation of serum and T3-peroxidase conjugate unbound enzyme conjugate is removed in the equilibrium state by washing. TMB/Substrate solution is added (step 2), and a blue colour develops. The intensity of this colour, which changes to yellow after stopping the reaction of T3 is inversely proportional to the amount of T3 in the specimen. The absorbance of calibrators and specimen is determined by using ELISA microplate readers like HUMAN´s HUMAREADER specimen's concentration is extrapolated from a dose response curve generated by utilizing serum calibrators of known antigen concentrations.

B-Solutions:

Calibrators: 0 (A), 0.50 (B), 1.00 (C), 2.50 (D), 5.00 (E)

And 7.50 (F) ng/ml

Enzyme – antigen conjugate (T3-HRP-conjugate)

Conjugate buffer (Phosphate buffer)

Wash Solution (Tris buffered saline)

Substrate Reagent A and B; mixing (3, 3', 5, 5'-tetramethylbenzidine (TMB), (Urea hydrogen peroxide) and (Sodium acetate buffer)

Stop solution (Sulphuric acid)

C-Procedure:

Note: This measurement is done for group (1) in duplicate

1-Triiodothyronine (T3) measurement in samples were conducted according to manufacture human / germany as the quantitative determination of human triiodothyronine concentration .50µL of standard (calibrators) and sample were added per well then 100µl of HRP-conjugated were added to each well (not to Blank well), mixed well and then incubated for 1 hour at(25)°C wells were wshed with washing buffer for (30 seconds) five times. Then.100µL of substrate A and substrate B were added to each well, mixed well and incubated for 15 minutes at(25)°C

Reaction was stopped by added 50µL of Stop Solution and mixed well. The concentrations were determined by measuring the absorption at 450 nm by using microplate reader.

2- The procedure was repeated twice for measuring T3 in group **(2)** and **(3)** respective.

D- Calculation:

Standard curve that was created by reducing the data using computer software and then by the program itself for calculation the concentration of samples.

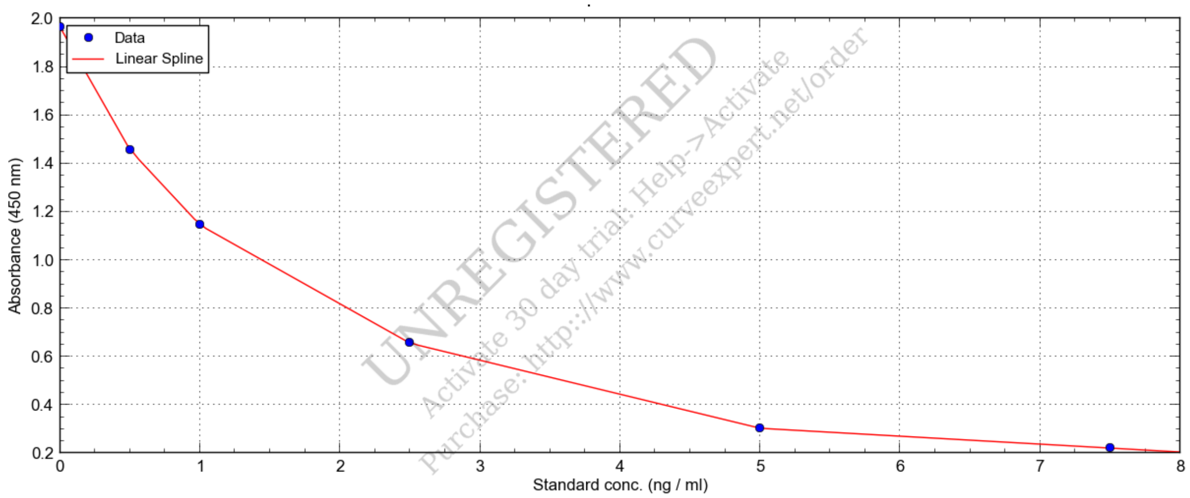

Figure (2-1) Standard curve for T3

2.3.7 Determination of Thyroxine (T4) in the sera of the three studied groups

A-principle:

The T4 ELISA technique is based on the principle of competitive binding between T4 in serum and T4-peroxidase conjugate for a limited number of binding sites on the anti-T4 coated well. Thus the amount of T4-peroxidase conjugate bound to the well is inversely proportional to the concentration of T4 in the specimen.

After incubation of serum and T4-peroxidase conjugate unbound enzyme conjugate is removed in the equilibrium state by washing. TMB/Substrate solution is added and a blue colour develops. The intensity of this colour, which changes to yellow after stopping the reaction of T4 is inversely proportional to the amount of T4 in the specimen. The absorbance of calibrators and specimen is determined by using ELISA microplate readers like HUMAN´s HUMAREADER .Serum concentration is interpolated from a dose response curve generated by utilizing serum calibrators of known antigen concentrations.

B- solution:

Calibrators: 0 (A), 2 (B), 5 (C), 10 (D), 15 (E), and 25 (F) µg/dl

Enzyme - antigen conjugate (T4-HRP-Conjugate)

Conjugate buffer (Phosphate buffer)

Wash Solution (Tris buffered saline)

Substrate Reagent A and B; mixing (3, 3', 5, 5'-tetramethylbenzidine (TMB), (Urea hydrogen peroxide) and (Sodium acetate buffer)

Stop solution (Sulphuric acid)

C-Procedures:

Note: This measurement is done for group (1) in duplicate

1-Thyroxine (T4) measurement in samples were conducted according to manufacture Human / Germany as the quantitative determination of endogenic human thyroxine concentration. 25µL of standard (calibrators) and sample were added per well then 100µl of HRP-conjugated were added to each well (not to Blank well), mixed well and then incubated for 1 hour at(25)°C . Wells were washed with washing buffer for (30 seconds) five times. Then 100µL of substrate A and substrate B were added to each well, mixed well and incubated for 15 minutes at (25)°C

Reaction was stopped by added 50µL of Stop Solution and mixed well. The concentrations were determined by absorption at 450 nm using microplate reader.

2- The procedure was repeated twice for measuring T4 in group **(2)** and **(3)** respective.

D- Calculation:

Standard curve that was created by reducing the data using computer software and then by the program itself for calculation the concentration of samples.

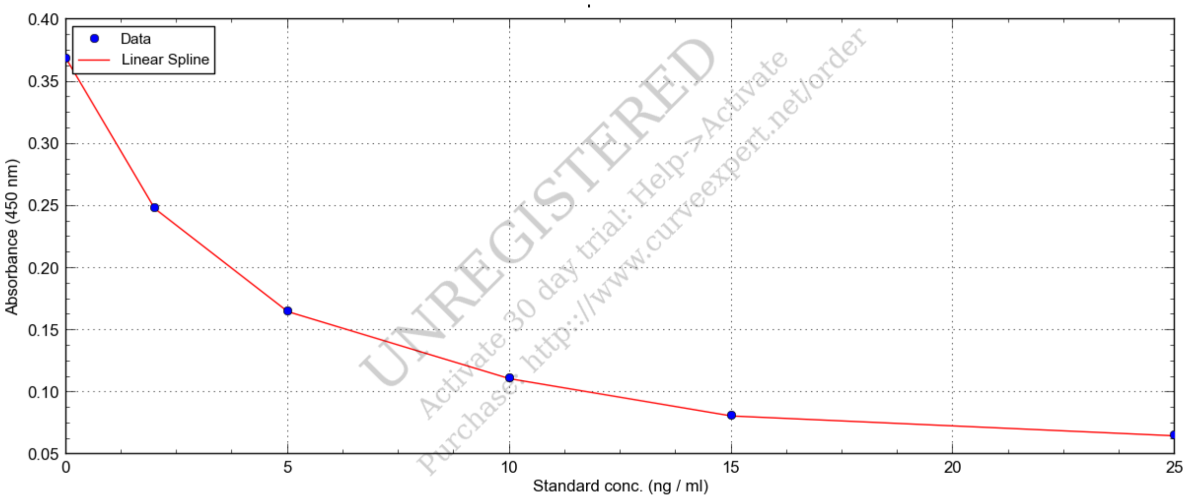

Figure (2-2) Standard curve for T4

2.3.8 Determination of Serum Thyrotropin (TSH)

A-principle:

In the first incubation step, sera, calibrators or controls and enzyme conjugate (peroxidase-labelled anti-TSH) are mixed to form the sandwich complex which is bound to the surface of the wells by the interaction with the immobilised antibody. At the end of the incubation excess enzyme conjugate is washed out. Substrate reagent is added and the

resulting colour, which turns into yellow after stopping the reaction with the stop solution, is measured photometrically. The intensity of colour is directly proportional to the TSH (Thyrotropin) concentration in the sample.
The absorbance of calibrators and specimen is determined by using ELISA microplate readers like HUMAN's HumaReader. The concentration is evaluated by calibration curve which is established from the calibrators supplied with the kit.

B- solution:

Calibrators: 0 (A), 0.5 (B), 3.0 (C), 6.0 (D), 15.0 (E), and 30.0
(F) mIU/l
Enzyme Conjugate
Wash Solution: mixing (Tris-Buffer) and (NaCl)
Substrate Reagent: mixing (3, 3', 5, 5'-tetramethylbenzidine (TMB) and (Hydrogen peroxide)
Stop solution (Sulphuric acid)

C-Procedures:

Note: This measurement is done for group (1) in duplicate

1-Thyrotropin (TSH) measurement in samples were conducted according to manufacture Human / Germany as the quantitative determination of endogenic human Thyrotropin (TSH) concentration. 50µL of standard (calibrators) and sample were added per well then 100µl of HRP-conjugated were added to each well (not to Blank well), mixed well and then incubated for 1 hour at(25)°C
Wells were wished with washing buffer for (30 seconds) five times. Then 100µL of substrate was added to each well, mixed well and incubated for 15 minutes at(25)°C

Reaction was stopped by added 100µL of stop solution and mixed well. The concentrations were determined by absorption at 450 nm using microplate reader.

2- The procedure was repeated twice for measuring TSH in group **(2)** and **(3)** respective.

D- Calculation:

Standard curve that was created by reducing the data using computer software and then by the program itself for calculation the concentration of samples.

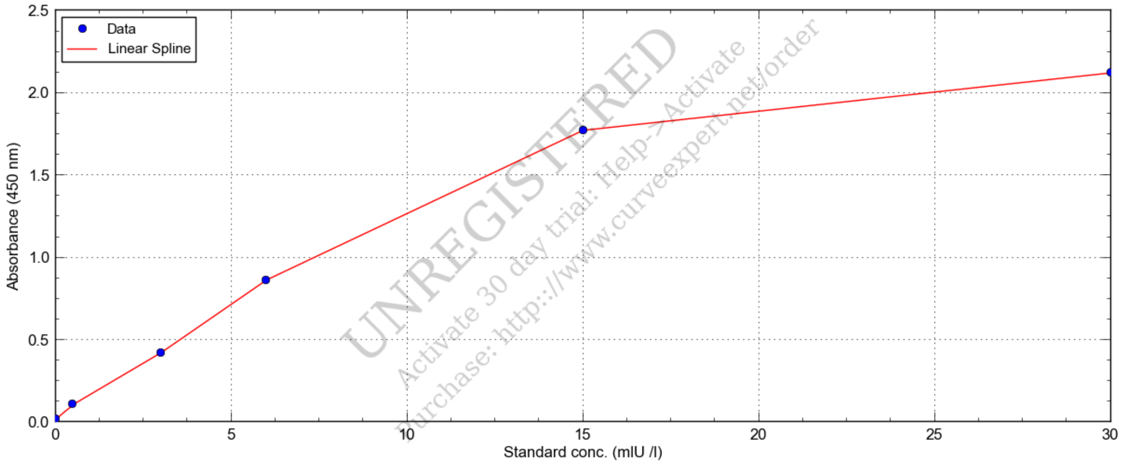

Figure (2-3) Standard curve for TSH

2.3.9 Determination of Thyroglobuline-Ab (Tg-Ab) in the sera of the studied groups

A-Principle:

Highly purified human thyroglobulin (TG) is bound to microwells. Tg-Ab Antibodies to this antigen, if existent in diluted sample serum, bind in the microwells. Washing of the microwells. Removes unbound sample serum antibodies.so, horseradish peroxidase (HRP) conjugated anti human IgG immunologically bind to the bound patient antibodies forming a conjugate antibody antigen complex. Washing of the microwells removes unbound conjugate. An enzyme substrate in the existent of bound conjugate hydrolyzes to form a blue color.so; the addition of an acid stops the reaction forming a yellow end product. The intensity of this yellow colour was measured photometrically at 450 nm wave length. The amount of colour was directly proportional to the concentration of IgG antibodies present in the original sample.

B- solution:

Calibrators: 0; 100; 300; 1000; 3000; 9000 IU/ml.

Thyroglobuline- Ab (Tg-Ab) Controls positive (1) and negative (2).

Sample buffer

Enzyme conjugate solution (polyclonal anti-human IgG)

Substrate solution of TMB (3, 3', 5, 5'-tetramethylbenzidine (TMB)

Stop solution (Sulphuric acid)

Wash solution

C-Procedures:

Note: This measurement is done for group (1) in duplicate

Thyroglobuline-Ab (Tg-Ab) measurement in samples was conducted according to manufacture human / germany as the quantitative determination of human Thyroglobuline-Ab (Tg-Ab) concentration. A sufficient number of microplate modules were prepared to accommodate controls and pre-diluted samples. And Pipet 100 µl of calibrators controls and pre diluted samples in duplicate into the wells, then incubated for 30 minutes at room temperature (25 °C) and discard the contents of the microwells and wells were washed 3 times with 300 µl of washing solution. Then dispense 100 µl of enzyme conjugate into each well, incubate for 15 minutes at room temperature .And the contents of the microwells were discard and wells were washed 3 times with 300 µl of washing solution. then 100 µl of TMB substrate solution was dispensed into each well and incubated for 15 minutes at room temperature (25°C), 100 µl of stop solution was added to each well of the modules and incubated for 5 minutes at room temperature, the optical density were determined by measuring aborpation at 450 nm and calculate the results.

2- The procedure was repeated twice for measuring Tg-Ab in group **(2)** and **(3)** respective.

D- Calculation:

For quantitative results plot the optical density of each calibrator versus the calibrator concentration to create a calibration curve of Tg-Ab.The concentration of samples may then be estimated from the calibration curve by interpolation. Using data of Tg-Ab reduction software a 4-parameter-Fit with lin-log coordinates for optical density and concentration is the data reduction method of choice.

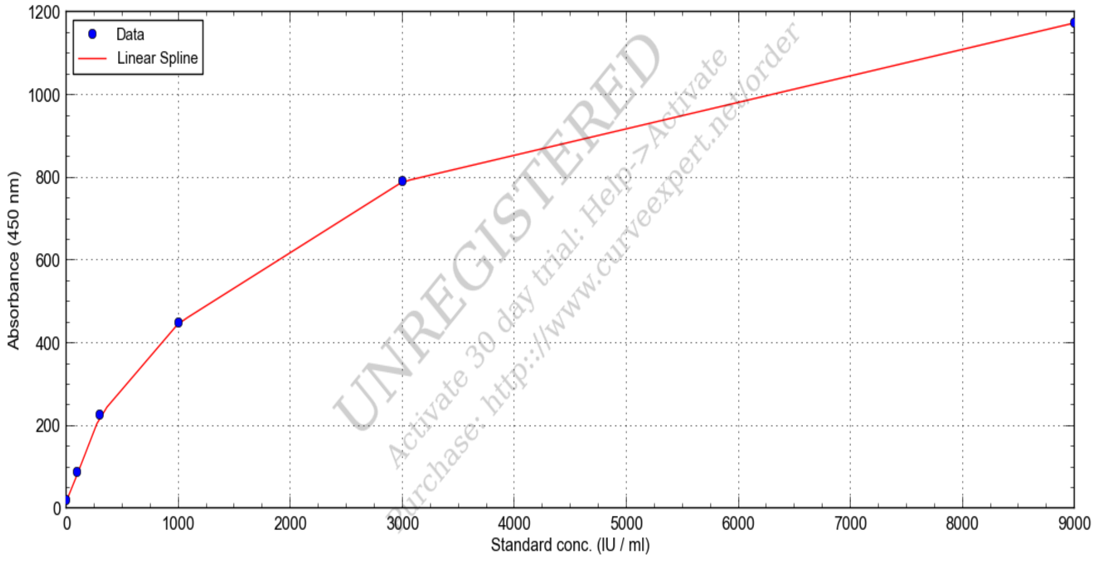

Figure (2-4) Standard curve for Tg-Ab

2.3.10 Measurement of lipid profile in the sera of the studied groups

Lipid profile including total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL), low density lipoprotein (LDL), and very low density lipoprotein (VLDL) were measured in serum of the three groups. Lipid levels were measured by using a roche diagnostics c111 cobas analyzer (Roche, Germany). [101]

2.4 Statistical Analysis

Statistical analysis of data was performed using SAS (Statistical Analysis System - version 9.1). One-way ANOVA and Least significant differences (LSD) post hoc test were performed to assess significant differences among means of three study groups. $P < 0.05$ was considered statistically significant. [102]

Chapter Three

Results and Discussion

3.1 Descriptive Data:

3.1.1 Distribution of Groups:

The present study included 75 volunteers with no symptoms of thyroid disease divided into three groups; first group is Al-karradah group (n=25 subjects), the second group is Abo-Gharib (n=25 subjects), and (n=25) apparently healthy individuals as control group Al-jadriah group, all shown in figure (3-1) with their percentage and body mass index shown in table (3-1) below

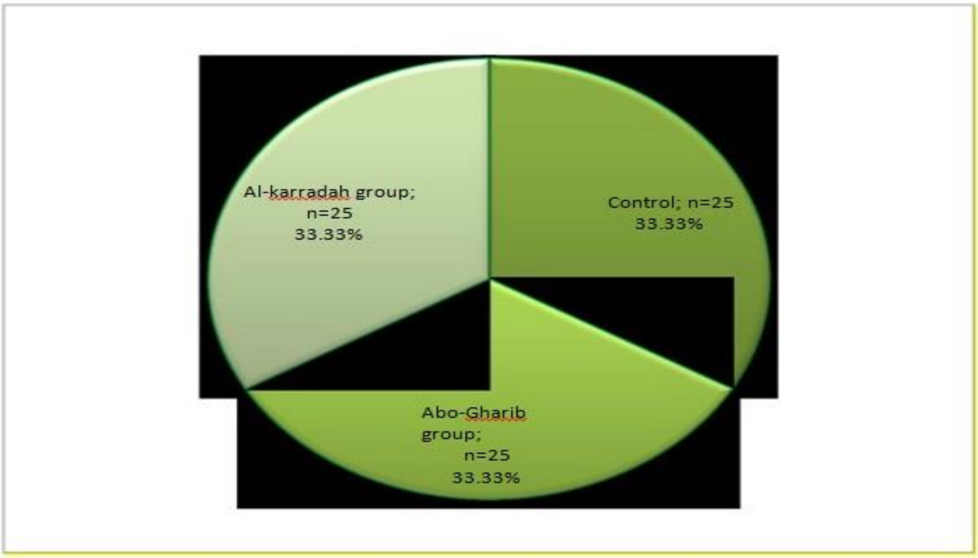

Figure (3-1): Distribution of studying group.

Table (3-1) Body mass index, age and gender from three different hospitals in Baghdad (Al-karradah , Abo-Gharib) compared with Al-Jadriah (control). In the studied groups

Groups	NO.	Age	Gender	BMI
Al-karradah group	25	25-65	5 Female 20 Male	22.51
Abo-Gharib group	25	18-65	17 Female 8 Male	25.49
Al-jadriah group (control)	25	20-60	18 Female 7 Male	19.7

3.2 Results of lead, Mercury and Cadmium level in the sera of the studied groups

Heavy metals (lead, mercury and cadmium) levels were determined in the sera of three studied group using graphite furnace atomic absorption spectrophotometer (GFAAS), and the result is illustrated in table (3-2)

Table (3-2) statistical analysis (mean ±standard error), maximum, minimum and standard deviation of heavy metals (Pb, Hg and Cd) for study groups in Baghdad

Region	Pb(**µg/L**)	Hg(**µg/L**)	Cd(**µg/L**)
Al-Karradah Min-Max STD	52.41±0.81a (50.30-55.80) 2.00	2.82±0.12b (2.27-3.12) 0.30	107.02±2.33a (99.32-114.11) 5.72
Abo-Gharib Min-Max STD	47.13±0.41b (45.90-48.70) 1.00	3.88±0.17a (3.25-4.50) 0.42	94.47±0.76b (91.93-96.54) 1.88
Al-Jadriah Min-Max STD	42.73±1.02c (39.80-45.50) 2.51	2.09±0.12c (1.55-2.43) 0.31	75.99±2.05c (68.68-82.56) 5.02
LSD	2.3929	0.4305	5.5718
P	<0.0001	<0.0001	<0.0001

a,b,c: The difference letters in the same column means a significant difference in parameters between groups.

3.3 Results of thyroxine T4, triiodothyronine T3, thyroglobuline-Ab (Tg-Ab) and thyroid stimulating hormone TSH in the sera of the studied groups

Thyroxine T4, triiodothyronine T3, thyroglobuline-Ab (Tg-Ab) and thyroid-stimulating hormone TSH were determined in the sera of the three studied group by an enzyme-linked immune-sorbent assay (ELISA) kit (Sandwich) technology for individual in three regions and the results are illustrated in table (3-3)

Table (3-3) statistical analysis (mean ±standard error), maximum, minimum and standard deviation of thyroid Parameters (thyroxine T4, triiodothyronine T3, thyroglobuline-antibody (Tg-Ab) and thyroid stimulating hormone TSH) for study groups in Baghdad

Region	T3(ng/ml)	T4(µg /dl)	Tg-Ab(IU/ml)	TSH(mIU/I)
Al-Karada Min-Max STD	1.13±0.07 (0.85-2.63) 0.36	9.14±0.37a (5.09-12.40) 1.87	69.87±6.30a (27.50-298.20) 66.53	2.20±0.30 (0.37-5.53) 1.51
Abo.Gharib Min-Max STD	1.28±0.08 (0.92-2.70) 0.44	9.42±0.37a (5.56-13.50) 1.89	65.61±5.21a (31.00-364.70) 76.06	2.06±0.26 (0.40-6.09) 1.32
Al-Jadriah Min-Max STD	1.13±0.04 (0.93-2.03) 0.21	8.44±0.38b (4.85-11.20) 1.86	56.03±3.75b (20.00-264.30) 48.79	1.98±0.23 (0.44-4.04) 1.14
LSD	0.1984	0.9628	8.532	0.7538
P	0.44	0.046	0.033	0.43

a,b,c: The difference letters in the same column means a significant difference in parameters between groups.

3.4 Results of Bisphenol -A in the sera of the three studied groups

Bisphenol -A was determined in the sera of the studied groups by high performance liquid chromatography (HPLC) for individual in three regions and the results are illustrated in table (3-4)

Table (3-4) statistical analysis (mean ±standard error), maximum, minimum and standard deviation of bisphenol -A for the three studied groups

Region	Bisphenol-A(µg/L)
Al-Karadah Min-Max STD	28.44±2.59a (14.1-35.20) 6.86
Abo.Gharib Min-Max STD	28.24±0.87a (24.50-31.30) 2.32
Al-Jadriah Min-Max STD	14.82±1.40b (10.40-20.00) 3.71
LSD	5.2827
P	<0.0001

a,b,c: The difference letters in the same column means a significant difference in parameters between groups.

3.5 Results of Polychlorinated biphenyls in the sera of the three studied groups

Polychlorinated biphenyl was determined in the sera of the studied groups by gas chromatography (GC) for individual in three regions and the results are illustrated in table (3-5)

Table (3-5) Statistical analysis (mean ±standard error), maximum, minimum and standard deviation of Polychlorinated biphenyls for the three studied groups

Region	PCBs(μg/L)
Al-Karadah Min-Max STD	0.00
Abo.Gharib Min-Max STD	0.54±0.47 (0.06-1.50) 0.82
Al-Jadriah Min-Max STD	0.00
LSD	0.9557
P	<0.0001

3.6 Results of lipid profile in the sera of the studied groups

Lipid profile including total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL), low density lipoprotein (LDL), and very low density lipoprotein (VLDL) were measured on human serum. Lipid levels were measured using a roche diagnostics c111 cobas analyzer, for individual in three regions and the results are illustrated in table (3-7)

Table (3-6) statistical analysis (mean ±standard error), maximum, minimum and standard deviation of lipid profile for the three studied groups

Region	Cholesterol(mg/dL)	Tri.(mg/dL)	HDL(mg/dL)	VLDL(mg/dL)	LDL(mg/dL)
Al-Karada Min-Max STD	330.30±24.34a (144.00-616.00) 108.87	205.30±17.21a (121.00-419.00) 76.97	37.75±2.05b (25.00-53.00) 9.21	40.56±3.35 (24.20-83.80) 15.00	224.99±26.22a (63.40-544.00) 117.26
Abo.Gharib Min-Max STD	223.60±20.35b (118.00-541.00) 91.01	168.80±11.49b (82.00-256.00) 51.42	43.45±1.86a (27.00-56.00) 8.35	33.76±2.29 (16.40-51.20) 10.28	144.89±22.35b (41.80-473.80) 99.98
Al-Jadriah Min-Max STD	284.90±23.55ab (161.00-587.00) 105.35	171.51±16.15b (78/00-303.00) 72.42	37.10±1.48b (26.00-48.00) 6.64	34.35±3.23 (15.60-60.60) 14.44	213.45±25.03ab (86.80-535.80) 86.80
LSD	64.617	28.931	5.1543	8.4941	69.639
P	0.042	0.046	0.031	0.215	0.049

a,b,c: The difference letters in the same column means a significant difference in parameters between groups.

	Unit	Cholesterol	Triglyceride	HDL	LDL
Normal	mg/dL	<200	<150	>60	<130
Intermediate	mg/dL	200-239	150-199	40-60	130-159
High	mg/dL	>239	>199	<40	>159

3.7 Results of the correlation coefficient between heavy metals (Pb, Hg, and Cd) and T3, T4, TSH and Tg-Ab parameters

We examined associations of human serum Pb, Hg , and Cd with T4, T3, TSH, and Tg-Ab, using separate regression models for each exposure outcome association.

Table (3-7) Correlation coefficient between heavy metals (Pb, Hg, and Cd) and T3, T4, TSH and Tg-Ab parameters in Al-karradah.

Al-karradah		Hg(µg/L)	Cd(µg/L)	T3(ng/ml)	T4(µg /dl)	Tg-Ab(IU/ml)	TSH(mIU/l)
Pb	Pearson Correlation	.799*	.913*	-.175	-.405	-.607-	-.775-
	P	.057	.011	.740	.426	.202	.070
Hg	Pearson Correlation		.900*	-.276*	-.087	.253	-.891-*
	P		.014	-.596	.869	.628	.017
Cd	Pearson Correlation			.489	.482*	.455*	-.714-
	P			.325	.333	.365	.111
T3	Pearson Correlation				-.702	-.210-	.143
	P				.120	.689	.787
T4	Pearson Correlation					-.611-	.144
	P					.197	.786
Tg-Ab	Pearson Correlation						.344
	P						.505
TSH	Pearson Correlation						
	P						

* : significant

** : Highly significant

Table (3-8) Correlation coefficient between heavy metals (Pb, Hg, and Cd) and T3, T4, TSH and Tg-Ab parameters in Abo-Gharib

Abo-Gharib		Hg(µg/L)	Cd(µg/L)	T3(ng/ml)	T4(µg /dl)	Tg-Ab(IU/ml)	TSH(mIU/l)
Pb	Pearson Correlation	.976**	.916*	.-319	.-089	.-226	-.177
	P	.001	.010	.537	.866	.667	.737
Hg	Pearson Correlation		.885*	-.904-*	-.102-*	.042	.-277
	P		.019	-.013	.848	.938	.595
Cd	Pearson Correlation			.298	.047*	.233*	-.220
	P			.567	.930	.657	.675
T3	Pearson Correlation				-.214	-.235	-.316-
	P				.683	.654	.542
T4	Pearson Correlation					-.848*	.229
	P					.033	.662
Tg-Ab	Pearson Correlation						.010
	P						.985
TSH	Pearson Correlation						
	P						

Table (3-9) Correlation coefficient between heavy metals (Pb, Hg, and Cd) and T3, T4, TSH and Tg-Ab parameters in Al-Jadriah

Al-Jadriah		Hg(µg/L)	Cd(µg/L)	T3(ng/ml)	T4(µg /dl)	Tg-Ab(IU/ml)	TSH(mIU/l)
Pb	Pearson Correlation	.878	.956**	.637	.423	.043	-.546
	P	.021	.003	.173	.403	.936	.263
Hg	Pearson Correlation		.964**	.322	.025	-.398	.062
	P		.002	.533	.962	.434	.908
Cd	Pearson Correlation			-.769*	-.234	.318	.324
	P						
T3	Pearson Correlation				.369	.403	-.183-
	P				.472	.428	.728
T4	Pearson Correlation						.496
	P						.317
Tg-Ab	Pearson Correlation						-.729-
	P						.100
TSH	Pearson Correlation						
	P						

3.8 Results of the correlation coefficient between heavy metals (Pb, Hg, and Cd) and lipid profile parameters

Table (3-10) Correlation coefficient between heavy metals (Pb, Hg, and Cd) and Cholesterol, Triglyceride, HDL, LDL, and VLDL parameters in Al-karradah

Al-karradah		Choles(mg/dL)	Trigly(mg/dL)	HDL(mg/dL)	VLDL(mg/dL)	LDL(mg/dL)
Pb	Pearson Correlation	.388	-.669-*	.773	-.669-*	.634
	P	.447	.146	.071	.146	.176
Hg	Pearson Correlation	.004	-.960-**	-.586-	-.960-**	.379
	P	.994	.002	.222	.002	.459
Cd	Pearson Correlation	-.058-	-.794-	-.575-	-.794-	.369
	P	.914	.059	.233	.059	.471
Chol.	Pearson Correlation		.040	-.732-	.040	.925**
	P		.941	.098	.941	.008
Trigly	Pearson Correlation			.449	1.000**	-.339-
	P			.372	.000	.511
HDL	Pearson Correlation				.449	-.883-*
	P				.372	.020
VLDL	Pearson Correlation					-0.339-
	P					.511

Table (3-11) Correlation coefficient between heavy metals (Pb, Hg, and Cd) and Cholesterol, Triglyceride, HDL, LDL, and VLDL parameters in Abo-Gharib

Abo-Gharib		Choles(mg/dL)	Trigly(mg/dL)	HDL(mg/dL)	VLDL(mg/dL)	LDL(mg/dL)
Pb	Pearson Correlation	.302	-.883-*	.545	-.883-*	.262
	P	.561	.020	.263	.020	.616
Hg	Pearson Correlation	.141	-.884-*	-.432-	-.884-*	.100
	P	.790	.019	.392	.019	.850
Cd	Pearson Correlation	-.508-	-.928-**	-.769	-.928-**	.471
	P	.304	.008	.074	.008	.346
Chol.	Pearson Correlation		.247	-.887-*	.247	.999**
	P		.636	.018	.636	.000
Trigly	Pearson Correlation			-.625-	1.000**	.206
	P			.185	.000	.695
HDL	Pearson Correlation				-.625-	-.871-*
	P				.185	.024
VLDL	Pearson Correlation					.206
	P					.695

Table (3-12) Correlation coefficient between heavy metals (Pb, Hg, and Cd) and Cholesterol, Triglyceride, HDL, LDL, and VLDL parameters in Al-Jadriah

Al-Jadriah		Choles(mg/dL)	Trigly(mg/dL)	HDL(mg/dL)	VLDL(mg/dL)	LDL(mg/dL)
Pb	Pearson Correlation	-.354-	.847	-.108-	.847	-.147-
	P	.491	.033	.839	.033	.782
Hg	Pearson Correlation	-.558-	.782	.369	.782	-.406-
	P	.249	.066	.472	.066	.425
Cd	Pearson Correlation	.473	.777	.304	.777	.311
	P					
Chol.	Pearson Correlation		.611	-.856-*	.611	.964**
	P		.198	.030	.198	.002
Trigly.	Pearson Correlation			-.211-	1.000**	.381
	P			.688	.000	.456
HDL	Pearson Correlation				-.211-	-.942-**
	P				.688	.005
VLDL	Pearson Correlation					.381
	P					.456

3.9 Results of the correlation coefficient between heavy metals (Pb, Hg, and Cd) and Bisphenol-A parameters

Table (3-13) Correlation coefficient between heavy metals (Pb, Hg, and Cd) and bisphenol -A parameters in Al-karradah

Al-karradah		Bisphenol-A(µg/L)
Pb	Pearson Correlation	-.818-*
	P	.046
Hg	Pearson Correlation	-.385-
	P	.451
Cd	Pearson Correlation	-.647-
	P	.165

Table (3-14) Correlation coefficient between heavy metals (Pb, Hg, and Cd) and bisphenol-A parameters in Abo-Gharib

Abo-Gharib		Bisphenol-A(µg/L)
Pb	Pearson Correlation	-.601-
	P	.207
Hg	Pearson Correlation	-.583-
	P	.224
Cd	Pearson Correlation	-.774-
	P	.071

Table (3-15) Correlation coefficient between heavy metals (Pb, Hg, and Cd) and bisphenol-A parameters in Al-Jadriah

Al-Jadriah		Bisphenol-A(µg/L)
Pb	Pearson Correlation	.346
	P	.501
Hg	Pearson Correlation	.498
	P	.315
Cd	Pearson Correlation	.331
	P	

3.10 Results of the correlation coefficient between Bisphenol-A and Lipid profile parameters

Table (3-16)Correlation coefficient between Bisphenol-A and Cholesterol, Triglyceride, HDL, LDL, and VLDL parameters in Al-karradah

Al-karradah		Bisphenol-A(µg/L)
Chol.	Pearson Correlation	.427**
	P	.340
Trigly.	Pearson Correlation	.149**
	P	.750
HDL	Pearson Correlation	-.612-*
	P	.144
VLDL	Pearson Correlation	.149
	P	.750
LDL	Pearson Correlation	-.476-**
	P	.280

Table (3-17)Correlation coefficient between Bisphenol-A and Cholesterol, Triglyceride, HDL, LDL, and VLDL parameters in Abo-Gharib

Abo-Gharib		Bisphenol-A(µg/L)
Chol.	Pearson Correlation	.045**
	P	.924
Trigly.	Pearson Correlation	.187**
	P	.688
HDL	Pearson Correlation	-.079-*
	P	.866
VLDL	Pearson Correlation	.187
	P	.688
LDL	Pearson Correlation	-.035-**
	P	.941

Table (3-18)Correlation coefficient between Bisphenol-A and Cholesterol, Triglyceride, HDL, LDL, and VLDL parameters in Al-Jadriah

Al-Jadriah		Bisphenol-A(µg/L)
Choles	Pearson Correlation	-.329-
	P	.471
Trigly	Pearson Correlation	-.557-
	P	.194
HDL	Pearson Correlation	.045
	P	.924
VLDL	Pearson Correlation	-.557-
	P	.194
LDL	Pearson Correlation	.194
	P	.677

3.11 Results of the correlation coefficient between Bisphenol-A and T3, T4, TSH, and Tg-Ab parameters

Table (3-19) Correlation coefficient between Bisphenol-A and T3, T4, TSH and Tg-Ab parameters in Al-karradah

Al-karradah		Bisphenol-A (μg/L)	T3(ng/ml)	T4(μg /dl)	Tg-Ab(IU/ml)	TSH(mIU/l)
Bisphenol-A	Pearson Correlation		-.016-	-.519-	.459	.386
	P		.976	.291	.360	.450

Table (3-20) Correlation coefficient between Bisphenol-A and T3, T4, TSH and Tg-Ab parameters in Abo-Gharib

Abo-Gharib		Bisphenol-A (μg/L)	T3(ng/ml)	T4(μg /dl)	Tg-Ab(IU/ml)	TSH(mIU/l)
Bisphenol-A	Pearson Correlation		-.741-	-.024-	-.247-	.023
	P		.092	.964	.636	.966

Table (3-21) Correlation coefficient between Bisphenol-A and T3, T4, TSH and Tg-Ab parameters in Al-Jadriah

Al-Jadriah		Bisphenol-A (μg/L)	T3(ng/ml)	T4(μg /dl)	Tg-Ab(IU/ml)	TSH(mIU/l)
Bisphenol-A	Pearson Correlation		.597	.056	-.062-	-.527-
	P		.210	.916	.906	.283

3.12 Results of the correlation coefficient between Lipid profile and T3, T4, TSH and Tg-Ab parameters

Table (3-22) Correlation coefficient between lipid profile and T3 ,T4 ,TSH and Tg-Ab in Al-karradah

Al-karradah		Choles(mg/dL)	Trigly(mg/dL)	HDL(mg/dL)	VLDL(mg/dL)	LDL(mg/dL)
T3	Pearson Correlation	-.449-	-.291-	-.295-	-.291-	-.323-
	P	.372	.576	.571	.576	.533
T4	Pearson Correlation	-.179-	.025	.121	.025	-.175-
	P	.734	.962	.819	.962	.740
Tg-Ab	Pearson Correlation	-.259-	.255	.160	.255	-.322-
	P	.621	.626	.763	.626	.533
TSH	Pearson Correlation	.212	.867*	.680	.867*	-.537-
	P	.687	.026	.137	.026	.272

Table (3-23) Correlation coefficient between lipid profile and T3 ,T4 ,TSH and Tg-Ab in Abo-Gharib

Abo-Gharib		Choles(mg/dL)	Trigly(mg/dL)	HDL(mg/dL)	VLDL(mg/dL)	LDL(mg/dL)
T3	Pearson Correlation	-.099-	-.225-	-.124-	-.225-	-.119-
	P	.852	.668	.814	.668	.822
T4	Pearson Correlation	-.424-	.196	.119	.196	-.428-
	P	.402	.709	.823	.709	.397
Tg-Ab	Pearson Correlation	-.765-	.066	.457	.066	-.768-
	P	.076	.902	.362	.902	.074
TSH	Pearson Correlation	.258	.408	.441	.408	-.246-
	P	.622	.422	.382	.422	.638

Table (3-24) Correlation coefficient between lipid profile and T3, T4, TSH and Tg-Ab in Al-Jadriah

Al-Jadriah		Choles(mg/dL)	Trigly(mg/dL)	HDL(mg/dL)	VLDL(mg/dL)	LDL(mg/dL)
T3	Pearson Correlation	.586	.664	.445	.664	.475
	P	.221	.150	.377	.150	.341
T4	Pearson Correlation	.034	-.350-	-.280-	-.350-	.163
	P	.949	.496	.590	.496	.757
Tg-Ab	Pearson Correlation	-.337-	.163	.539	.163	-.455-
	P	.513	.757	.270	.757	.364
TSH	Pearson Correlation	-.215-	-.791-	-.205-	-.791-	.018
	P	.682	.061	.697	.061	.973

3.13 Discussion

According to the results of the BMI analysis. AL-Karradah group consisted of 25 individual with normal BMI**,** abo-Gharib group contained 25 individual with overweight BMI**,** al-Jadriah group (control) comprised of 25 individual with normal BMI.

Table (3- 2) shows Statistical analysis of Pb, Cd and Hg of the three different hospitals in Baghdad (Al-karadah , Abo-Gharib, Al-Jadriah). Lead, mercury and cadmium levels had a highly significant differences at (p <0.0001) in the two regions (AL-Karradah and Abo-Gharib) as compared with AL-jadriah (control).

This work is the first to study the pollution as consequences of terrorism of Baghdad regions.

As mercury is known as environmental toxicant; but only a few studies have examined its associations with T4, T3, or TSH. In addition to the Brain, metallic mercury is also deposited in the thyroid and may associate with thyroid dysfunction, environmental exposures to mercury correlate with thyroid dysfunction. (103)

Cadmium has been declared to accumulate in the thyroid after chronic exposure to be association with increased thyroid hormones levels and pre-neoplastic thyroid abnormalities. Moreover, levels of Cd are higher in thyroid tissue of patients with advanced thyroid cancer. (104)

Blood lead levels in the studies were significantly higher than in the control groups. Our results agree with the findings of a previous study. (105)

Lead poisoning causes functional and structural changes in many organs such as liver dysfunction, renal dysfunction thyroid dysfunction, nervous system disorders, hematological changes, and glucose metabolism abnormalities, also lead adversely affects the secretion, production, and biological activities of thyroid and stress Hormones and of hormone related metabolism. So, in agreement with the present study, TSH blood level increased among workers exposed to lead and source of lead. (106)

Pb, Cd, and Hg are defined as metallic chemical elements that have a relatively high density and are toxic or poisonous at even low levels. (107)

A recent animal study noted an effect of Pb levels on thyroid hormone level in rates. (108)

The thyroid gland is the only organ involved in T4 synthesis, the decrease of this hormone level system in the serum of Pb and cadmium exposed mice, may suggest that Cd and Pb influences the production and/or secretion of T4 by follicular cells. The probability of Cd and Pb interference in the synthesis and/or secretion of T4 by the thyroid follicular cells are supported by the results of morphological examinations. These revealed a damaging action of Cd and Pb on the structure of follicular cells of thyroid gland. So, a tendency towards an increase in the sample serum TSH concentration observed at exposure to Cd and Pb is a likely response to decreased serum T4 and T3 level. Thus the lack of significant response of thyrotropin to decreased serum T4 and T3 level may suggest Pb and Cd involvement with pituitary regulation of thyroid hormones Production and secretion. Serum levels of thyroid hormones, consist of TSH, T4 and T3, are commonly used as reliable indicators of the thyroid function in humans and experimental animals. [109]

The TSH reference intervals may vary from one population to another. The relationship between TSH and thyroid antibodies and the prevalence of thyroid antibodies (Tg-Ab) has never been studied in a Middle Eastern population. [110]

Currently, serum-based immunoassays techniques are available for measuring thyroid hormones thyroxine and triiodothyronine, as well as the pituitary thyroid stimulator, thyroglobulin (Tg) and thyrotropin (Thyroid Stimulating Hormone) TSH. In addition, methods to detect the thyroid autoantibodies: thyroglobulin antibodies have been developed in response to the recognition that autoimmunity is a major cause of thyroid dysfunction. Currently, most thyroid testing is performed on serum specimens using manual or automated immunoassays employing specific antibody reagents targeting these ligands.

Thyroglobulin autoantibodies predominantly belong to the immunoglobulin G class, serum thyroglobulin antibodies (Tg- Ab) were the firs thyroid antibody to be detected in patients with autoimmune thyroid disorders subsequently, methodologies for detecting Tg-Ab have evolved in parallel with those for TPOAb measurement from semi quantitative with techniques, to more sensitive ELISA and most recently non-isotopic competitive or non-competitive immunoassays . [111]

Bisphenol -A is widely used as a raw material in manufacture, resulting in its ubiquitous distribution in natural environment pollutants, including the aqueous environment. However, the effect of BPA on the thyroid endocrine system is largely unknown, bio concentration of BPA and whole-body thyroid hormones, thyroid stimulating hormone concentrations related to the hypothalamic-pituitary-thyroid (HPT) axis were examined. The significant adverse effects of bisphenol-A on human health, demonstrated that developmental exposure to BPA caused developmental poisoning, disturbed the balance of hormones (sex steroids and thyroid hormones).The pollutants of BPA and its analogs have gained great concern because of their potentially adverse health impacts in this study, we evaluated the mechanism of thyroid endocrine disruption caused by BPA. The results demonstrated that BPA significantly changed whole-body TH and TSH concentrations suggesting the thyroid endocrine disrupting effects of BPA, so the emergence of a large number of bisphenol -A pollutants found many pollute in the areas of Karradah and Abo- Gharib compared with the control Al-Jadria region, show that in (appendix B). (112)

In addition, BPA can alter thyroid-specific gene expression and functions. (113)

Concentrations of PCBs a compound detected in the human serum samples are summarized only in abo-Gharib region and shows the chromatogram obtained by GC–ECD for human serum, because of the high selectivity and, no interferences were noticed in the retention time of the target pesticides, PCBs components were successfully separated with good resolution.

The analytical conditions of PCBs concentrations detected in the human serum samples are summarized only in abo-Gharib region compared with control al-Jadria region.

Within PCBs risk survey when searching further for additional signs of hyperthyroidism e.g. increased T4 plus increased T3 among the subjects causes with very low TSH and very high PCBs level, So, identified a total of level we called these cases “high PCBs related subclinical hyperthyroidism” since they showed fundamental laboratory signs of hyperthyroidism (very low TSH and very high T4 and T3), though more detailed clinical examinations were not done this view is in agreement with recently suggested revision of thyroid diseases classification by Monaco who admitted that “environmental factors can affect thyroid function without a modification of thyroid morphology“ and defined “subclinical hyperthyroidism as an asymptomatic state in which circulating T3 and T4 are normal, but sample serum sensitive thyrotropin (TSH) is suppressed which shows a mild stage of thyroid hyper function thus, from our findings it may be concluded that TSH level tends to decrease with increasing levels of PCBs which is contrasting to several findings of increased TSH level by others, the important role of individual susceptibility in the development of adverse health effects related To PCBs. Previously study identified cases with very high PCBs and at the same time low TSH and high T4, this further possibly results in increased input of T4 to the cells and increased intracellular T4 to T3 conversion including pituitary cells which contributes to a final decrease of TSH. (114)

The serum VLDL levels were similar across each group ($P > 0.05$). But different cholesterol, triglyceride and LDL in al-Karradah reagion compared to controls al-Jadria reagion.

Thyroid disorder is the most common endocrine disorder which is associated with dyslipidemia.it affects the synthesis, mobilization and metabolism of lipids. (115)

In general, subclinical and overt hypothyroidism is associated with hypercholesterolemia which is mainly due to elevation of low density lipoprotein cholesterol levels, whereas high density lipoprotein cholesterol concentration is usually normal or even elevated, decreased thyroid secretion greatly increases the plasma concentration of cholesterol because of decreased rate of cholesterol secretion in the bile and consequent diminished loss in the faeces due to decreased number of low density lipoprotein receptors on liver cells. (116)

Table (3-7) and (3-8) statistically significant negative associations between human serum Hg, T4 and T3 were observed in al-karadah &abo. Gharib when comparing with control group (Al-jadria group), human serum Cd was positively associated with T3. Our results agree with the findings of a previous study. (117)

In the three-metal analysis in al-karada &Abo. Gharib, the negative association between Hg and T4 and T3 was evident with and without exposures to Cd or Pb above median levels, and the positive association between Cd and Tg was evident for all combinations with exposure to Cd above the median, regardless of exposure to Hg or Pb. (107)

A negative association between blood serum lead Pb and thyroid function parameters (T3, T4 and TSH) in the group of al-karadah &Abo. Gharib poisoned with lead compared with the control group, TSH level increased among workers exposed to lead. Our results were not agreed with other study. (118) who reported no correlation between blood lead levels and thyroid function.

Human serum Cd was positively associated with thyroid hormones in this study which agreed with a previous study. (119) who suggested a positive correlation between blood serum cadmium levels and serum thyroid hormones.

Human serum Hg was positively associated with thyroglobulin-Ab (Tg-Ab) was observed in this study which agreed with a previous study. [120] who found a positive association between blood serum mercury levels and serum thyroglobulin-antibody (Tg-Ab).

A cross-sectional investigation study in the United States revealed that metabolites T4 and triiodothyronine (T3) were negatively correlated with thyroglobulin-antibody (Tg-Ab), and were positively correlated with thyroid stimulating hormone (TSH). [121]

A negative correlation between blood serum lead and T4 levels in the group of al-karadah &Abo.Gharib poisoned with lead compared with the control group our results agree with the findings of a previous study. [122]

In adults, mercury exposure negatively associates with thyroid hormones levels. [123] Our finding of a relationship between mercury (Hg) and thyroglobulin antibodies (Tg-Ab) suggested a possible health implications of elevated Tg-Ab.

Thyroglobulin antibody (Tg-Ab) positivity alone is not a last diagnostic Indicator of thyroid disease; however, thyroglobulin antibodies (Tg-Ab) are elevated in more than 90% of patients with Hashimoto autoimmune thyroiditis.

Thyroglobulin antibodies are elevated in patients with other autoimmune related diseases, for example, in %50 of patients with pernicious anemia and 20% of patients with systemic lupus erythematosus . Therefore, associations observed between mercury Hg and Tg-Ab may more broadly indicate a relationship antibody positivity, mercury (Hg) was associated with increased odds for thyroid cancer. (118)

Finally, there were significant positive correlations between the heavy metals Pb, Hg, Cd themselves. This is suggestive of a similar, if not identical, radix of the heavy metals (Pb, Hg, Cd) and referring that anthropic activities could promoting the mobility of these elements. (124)

We conclude that serum lead level is positively associated with levels of sample serum total cholesterol TC, HDL cholesterol and LDL cholesterol. The positive association between serum lead level and serum cholesterol among exposed subjects may have important clinical implications. Our results agree with the findings of a previous study. (125)

To confirmed previous findings that Cd can adversely affect the lipid and lipoprotein profile. In the current study, considerable increases in total cholesterol TC, triglyceride TG and LDL-C exposed to low dose of Cd as compared with the control group. So, other studies have suggested similar increases in serum levels of total cholesterol TC, triglyceride TG and LDL after high dose administration of Cd to rats. (126)

We suggest that serum cadmium level is negatively associated with levels of serum total cholesterol, HDL cholesterol, TG, and VLDL cholesterol. Our results agree with the findings of a previous study. (127)

Mercury is a common environmental pollutant and toxicant which is not necessary in the biological processes of our body. Humans are continuously exposed to mercury, which is mainly produced from fossil fuel combustion, mining, and incineration plants, also from natural sources, without occupational exposure to mercury. The primary source of mercury Hg is the diet especially fish and shellfish in the general population. In a previous study, a positive correlation of LDL with mercury (Hg) and a negative relation of HDL with mercury (Hg) were reported, while no significant association of blood mercury was observed with LDL in the present study. So, in our study regardless of gender and age, mercury was positively correlated with an increase of total cholesterol. Previous studies reported that mercury exposure might increase the risk of metabolic syndrome which is it including obesity, increased fasting glucose, low high density lipoprotein, high triglyceride and hypertension. Although a possible relationship triglyceride, and hypertension, although a possible relationship between the deregulation of lipid and glucose metabolism and mercury has been suggested, the mechanism of obesity by mercury is not yet clear. Our results agree with the findings of a previous study. [128]

Asignificant negative correlation was found between bisphenol-A ($p< 0.05$) and lead and negative correlation was found between bisphenol-A and both mercury and cadmium.

There was a highly significant positive correlation found between bisphenol-A and cholesterol and triglycerides ($p<0.001$). A significant negative correlation was found between bisphenol-A and HDL ($p< 0.05$). A highly significant negative correlation was found between bisphenol-A and LDL ($p<0.001$) and positive correlation was found between bisphenol-A and VLDL. Our results agree with the findings of a previous study. [129]

Our study was supported by the results of the hormonal levels which showed significant increase in the level of lipid profile such as cholesterol TC, triglycerides TG, LDL with a significant decrease of the level of HDL concluded that BPA may interfere with the steroid genesis by inhibiting cholesterol uptake, which regular with our study concerning the results of lipid profile. [130]

The high bisphenol-A of group aL-Karrada and abo-Gharib was having changes in parallel with higher levels of serum cholesterol, LDL, TG in compared to the low one, which expounds in al-Jadria group observed in this study. The difference was statistically significant for lipid profile. Similar results were obtained by another study [131] Who found that higher total serum BPA was associated with higher levels of low density lipoprotein, and cholesterol levels. Population characteristics and distributions of BPA, and serum thyroid measures are presented in supplemental material, the suggestive inverse relationships between BPA and T4. In a recent study of people recruited through an infertility clinic, BPA was inversely associated with TSH but not related to T4 or T3 potentially consistent with our observation of suggestive inverse associations between BPA and both T4 and TSH, that BPA repress TSH release from amphibian pituitary in a manner independent of both estrogenic activity of BPA and the thyroid hormone feedback mechanism. So, these studies and the present analysis suggest that BPA may alter thyroid signaling but more research is necessary. Our results were not agreed with other study. [132] that suggested inverse association between BPA and TSH. So, in the present study, we suggestion positive association between bisphenol-A (BPA) and thyroid stimulating hormones (TSH). Human exposures to BPA and its effects on thyroid measures, possible thyroid damaging properties of BPA have been mostly studied in vitro or in animal studies . In fact, a positive association between BPA and serum TSH levels were observed in a U.S. representative general population adult group (2007–2008), albeit not significant ($p = 0.2$). Our results agree with the findings of a previous study. [133] For instance, bisphenol-A, which is ubiquitous in the environment and large amounts of it can leach into liquids and food from plastic water bottles and the lining of aluminum cans, is shown to significantly prevent thyroid activity in all tissues except the pituitary, potentially causing weight gain or contributing to fatigue and depression but not detected by TSH testing. Levels of number of thyroid blocking toxins, including BPA is significantly very higher in individuals in the United States resulting in reduced triiodothyronine T3 effect in all tissues in almost all individuals in compared to the rest of the world , this is potentially a significant contributor to the epidemic of obesity and depression in the US. (134)

A previous study clearly showed positively association between TSH levels and serum cholesterol and triglyceride levels. (135)

In correlation coefficient, TSH was positively associated with cholesterol. TSH was positively and significantly associated with triglyceride. The TSH level is directly proportional to the lipid level. T3 was negatively correlated to serum HDL, T4 was positively correlated to serum HDL. Our results agree with the findings of a previous study. (136)

In the current study, there was a positive relationship between TSH and HDL in addition to negative correlation between TSH and LDL. Other studies observed a negative relationship between TSH and lipid profile.

They suggest that TSH level was significantly and negatively associated with HDL, and positively with LDL. Also, T3 was negatively correlated to serum TC, triglyceride and LDL. Thyroid hormones (T3 and T4), especially T3 have been demonstrated to regulate LDL receptors by binding directly to thyroid hormone responsive elements and controlling sterol regulatory element binding protein, in the current study T4 was negatively correlated to serum TC, LDL. (137)

Finally, in the current study, thyroglobulin antibodies did not show any significant correlation with lipid profile. Lipid profile results were not significantly associated with thyroid antibodies thyroglobulin antibodies. It is well known that alterations in thyroid function result in changes in the composition and transport of lipoproteins. [138]

Conclusions

In general, in population of al-karradah and abo.Gharib an inverse association were observed between the sera mercury (Hg) and lead and T3, TSH and T4 levels, and positive associations between cadmium (Cd) and TH levels and thyroglobuline-Ab (Tg-Ab). T4 and T3 were negatively correlated with thyroglobulin-Ab (Tg-Ab), and positive associations between mercury (Hg) and thyroglobulin-antibodies (Tg-Ab).There were significant positive correlations between the heavy metals themselves. It seen that heavy metals and persistent organic pollutants as poisons to health. However, our study is unique in that we have measured three groups of POPs and heavy metals and all thyroid hormones in serum samples, the results of the present study provide another line of evidence that the current exposure among humans could influence the levels of thyroid hormones. The observed association between POPs and heavy metals exposure toward thyroid hormone disruption. Thus, considering the importance of thyroid hormones in rapidly developing bodies, public health implications of thyroid hormone disturbance should receive further investigations.On the other hand an emergence of a large number of bisphenol -A and polychlorinated biphenyls pollutants found in most residents of al-Karradah and abo-Gharib areas compared to al-Jadria region (control group).The effect of war(terrorist operation) on the environment in Iraq results of pollution of heavy metals and Persistent Organic Pollutants indicating that increased heavy metals and POPS in the blood are likely to decrease thyroid hormone production. Environmental factors have been hypothesized to be influential in thyroid hormone production. This study offers an additional indication that heavy metals and persistent organic pollutants are correlated to thyroid hormone levels. Future research should continue studying the content of this study in order to continue increasing research accuracy by taking into account additional environmental and biological factors that influence heavy metals and thyroid hormones.

Recommendations

1. Study the epigenetic modification due to heavy metal exposure.

2. Study the effect of heavy metal exposure on neonatal and children health in areas that were military operations.

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Questionnaire

Number:

Name:

Age:

Gender:

Address:

Diseases:

Medication:

Smoker:

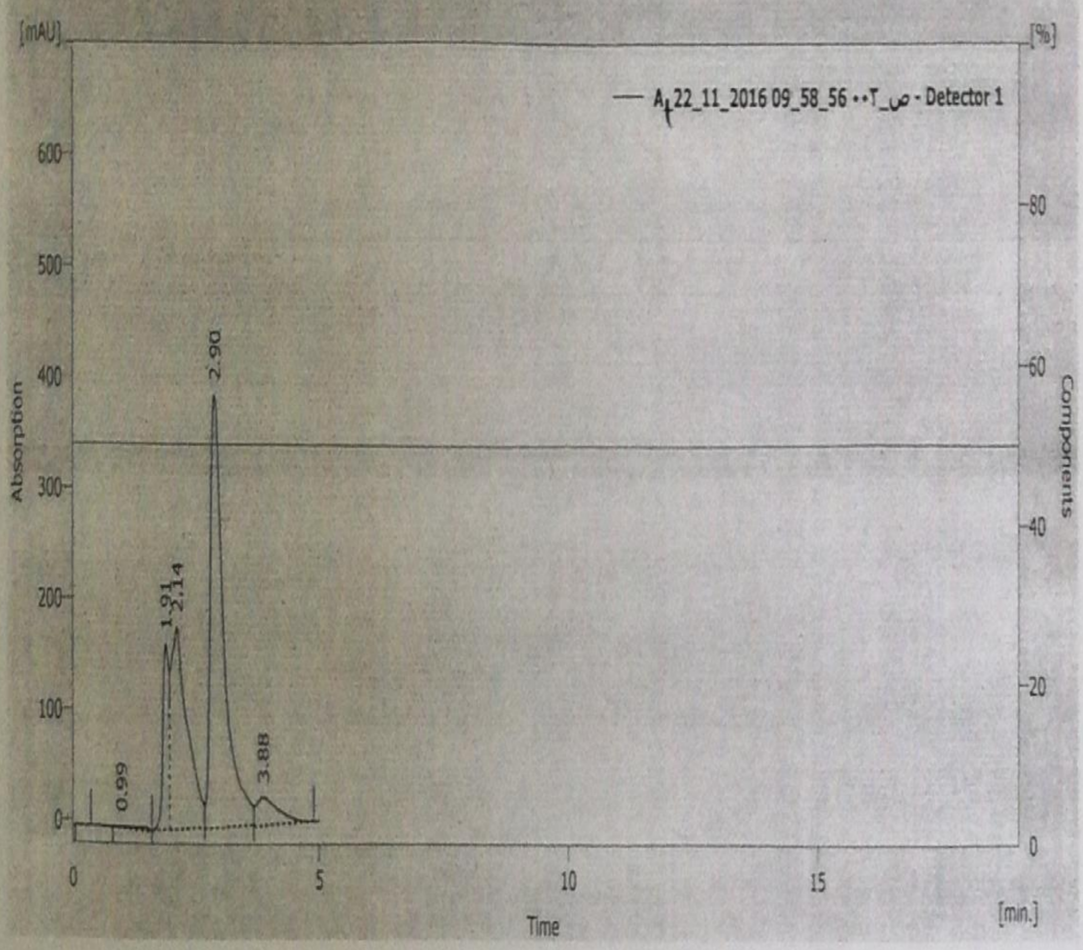
Pregnancy:

Biochemical Test :

Test	Result
CHO	
VLDL	
LDL	
HDL	
TG	
Hg ion	
Pb ion	
Cd ion	
Bisphenol-A	
PCBs	
TSH	
T3	
T4	
Tg-Ab	

Appendix (B)

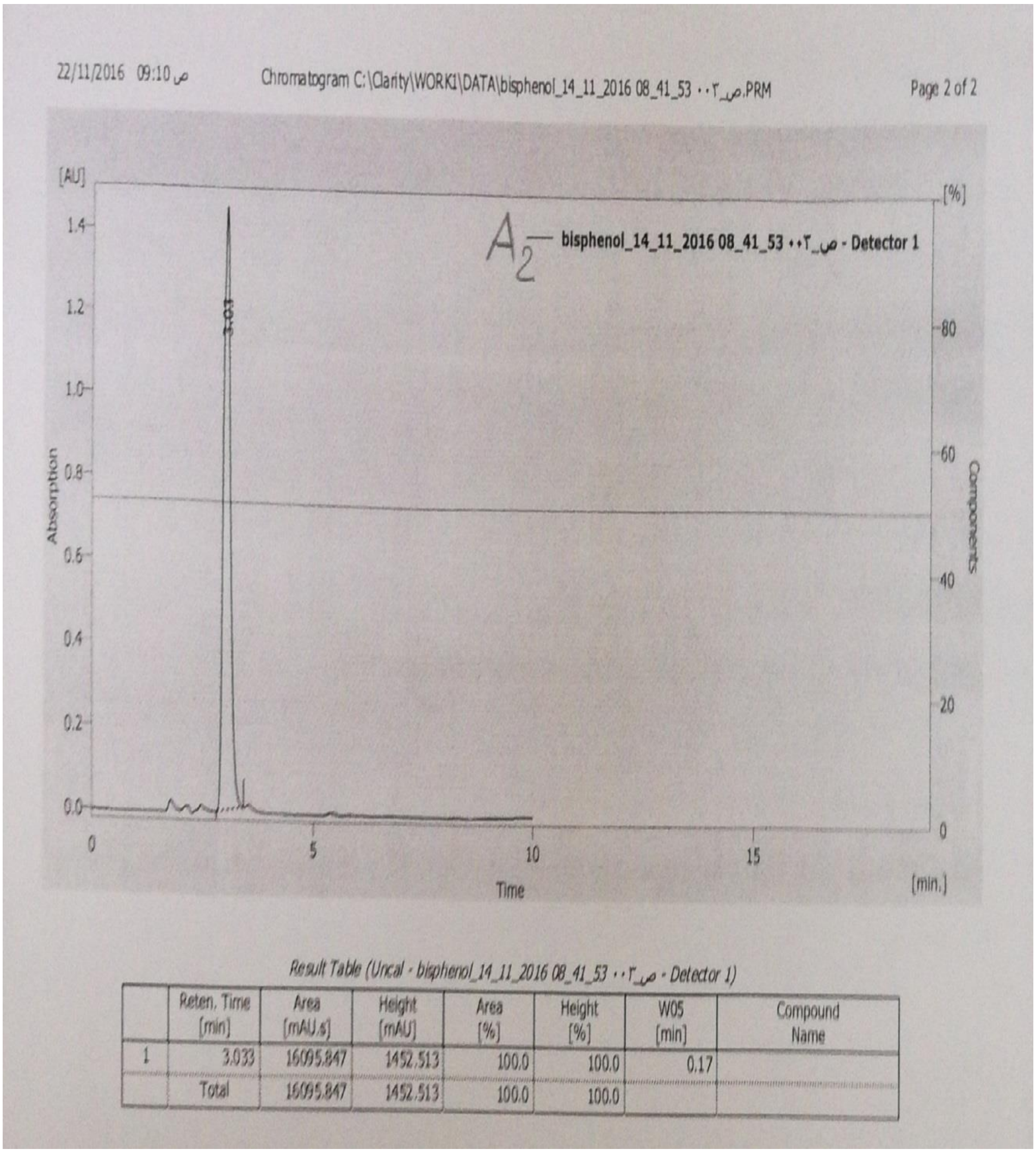
Bisphenol A concentration measured by HPLC



Result Table (Uncal - A_22_11_2016 09_58_56 ٠٠٢_ص - Detector 1)

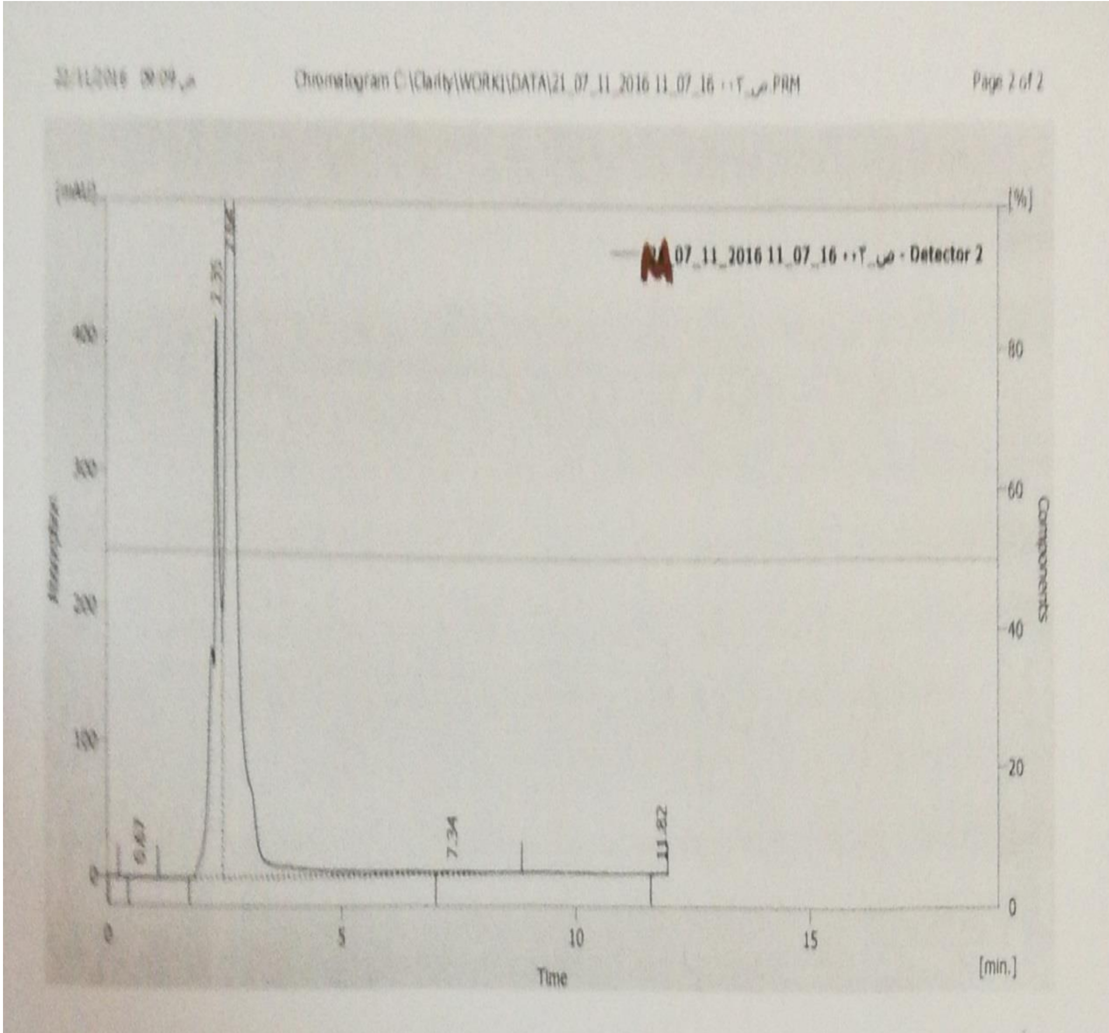
	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	0.113	4.242	0.454	0.0	0.1	0.22	
2	0.993	50.337	0.895	0.4	0.1	0.34	
3	1.913	1417.618	166.975	10.1	21.8	0.15	
4	2.143	4157.249	182.276	29.7	23.8	0.37	
5	2.903	7582.355	389.841	54.2	51.0	0.26	
6	3.877	780.629	24.673	5.6	3.2	0.54	
	Total	13992.430	765.113	100.0	100.0		

Figure B.1: UV280 nm chromatogram of HPLC analysis of a mixture of Bisphenol A in Al-Karradah Region.



	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	3.033	16095.847	1452.513	100.0	100.0	0.17	
	Total	16095.847	1452.513	100.0	100.0		

Figure B.2: UV280 nm chromatogram of HPLC analysis of a mixture of Bisphenol A in Al-Karradah Region.

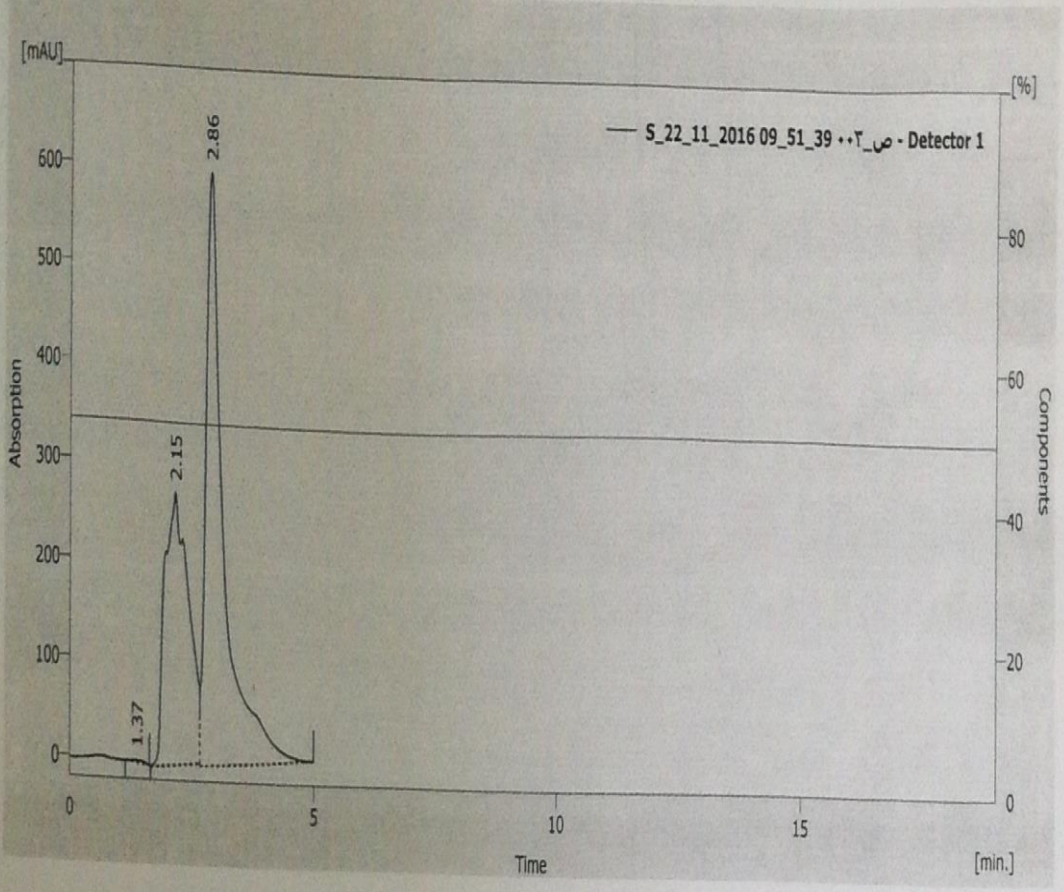


Result Table (Uncal - 21_07_11_2016 11_07_16 ٠٠٢_ص - Detector 2)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	0.103	2.017	0.328	0.0	0.0	0.11	
2	0.673	3.568	0.190	0.0	0.0	0.20	
3	2.350	4451.737	413.814	22.8	28.4	0.14	
4	2.640	14990.388	1038.429	76.7	71.4	0.18	
5	7.343	98.227	1.934	0.5	0.1	1.13	
6	11.820	2.264	0.183	0.0	0.0	0.23	
	Total	19548.200	1454.878	100.0	100.0		

Figure B.3: UV280 nm chromatogram of HPLC analysis of a mixture of Bisphenol A, in Abo-Gharib region.

22/11/2016 09:57 ص Chromatogram C:\Clarity\Work1\DATA\S_22_11_2016 09_51_39 ٠٠٣_ص.PRM Page 2 of 2

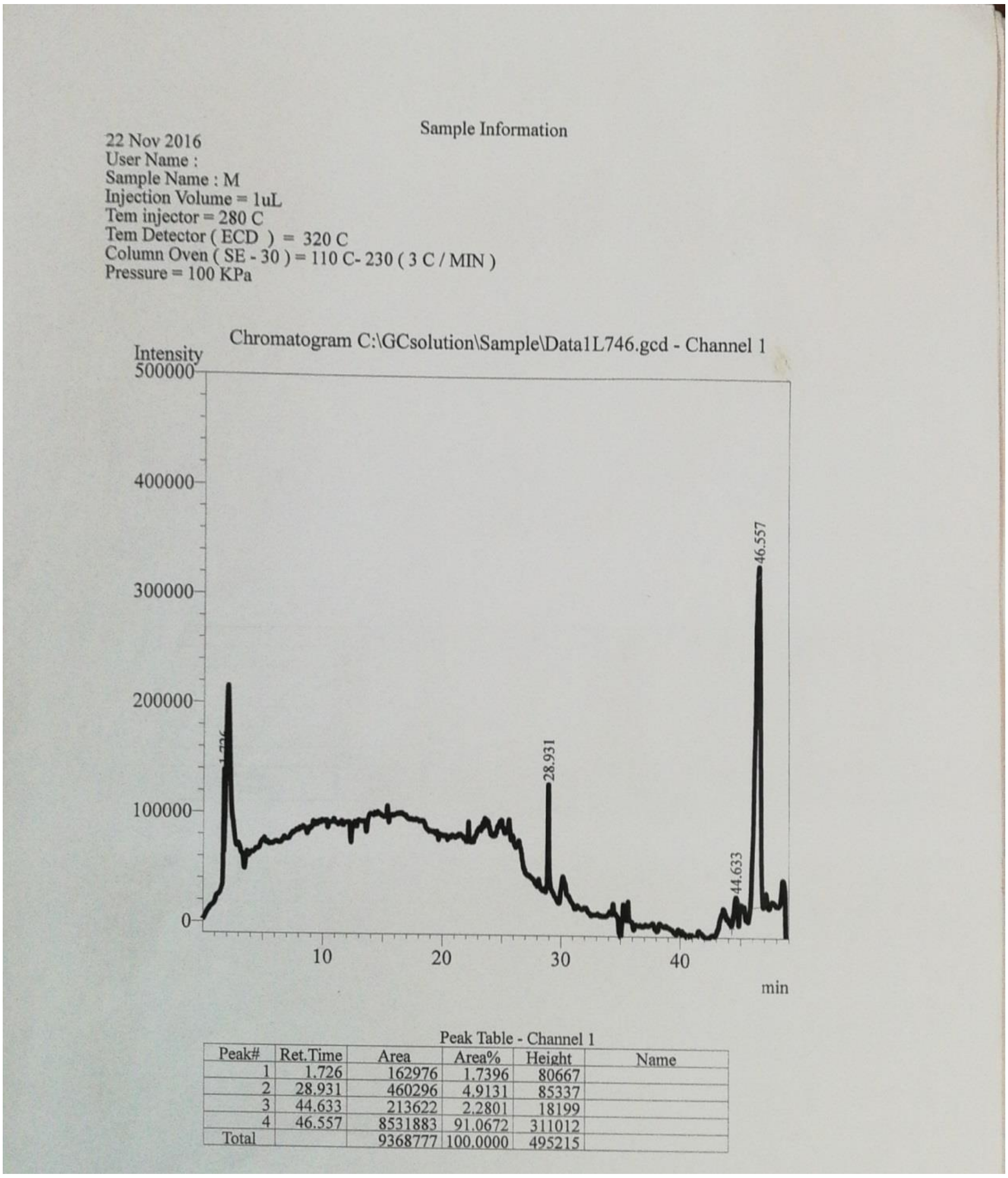


Result Table (Uncal - S_22_11_2016 09_51_39 ٠٠٣_ص - Detector 1)

	Reten. Time [min]	Area [mAU.s]	Height [mAU]	Area [%]	Height [%]	W05 [min]	Compound Name
1	1.367	45.429	2.223	0.2	0.3	0.38	
2	2.150	9334.044	274.591	37.9	31.4	0.63	
3	2.860	15218.233	597.828	61.9	68.4	0.31	
	Total	24597.706	874.642	100.0	100.0		

Figure A.4: UV280 nm chromatogram of HPLC analysis of a mixture of Bisphenol A in Al-Jadria region.

Polychlorinated biphenyl concentration measured by gas Chromatography (GC)



Sample Information

22 Nov 2016
User Name :
Sample Name : M
Injection Volume = 1uL
Tem injector = 280 C
Tem Detector (ECD) = 320 C
Column Oven (SE - 30) = 110 C- 230 (3 C / MIN)
Pressure = 100 KPa

Peak Table - Channel 1

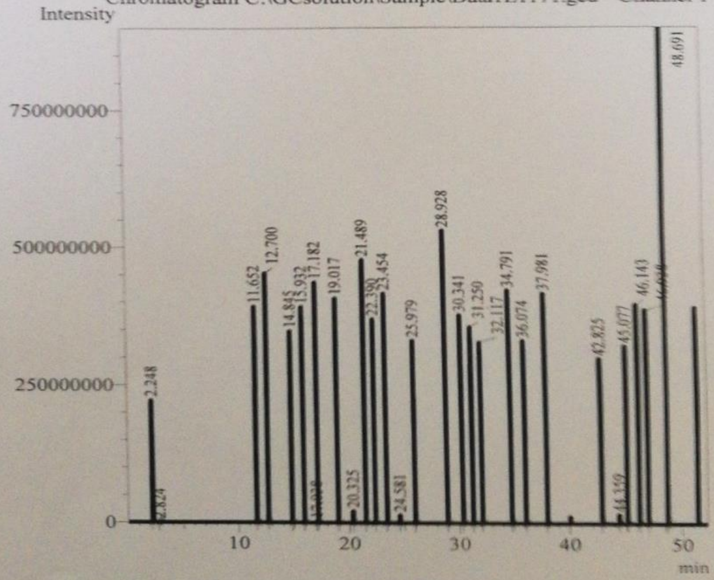
Peak#	Ret.Time	Area	Area%	Height	Name
1	1.726	162976	1.7396	80667	
2	28.931	460296	4.9131	85337	
3	44.633	213622	2.2801	18199	
4	46.557	8531883	91.0672	311012	
Total		9368777	100.0000	495215	

Figure A.6: gas Chromatography (GC) analysis of a commercial mixture of polychlorinated biphenyls, in Abo-Gharib region

Sample Information

07 Mar 2017
User Name :
Sample Name : PCB Standerd (mix 10 ppm)
Injection Volume = 1uL
Tem injector = 280 C
Tem Detector (ECD) = 320 C
Column Oven (SE - 30) = 110 C- 230 (3 C / MIN)
Pressure = 100 KPa

Chromatogram C:\GCsolution\Sample\Data1L1171.gcd - Channel 1



Peak Table - Channel 1

Peak#	Ret.Time	Area	Area%	Height	Name
1	2.248	725144287	7.3220	21058716	
2	2.824	2409	0.0000	705	
3	11.652	376605875	3.8027	80323013	PCB - 18
4	12.700	443915066	4.4823	14951708	PCB - 31
5	14.845	334162383	3.3741	34235937	PCB - 28
6	15.932	375506213	3.7916	76045948	
7	17.038	1912458	0.0193	1355520	PCB - 20
8	17.182	419566021	4.2365	20982113	PCB - 20
9	19.017	390902039	3.9470	93754703	PCB - 52
10	20.325	32991826	0.3331	19585817	
11	21.489	459436243	4.6390	61885322	PCB - 44
12	22.390	362698800	3.6623	55872688	PCB - 44
13	23.454	404723847	4.0866	03866284	
14	24.581	18777519	0.1896	13134754	
15	25.979	325239215	3.2840	15688383	PCB - 101
16	28.928	514062285	5.1906	15652137	PCB - 149
17	30.341	361319553	3.6483	60632169	PCB - 118
18	31.250	342872370	3.4621	29443806	PCB - 153
19	32.117	322573169	3.2571	99611017	PCB - 153
20	34.791	406612535	4.1057	93475581	PCB - 105
21	36.074	316731132	3.1981	97270351	PCB - 138
22	37.981	402139626	4.0605	03642820	
23	42.825	286110281	2.8889	90018064	PCB - 180
24	44.359	21058289	0.2126	15525634	PCB - 170
25	45.077	317483631	3.2057	97825196	PCB - 170
26	46.143	384200963	3.8794	83791967	PCB - 194
27	46.938	374261125	3.7790	57418565	PCB - 101
28	48.547	2176140	0.0220	1752227	PCB - 156
29	48.691	1180515933	11.9199	24209698	PCB - 156
Total		9903701233	100.0000	83010843	

Figure A.7: gas Chromatography (GC) analysis of a commercial mixture of polychlorinated biphenyls, in Abo-Gharib region

الخلاصة

المعادن الثقيلة تشمل الزئبق (Hg) والرصاص (Pb) والكادميوم (Cd) المعروفة على نطاق واسع كونها من السميات, وكذلك التعرض للتاثير السام على جميع البشرمن قبل الملوثات العضوية الثابتة مثل ثنائي الفينيل متعدد الكلور (PCBs) وبيسفينول A (BPA).

لذلك سوف ندرس تأثير الملوثات العضوية الثابتة والمعادن الثقيلة السامة والتلوث في أي نوع من التلوث البيئي الناجم عن العمليات الإرهابية والعسكرية في ثلاث مناطق من بغداد على الغدة الدرقية وعلى الدهون في عينة الدم من العراقيين في منطقتين الكرادة وابوغريب مقارنة مع منطقة الجادرية (المجموعة المسيطرة) .

العلاقة بين هرمونات الغدة الدرقية thyroxine (T4), triiodothyronine(T3), Thyrotropin (TSH), Thyroglobulin-Ab (Tg-Ab) ومستويات الزئبق (Hg) والرصاص (Pb) والكادميوم (Cd) وثنائي الفينيل متعدد الكلور (PCBs) وبيسفينولA (BPA). درست في الأمصال خمسة وسبعون من المتطوعين العراقيين في ثلاث مناطق التي تم تضمينها في هذه الدراسة.تراوحت أعمار الاشخاص تحت الدراسة من 15-65 سنة. تم استبعاد المرضى الذين يعانون من أمراض الغدد الصماء وأمراض الغدة الدرقية .وتحليلنا يشير إلى علاقة عكسية بين التعرض للزئبق وهرمونات الغدة الدرقية, علاقة عكسية بين التعرض للرصاص وهرمونات الغدة الدرقية وثايروجلوبولينTg-Ab, ارتباط إيجابي بين التعرض للزئبق و ثايروجلوبولين Tg-Ab, علاقة طردية بين التعرض للكادميوم وهرمونات الغدة الدرقية و Tg-Ab.وعلاقة طردية بين العناصر الثقيلة مع بعضها . وبالتالي زيادة تعرض للمعادن الثقيلة والملوثات العضوية الثابتة قد يكون عاملا في مسببات أمراض قصور الغدة الدرقية وتعطيل وظيفة الغدة الدرقية.

نتائج هذه الدراسة أظهرت تأثير مصل الدم Hg, مصل الدمPb , مصل الدم Cd, مصل الدم ثنائي الفينيل متعدد الكلور مصل الدم BPA على هرمونات الغدة الدرقية وأثر العمليات العسكرية والعمليات الإرهابية على الغدة الدرقية وثايروجلوبولينTg-Ab

في النهاية نستنتج أن المعادن الثقيلة مثل الزئبق والكادميوم والرصاص وأيضا الملوثات العضوية الثابتة مثل ثنائي الفينيل متعدد الكلور والبسفينول- A الناجمة عن الانفجارات والعمليات الإرهابية في منطقتين (الكرادة و ابوغريب) عالية مقارنة مع منطقة (الجادرية) المجموعة المسيطرة، وهذا يؤدي إلى العديد من الأمراض على صحة جسم الإنسان، وكذلك تأثير المعادن الثقيلة والملوثات العضوية الثابتة على الغدة الدرقية وتأثيرها السلبي على هرمونات الغدة الدرقية وتسبب أمراض الغدة الدرقية.

جمهورية العراق

وزارة التعليم العالي والبحث العلمي

جامعة النهرين

كلية العلوم

قسم الكيمياء

تأثير بعض المعادن الثقيلة على وظائف الغدة الدرقية

رسالة

مقدمة إلى كليه العلوم , جامعة النهرين , وهي جزء من متطلبات نيل درجة

الماجستير في علوم الكيمياء (الكيمياء الحياتية)

من قبل

سارة جواد كاظم

بكالوريوس علوم كيمياء / كلية العلوم/ جامعة النهرين

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