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AN ANALYSIS OF THE QUANTITY OF ZINC AND INTERFERON-GAMMA IN THE SERUM OF INDIVIDUALS SUFFERING FROM CUTANEOUS LEISHMANIASIS IN THE CITY OF SALADIN

RUNNING TITLE : QUANTITY OF ZINC AND INTERFERON-GAMMA IN THE SERUM OF INDIVIDUALS SUFFERING STATUS IN CUTANEOUS LEISHMANIASIS PATIENTS

Author affiliation:

Al-Gburi, Khatab O.1,2,3 and Rebai, Ahmed3

1General Hospital Salahuddin, Qadisiyah, Tikrit, Iraq

2Faculty of Science of Sfax, University of Sfax, Tunisia

3Laboratory of Molecular and Cellular Screening Processes, Centre of Biotechnology of Sfax, University of Sax, Tunisia

Corresponding author:

A. Rebai, Centre of Biotehnology of Sfax, PoBox 1177, 3018 Sfax, Tunisia

Email : ahmed.rebai@cbs.rnrt.tn , Fax :+216.74.875.818

Email (Dr Al-Gburi): communityhealth557@gmail.com

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Ethics : All participants have provided informed consent to the use of their clinical data and biological samples, after anonymization, for the dosage of immunoglobulins, cytokines and others relevant biological analyses. The study have been approved by the ethics committee of the General Hospital Salahuddin, Qadisiyah, Tikrit, Iraq **(GHS1/2019).**

Summary

Zinc is one of the most essential cytokines because it plays a role in the proliferation of cells and tissues and also plays an active part in the body's immune system. Zinc also plays a role in the production of antibodies. In addition to being one of the most important cytokines, kama-interferon

is noteworthy since it is an essential component of the immune system that is found in the human body.

The objective of this study was to first assess how high the levels of gamma-interferon and zinc were in the blood serum of patients who had been diagnosed with cutaneous leishmaniasis and then compare those levels to the levels that were discovered in the control groups.

48 people with cutaneous leishmaniasis were taken during the time period of October 2020 to the end of September 2021 in the dermatology department of the outpatient clinic in Tikrit Teaching Hospital. The percentage of males was 61, which is equivalent to 60.39%, and the percentage of females was 40, which is equivalent to 39.60%. They ranged in age from one year old all the way up to 71 decades old. The youngest was one year old

A spectrophotometer was used to assess the mean concentration of zinc in the serum of all patients with cutaneous leishmaniasis as well as in the serum of control groups. The results of this measurement were compared with one another. The mean concentration of zinc in patients with cutaneous leishmaniasis was found to be 9.6 mmol/L, while in the control groups of those aged 15 years and below, it was 11.4 mmol/L. In males with cutaneous leishmaniasis, the average zinc concentration was 10 mmol/L, whereas in the control groups, it was 11.6 mmol/L. The average zinc content in females with cutaneous leishmaniasis was 9.4 mmol/L, whereas the percentage was significantly higher in the control group, reaching 10.8 mmol/L

In addition, the findings of the research indicated a statistically signifi cant increase in the concentration of gamma-interferon compared with the groups61control (1P0.01) for those aged 15 years and below, where the rate of gamma-interferon in patients was (0.8) unit/ml and in the control groups (0.5) unit/ml, as well as for those aged mor than 15 years, where the rate of gamma-interferon in patients was (0.8 Where the rate of interferon-gamma in males was (1.1) units/ml while in the control groups it was just (0.6) units/ml. In a similar fashion, the average concentration of gamma-interferon in female patients was (0.7) alone/ml, whereas the average concentration in control groups was (0.5) alone/ml

The initial portion of the book, which includes the introductory paragraph

The protozoan parasites that are a part of the genus Leishmania are the organisms that are responsible for the disease known as leishmaniasis. The bite of some species of the sand fly, such as flies belonging to the genus Lutzomyia in the New World and the genus Phlebotomus in the Old World, is how this disease is transmitted from person to person. In the year 1901, a Scottish pathologist by the name of William Pogue Leishman was the one who first referred to the illness by its current name. (1) This disease is also referred to as leishmaniasis, leishmaniasis, Baghdad boil, eastern ulcer, tropical leishmaniasis, tropical leishmaniasis, tropical leishmaniasis, biskra zir, Delhi boil, Aleppo boKandaharahar ulcer, black fever, Kalazar fever, sandfly side, use, and Lahore ulcer.(2 ,1)

Certain strains of the disease can be transmitted from person to person, although the vast majority of the disease can only be transmitted between animals (inside a zoo). 21 of the 30 different kinds of parasites that can infect other mammals are responsible for the infection that affects humans.

They are made up of the letter L. donovani complex, which is made up of three distinct species (L. donovani, L. infantum, and L. chagasi); the L. Mexicana complex, which is made up of three principal species (L. Mexicana, L. amazonensis, and L. venezuelensis); the L. chagasi complex; and the L. chagasi complex. L. Tropica, L. aethiopica, and L. major are the three separate species that make up the L. Tropica complex. L. braziliensis is a complex species that consists of three different species: L. braziliensis, L. guyanensis, and L. panamensis. In spite of the fact that it is not able to identify between the various species based on their outward appearance, it is possible to do so through the utilization of homologous enzyme analysis, DNA sequence analysis, or monoclonal antibodies. (1) The infectious disease known as leishmaniasis is prevalent in 88 different countries spread over the continents of Africa, Asia, Europe, and both the North and South American continents.

The infectious disease leishmaniasis is spread from person to person by the bite of some species of the phlebotomine sandfly. When a sandfly bites a human being or an animal that is already affected with a disease (like a mouse or a dog, for example), the sandfly will also become infected with the disease. In addition, leishmaniasis can be transmitted by blood transfusions, needles that have been contaminated, and even, on the extremely rare occasion, from a pregnant mother to her unborn child. This, however, occurs very infrequently. [5(

There are primarily three different types of leishmaniasis, which can be broken down as follows : [6]

•Cutaneous leishmaniasis, also known as CL, is the most common form of the disease, and its symptoms include the development of a painful sore at the place where the insect bite occurred. This wound will heal within a few months to a year, but it will leave an unattractive scar behind after it does. This form is flexible, and it can be used with either of the other two forms. It also stands alone as a valid form. [6) Visceral leishmaniasis, also known as VL, is the most severe form of the illness and can be fatal if it is not treated. Visceral leishmaniasis is also abbreviated as VL. Fever, malaise in both the liver and the spleen, weight loss, leukopenia, and decreased white blood cell count are all symptoms of VL.

•The formation of skin ulcers, which eventually spread and cause tissue damage (especially to the nose and mouth), is a defining feature of mucocutaneous leishmaniasis. [6(

The infection that is induced by leishmania kicks off a convoluted chain of events in macrophages, each of which has an impact on the immune response that comes after it. One of the most important early signaling events is when infected macrophages start releasing cytokines into the surrounding environment. In response, these cytokines cause the beginning stages of a Th1 response as well as the creation of

interferon-gamma (also known as IFN-). The generation of interferon-gamma is important for the activation of macrophages, which is required for the elimination of pathogens and the protection of the host cell against infection.

The aims and targets in question

The goal of the study was to assess the levels of interferon-gamma (IFN-) and zinc (Zn) in the serum of people who had cutaneous leishmaniasis (CL) and to see if there was any correlation between the two .

The following are some of the goals of this research:

1. Determine how people who have CL are dispersed geographically according to where they live.
2. Determination of the amount of IFN- in the serum. Zinc levels in persons who have chronic lymphocytic leukemia

Differentiating the levels of IFN activity 3

4. Determine how the relationship between IFN and zinc changes with increasing age

An investigation of the part that zinc plays in the immune system 5.

The following are included in the second chapter:

Immunotherapy for those who have chronic lymphocytic leukemia:

(1Conversion factor: A successful treatment outcome that was accomplished by utilizing stable leukocyte extract (transfer factor) acquired from healthy donors who had fully recovered from CL. The patient receives injections of the drug under their skin, subcutaneously, in the area surrounding the skin lesions.

(2Gamma interferon (intralesional): Interferon gamma (IFN-), also known as gamma interferon, is one of the key cytokines produced by T-helper type 1 (Th - 1) cells in experimental leishmaniasis. This cytokine is also known as gamma interferon. It accomplishes this goal by causing macrophages to become more effective at removing intracellular parasites and by lowering the number of immature macrophages that are entering cells. IFN has been shown to be successful in the treatment of disease, but it was not until recently that it was discovered to be beneficial in human situations when it is administered locally or in combination with anti-chhormonal medicines. (7) The T cell, also known as the Th-1 cell, is the cell that is responsible for the production of the co-stimulator of interferon-gamma. This, in turn, encourages the activation of macrophages. The Leishmania parasites will be ingested by these macrophages, and then they will be destroyed by the free oxygen radicals that are produced by oxygen mediators such as H2O2. As a result, the local injection of IFN- it increases cellular immune responses and, as a consequence, assists patients in recovering from cutaneous leishmaniasis in a more expedient manner. (7, 8(

(3BCG: The efficacy of a combination vaccine (thermal killer L.Amazonas is plus viablCalmettete Guerin [BCG]) in the immunotherapy of American cutaneous leishmaniasis was evaluated in a clinical research study that included 217 patients. Over ninety percent of those who were given the immunization saw a complete clinical remission of their symptoms; the median amount of time it took to recover ranged between sixteen and eighteen weeks, which was approximately the same amount of time it took for those who were administered meglumine antimonite (glucantime.(

The field of study known as immunology:

Cytokines are a sort of signaling protein as well as a glycoprotein, and they play a key role in the communication that occurs between cells. Cytokines may be broken down into two subtypes. Cytokines are a family of substances that, in comparison to other types of molecules, contain a greater variety of subtypes and functions. Their origins can also vary. They are created by a wide variety of hematopoietic and non-hematopoietic cell types, and they have the ability to affect cells that are nearby as well as cells located throughout the body. These effects are frequently and significantly influenced by the presence of many additional drugs. The glycoproteins and other water-soluble, smaller proteins that make up the vast majority of the cytokine family are responsible for the majority of its composition. Cytokines are proteins that are involved in the innate as well as the adaptive immune response systems. They play a significant role in both. It is typically secreted by immune cells that come into touch with the pathogen as a method of activating and recruiting more immune cells and increasing the system's response to pathogens. This is done in order to improve the immune system's ability to combat pathogens. This is done in order to boost the system's capacity to fight against infections, which is the primary reason why it is done.

The following is a list of the several types of cytokines:

There is a wide variety of classifications for cytokines, and even within those classifications, there are further subclassifications. The cytokines that are created naturally by the body are listed below, along with the immune cells that are responsible for their production.

Interferons, often known as IFNs, can be broken down into three basic subtypes: the, the, and the. It is brought on by a number of different cells that are found inside the immune system, specifically white blood cells.

•There are more than ten distinct types of interleukins, which are more commonly referred to as ILs. The production of this protein is the responsibility of the leukocytes, which are the white blood cells.

•There are two primary types of tumor necrosis factors, which are also referred to as TNF in some contexts. It is brought on by a variety of cells that are found in the immune system, such as T cells and white blood cells, amongst others.

•Colony-stimulating factors, commonly known as CSFs, are molecules that induce latent stem cells in the bone marrow to differentiate into immune cells known as neutrophils. This differentiation process takes place in response to the presence of CSFs. Neutrophils provide a substantial amount of support for the inflammatory response that is built by the body in response to an infection.

•The kidneys are responsible for the production of the vast majority of erythropoietin in the body. This is accomplished by increasing the number of mature red blood cells produced from stem cells that are already present in the bone marrow.

Cytokines and hormones both exert their effects in remarkably comparable ways. They are secreted into the bloodstream or locally into the tissues that the immune cells are present in by immune cells. Cytokines and the receptors that are located on the cells that are the targets of the immune system interact. This contact sets off a cascade of metabolic responses, which among other cellular activities includes the generation of additional cytokines, cell division, and cell differentiation. The

two distinct populations are referred to by their respective designations, T-helper-1 (Th-1) and T-helper-2 (Th-2). T-helper-1 cells are responsible for the production of interleukin 2, interferon alpha, and tumor necrosis factor, whereas T-helper-2 cells are responsible for the production of interleukin 4, interleukin 5, and interleukin 10.

On their surfaces, lymphocytes and other types of leukocytes express a vast variety of unique molecules that can be utilized to discriminate between (mark) the different types of cell subsets. These molecules are also expressed by several other types of leukocytes. A systematic terminology has been developed, and within this nomenclature, the term "cluster differentiation" (CD) refers to clusters of monoclonal antibody clusters (mAb clusters). This terminology has led to the establishment of a systematic terminology. Each group is firmly attached to a separate molecule in a way that is completely unique to them. The T cell has a variable constant region, which is mirrored in the T cell receptor, which is a transmembrane glycoprotein that is found on the surface of the T cell. The variable constant region of the T cell is located on the surface of the T cell. While the variable regions are the ones that are responsible for binding to a specific antigen, the constant regions only penetrate the cytoplasm to a very limited extent. T cells can be divided into two categories: cytotoxic T cells (CD8+) and helper T cells (CD4+). Cytotoxic T cells are responsible for killing cancer cells

The role of interferon-gamma: 2.1.2 Interferon-gamma 2.1.2. (IFN-) is the sole member of the interferon family that belongs to the class II subfamily. It is the only type of interferon that can be found in this class and is a soluble two-dimensional cytokine. The macrophage activating factor was the previous name that was given to this interferon before it was renamed.

.2.1.3The structure of the IFN: The organization of the IFN A monomer is made up of six different nuclei that are referred to as Hops, in addition to a prolonged unfolded sequence at the C-terminal region. The structure is given a shorter overall length as a consequence of the removal of 17 amino acids from the C-terminal portion of the structure. The sequence has been completely determined, and it has a length of 143 amino acids. The glycosaminoglycan heparin sulfate affinity could not be explained by any of the remaining amino acids in the sequence; it could be explained only by the 17 amino acids that were deleted(12 ,10) .

.2.1.4Biological activity: in contrast to interferon- and interferon-, which are both able to be expressed by any cell, IFN- is only produced by Th-1 cells, dendritic cells, and natural killer (NK) cells. These three cell types are the only ones capable of producing this interferon. IFN-, also known as immunoglobulin interferon, is the only type of interferon that comes in a second iteration. It is also the only type of interferon that can interact with immunoglobulins. It is distinct from type I interferon in terms of its serological characteristics and is susceptible to the effects of acid, whereas variations of type I interferon are resistant to the effects of acid. Interferon-gamma has properties that control the immune system, combat viruses, and limit the growth of tumors. It also helps in the battle against cancer. (10) It has the potential to alter the transcription of up to 30 genes, each of which is responsible for a different cellular and physiological response. The following are some examples of influences: • An increase in the presentation of antigen by macrophages.

•The activation of macrophages, which leads to an increase in the amount of lysosomal activity produced by the macrophages.

•A decrease in the amount of activity seen in the Th2 cell subset.

•The presence of normal cells acts as a trigger for the production of major histocompatibility complex (MHC) class II molecules.

•Stimulates leukocyte adhesion and binding, two processes that are essential to the migration of leukocytes.

•Boosts the effectiveness of the natural killer cells found throughout the body.

IFN-it is able to activate its target cells as a result of its engagement with heterologous receptors that are composed of IFNGR1 and IFNGR2 (interferon-gamma receptors). In contrast to Th-2 cells, which are responsible for the generation of IL-4, Th-1 cells are distinguished by their ability to produce interferon-gamma. Not only natural killer (NK) cells but also CD8+ cytotoxic T cells are capable of producing IFN(10).-

2.1.5The function of IFN- inside the immune system :

Within thirty seconds after an infected female sandfly inoculating a promastigote that binds to immunoglobulin M (IgM), there is an activation of classical complement pathways that leads in the obliteration of the promastigote by the third component of the complement system. This occurs as a result of the third component of the complement system binding to the promastigote and destroying it. This causes the disease that is known as leishmaniasis to start in its early stages. Anti-quake antibodies are deposited on the surface of the parasite, where they enable the parasite connect to its host by interacting with complementary macrophage receptors (CR1, CR2), mannose/fructose fibrils, and FC receptors (104). Antibodies against earthquakes are deposited on the surface of the parasite. Parasites that reside within macrophages are compelled to rely on a variety of bactericidal processes in order to maintain their viability within the cell. Toxic byproducts of oxygen metabolism, lysosomal hydrolysis, a low pH, and cationic protein are all components of these systems, which determine who is hosting(9) .

The production of subsequent phagocytosis and the stimulation of respiratory burst are both outcomes of macrophages' use of intermediate reactive oxygen (ROI), another mechanism by which they exercise their actions. When stimulated by cytokines, typical resident macrophages release significantly more superoxide and hydrogen peroxide than they would under normal circumstances. O2-independent killing mechanisms are present in both types of macrophages. h. These macrophages have the capacity to undergo reactivation on several occasions, which enables them to express a level of (no) synthase that is comparable to the quantity that was initially present. It is not the newly proliferating cells that are to blame for the activation; rather, the re-expression of the absence of a synthase is what is to blame for the activation. Reactivated macrophages have the capability of completely eliminating intracellular protozoans in their whole. There is an insufficient amount of the soluble inducer in the sensitive amice strain. Although there is an increased Th-1 response because IL-10 suppresses s IFN-, nitric oxide is very vulnerable to infection with Leishmania species. This is despite the fact that IL-10 causes there to be an increased

Th-1 response. The continued existence of the parasite within the host cell is made feasible by macrophages' ability to induce a state of non-synthesis in the parasite. The role of IFN- in the regulation of MHC class II Interaction between cytotoxic T lymphocytes (CD8+) and MHC class I (13), which occurs both at the transcriptional level and in repeated infections caused by CL. Effective activation of macrophages in response to an infection with Leishmania if the individual chose to expand active antigen-specific CD4+ T cells. The products that are generated by activated cells as a reaction to Leishmania have an effect on the progression of the disease in mouse strains that are both vulnerable to the infection and resistant to it. an enzyme that can be identified within the cell that can kill it.

When a patient has fully recovered from cutaneous leishmaniasis, the IFN- response that they produce is likely to be their primary immune response. The production was modest, and IL-4 was only infrequently discovered in the supernatants of the peripheral blood mononuclear cells (PBMC) of the patients. The goal of the research that were made more challenging was to determine whether the cells in cultures of Leishmania-activated PBMC had a CD4+ or CD8+ phenotype and what pattern of cytokine production they presented. This was done in an effort to determine which of these two phenotypes the cells displayed. It is usual for IFN- and IL-4 to be produced at the same time in these cultures, which enables the identification of cells that produce IFN-. as CD3+ T cells, and IL-4 and IL-10 respectively. Cytokines have been found in just a tiny fraction of CD8+ cells; nevertheless, the vast majority of these cytokines are found in CD4+ cells. During our research on the simultaneous production of cytokines by T cells in culture, we came upon an unexpected cleavage that involved both IFN and IL-4. This is due to the fact that no cells are capable of carrying both cytokines; as a result, we anticipated discovering a cleavage. production of ce and its derivatives. As a result, the cells that produce cytokines can be broken down into the following categories: (i) individuals who generate IFN-, (ii) individuals who produce IL-4, and (iii) individuals who produce both IFN- and IL-10. (15) The characteristics of the first group of cells correspond to those of type Th-1 cells, whereas the characteristics of the second group of cells correspond to those of type Th-2 cells. On the other hand, the group of cells that produce IFN- and IL-10 does not conform to the conventional concept of Th0, Th-1, or Th-2 cells. These cells produce both of these cytokines.

In addition to the pathways exploited by L, an infection produced by L. major is responsible for activating a number of pathways in the host cell that are necessary for primary infection. These pathways are activated as a result of primary infection. in order to boost the chances of its reproduction and occurrence. There are three possible ways in which Leishmania major might infect a human monocyte cell line: in the presence of interferon-gamma, in the absence of interferon-gamma, or in the presence of IFN-. This is done so that the molecular events that take place in the host cell as a reaction to Leishmania may be analyzed and characterized. In order to examine alon, a high-density human oligonucleotide microarray was deployed. It has been proven that L. major is responsible for the phenomena of reduced phosphorylation of the IFN- receptor in cells that have been infected with Leishmania donovani. This phenomenon has also been demonstrated. When Donovani amastigotes are present, there is a significant and negative effect

on the expression of class II MHC molecules. It is essential to note that the Leishmania parasites prevent the primary synthesis of IL-12 from occurring in the macrophages of the host. This prevents the Canadian signaling from taking place, which, in a healthy immune-complementary host, would trigger the production of IFN-..through the utilization of T lymphocytes and natural killer cells as targets

.1.2.2 interferon-gamma, more commonly referred to as IFN-. The production of interferon-gamma is essential to the activation of macrophages, which is necessary for the clearance of pathogens and the protection of the host cell against infection. Interferon-gamma is produced when the host cell is exposed to a virus or other infectious agent.

The questions at hand concern the goals and objectives.
The objective of the study was to determine whether or not there was a connection between the levels of interferon-gamma (IFN-) and zinc (Zn) in the serum of patients who had cutaneous leishmaniasis (CL) and to determine whether or not there was a correlation between the two.

The following is a list of some of the goals that this research intends to accomplish: 1. Find out how people with CL are spread out across the country in relation to where they live.
.2Ascertain the total amount of IFN- that is present in the serum. Zinc levels in patients with chronic lymphocytic leukemia (CLL). [Medline] Zinc levels in patients with CLL.
.3Putting the various degrees of IFN activity into perspective.
.4Determine how the interaction between IFN and zinc shifts as one's age increases.
.5An examination of the impact that zinc has on the immune system is looked into here.

The following are some of the things that are discussed in the second chapter:
Immunotherapy for patients diagnosed with chronic lymphocytic leukemia aims to:
(1The term "conversion factor" refers to the effective treatment outcome that was attained by utilizing stable leukocyte extract (also known as transfer factor) received from healthy donors who had fully recovered from CL. Injections of the medication are given to the patient subcutaneously, or just beneath the patient's skin, in the region that is surrounding the skin lesions.
Interferon gamma (IFN-), often known as gamma interferon, is one of the major cytokines produced by T-helper type 1 (Th - 1) cells in experimental leishmaniasis. Gamma interferon is administered intralesionally. It is also possible to refer to this cytokine as gamma interferon. It achieves this purpose by encouraging macrophages to become more effective at eliminating intracellular parasites and by reducing the amount of immature macrophages that enter cells. Both of these effects are a result of the reduction in the number of immature macrophages. IFN has been found to be effective in the treatment of disease, but it wasn't until recently that it was discovered to be beneficial in human conditions when it is taken locally or in combination with anti-chhormonal medications. Previously, IFN had been demonstrated to be successful in the treatment of disease. (7) The T cell, also referred to as the Th-1 cell, is the cell in the body that is in charge

of producing the co-stimulator that is needed for interferon-gamma to be produced. As a consequence of this, macrophage activation is promoted. These macrophages will consume the Leishmania parasites, and subsequently free oxygen radicals released by oxygen mediators like H2O2 will kill the Leishmania parasites once they have been digested by the macrophages. Because of this, the local injection of IFN-it boosts cellular immune responses, which, in turn, enables patients to recover from cutaneous leishmaniasis in a manner that is more expeditious ,7) . (8

(3BCG: The efficacy of a combination vaccine in the immunotherapy of American cutaneous leishmaniasis was tested in a clinical research trial that included 217 patients. The vaccine in question was called thermal killer L.Amazonas is plus viablCalmettete Guerin (BCG). Over ninety percent of those who were given the immunization experienced a complete clinical remission of their symptoms; the median amount of time it took to recover ranged between sixteen and eighteen weeks, which was approximately the same amount of time it took for those who were administered meglumine antimonite (glucantime); the time it took to recover ranged between sixteen and eighteen weeks; and the median amount of time it took to recover ranged between sixteen and eighteen weeks.

The scientific discipline that is known as immunology:

Cytokines are both a type of protein that transmits signals and a glycoprotein; in addition, they play an important part in the communication that takes place between different cells. There are two distinct subtypes of cytokines that can be distinguished. Cytokines make up a family of chemicals that, in comparison to other kinds of molecules, have a far wider range of subtypes and functions to choose from. Their beginnings can also be different. They are produced by a wide variety of hematological and non-hematopoietic cell types, and they have the ability to effect cells that are close as well as cells that are situated throughout the body. In other words, they are cytokines. The presence of a large number of other medications can frequently and considerably alter the effects of the primary drug. The majority of the cytokine family is composed of glycoproteins in addition to other water-soluble, smaller proteins. These two types of proteins are responsible for the majority of the family's makeup. Proteins known as cytokines have a role in both the innate immune response system and the adaptive immune response system. They have an important part to play in both of these. It is usually released by immune cells that come into contact with the pathogen as a technique of activating and recruiting more immune cells and enhancing the system's response to pathogens. This is done in order to increase the system's resistance to infections. This is done in order to enhance the immune system's capacity to defend the body against infectious agents. The fundamental motivation for this practice is to improve the body's resistance to infectious diseases, which is why it is carried out in this manner.

The various forms of cytokines can be broken down into the following categories:

Cytokines can be categorized in a broad range of ways, and even within those categories, there are more subcategories that can be applied. Below is a list of the cytokines that are naturally produced by the body, along with the immune cells that are responsible for their production.

Interferons, also referred to as IFNs, can be subdivided into three primary subtypes, which are denoted by the letters,, and respectively. It is brought on by a variety of cells that can be discovered within the immune system, more specifically white blood cells.

Interleukins, or ILs for short, are a group of proteins that are involved in a variety of biological processes. There are more than 10 unique types of interleukins. The leukocytes, also known as white blood cells, are the ones in charge of the production of this particular protein in the body.

•The term "tumor necrosis factor," which is abbreviated as "TNF," can refer to either of the two basic types of tumor necrosis factors. It is caused by a number of different cells that can be found in the immune system. These cells include T cells and white blood cells, amongst others.

•Colony-stimulating factors, also known as CSFs, are chemicals that cause dormant stem cells in the bone marrow to develop into immune cells called neutrophils. This process takes place in response to the presence of CSFs. This process of differentiation occurs as a direct result of the presence of CSFs in the environment. In reaction to an infection, the body mounts an inflammatory response, which is supported by neutrophils to a significant degree by the substantial quantity of assistance they provide.

•The kidneys are the organs in the body that are in charge of producing the great majority of the erythropoietin that is found in the body. Increasing the number of mature red blood cells that are created from stem cells that are already present in the bone marrow is the method that is used to achieve this goal.

Cytokines and hormones, in terms of the mechanisms in which they exert their effects, are very similar. Immune cells are responsible for secreting these substances into the circulatory system or directly into the tissues in which they are located locally. Interaction occurs between cytokines and the receptors that are found on the cells that the immune system is attempting to destroy or protect. This interaction triggers a chain reaction of metabolic responses, some of which include the production of more cytokines, cell division, and cell differentiation, amongst other cellular functions. T-helper-1 (Th-1) and T-helper-2 (Th-2) are the two different populations that are referred to by their respective identities. Interleukin 2, interferon alpha, and tumor necrosis factor are produced by T-helper-1 cells, whereas interleukin 4, interleukin 5, and interleukin 10 are produced by T-helper-2 cells. T-helper-1 cells are responsible for the generation of these cytokines. On their surfaces, lymphocytes and other types of leukocytes express a large array of one-of-a-kind molecules that can be exploited to differentiate between (mark) the many types of cell subsets. These molecules can be found on the surface of lymphocytes and other types of leukocytes. These molecules are also expressed by a variety of leukocytes that are not white blood cells. Within this systematic terminology, the word "cluster differentiation" (CD) refers to clusters of monoclonal antibody clusters, which are also referred to as mAb clusters. A systematic terminology has been devised. A more organized method of terminology has been developed as a result of using this terminology. Every group has its own one-of-a-kind method for securing a solid attachment to a different molecule from the other groups. A variable constant region is present in the T cell, and this region is mirrored in the T cell receptor, which is a transmembrane glycoprotein that is located on the surface of the T cell. On the surface of the T cell is where you'll find the variable constant

area of the T cell. Although the variable portions are the ones that are in charge of binding to a particular antigen, the constant regions can only penetrating the cytoplasm to a very restricted degree due to their structure. Helper T cells (CD4+) and cytotoxic T cells (CD8+) are the two types of T cells that may be distinguished from one another. Cytotoxic T cells are the cells that are in charge of eliminating cancer cells.

Interferon-gamma and its function: 2.1.2 Interferon-gamma and its function. There is only one member of the interferon family that is classified under the class II subfamily, and that member is (IFN-). The fact that it is a soluble two-dimensional cytokine and the fact that it is the only type of interferon that can be discovered in this class both make it unique. Before it was renamed, this interferon was known by its prior name, which was the macrophage activating factor (macrophage activating factor).

.2.1.3The organization of the IFN A monomer is made up of six distinct nuclei that are referred to as Hops, in addition to a longer unfolded sequence at the C-terminal region. This makes up the structure of the IFN. The removal of 17 amino acids from the structure's C-terminal region resulted in the total length of the structure being reduced as a direct consequence of this change. The sequence has been thoroughly analyzed, and it was found to consist of 143 different amino acids in total. Because of this, the glycosaminoglycan heparin sulfate affinity could not be described by any of the amino acids that were left in the sequence; rather, it could be explained only by the 17 amino acids that had been removed(12 ,10) .

.2.1.4Biological activity: in contrast to interferon- and interferon-, which can both be expressed by any cell, IFN- can only be produced by Th-1 cells, dendritic cells, and natural killer (NK) cells. Both interferon- and interferon- can be expressed by any cell. Only these three types of cells are able to produce this interferon. It cannot be produced by any other cells. The only type of interferon that comes in a second iteration is IFN-, which is also known as immunoglobulin interferon. In addition to this, there is no other form of interferon that is capable of interacting with immunoglobulins than this one. In terms of its serological properties, it is distinct from type I interferon. Additionally, it is susceptible to the effects of acid, whereas variations of type I interferon are resistant to the effects of acid. Interferon-gamma has qualities that have the ability to govern the immune system, fight viruses, and inhibit the formation of cancers. Additionally, it is useful in the fight against cancer. (10) It has the capacity to change the transcription of up to 30 genes, each of which is responsible for a different cellular and physiological response. Each gene is responsible for a different reaction. Some examples of influences include the following: • An increase in the presentation of antigen by macrophages.

•The activation of macrophages, which results in an increase in the quantity of lysosomal activity produced by the macrophages; this rise is caused by the activation of macrophages.

•A lessening in the overall level of activity that can be noted in the Th2 cell subset.

•The presence of normal cells serves as a trigger, which initiates the creation of major histocompatibility complex (MHC) class II molecules.

•Encourages the adhesion and binding of leukocytes, which are two processes that are necessary for the migration of leukocytes.

•Increases the efficiency of the body's own natural killer cells, which are located all throughout the body.

IFN-it is able to activate the cells it is targeting as a result of its interaction with heterologous receptors, which are made up of interferon-gamma receptors (IFNGR1 and IFNGR2). Interferon-gamma production is what differentiates Th-1 cells from their counterparts, Th-2 cells, which are responsible for the production of IL-4. Th-1 cells, on the other hand, have the capacity to make interferon-gamma. IFN- may be generated not only by natural killer (NK) cells but also by CD8+ cytotoxic T cells.(10)

2.1.5The role that IFN- plays inside the body's immune system :

Within thirty seconds after an infected female sandfly inoculating a promastigote that binds to immunoglobulin M (IgM), there is an activation of classical complement pathways that leads in the obliteration of the promastigote by the third component of the complement system. This occurs when an infected female sandfly inoculates the promastigote that binds to immunoglobulin M (IgM). This is because the third component of the complement system binds to the promastigote and causes it to be destroyed as a result of the interaction. This triggers the beginning stages of leishmaniasis, which is a disease that affects the body's immune system. Anti-quake antibodies are deposited on the surface of the parasite, where they enable the parasite to attach to its host by engaging with complementary macrophage receptors (CR1, CR2), mannose/fructose fibrils, and FC receptors (104). Antibodies against earthquakes are deposited on the surface of the parasite. On the surface of the parasite, there are earthquake-fighting antibodies that have been deposited. Within macrophages, parasites are forced to rely on a variety of bactericidal activities in order to preserve their viability within the cell. This is necessary for the parasites to be able to survive. Components of these systems, which together decide who is hosting, include toxic byproducts of oxygen metabolism, lysosomal hydrolysis, a low pH, and cationic protein(9) .

The utilization of intermediate reactive oxygen (ROI) by macrophages, which is another way by which they carry out their operations, results in the generation of subsequent phagocytosis and the stimulation of respiratory burst. The emission of much more superoxide and hydrogen peroxide from ordinary resident macrophages than they would under normal circumstances occurs when the macrophages are stimulated by cytokines. Killing mechanisms that are not dependent on oxygen can be found in both types of macrophages. h. These macrophages have the ability to go through reactivation on multiple occasions, which enables them to express a level of (no) synthase that is comparable to the quantity that was initially present. This capacity to undergo reactivation multiple times gives these macrophages the ability to express this level. The activation is not caused by the newly proliferating cells; rather, it is caused by the re-expression of the absence of a synthase, which is what is to blame for the activation. Reactivated macrophages have the potential to eradicate intracellular protozoans in their whole, making them capable of performing their function to the fullest. Within the sensitive amice strain, the amount of the soluble inducer that is present is insufficient. Nitric oxide is extremely susceptible to infection with Leishmania species, despite the fact that there is an increased Th-1 response as a result of IL-10's ability to inhibit s IFN-. This is

despite the fact that IL-10 is responsible for an enhanced Th-1 response being produced in the body. Because macrophages have the potential to produce a state of non-synthesis in parasites, it is possible for parasites to continue to live inside the cells of their hosts for an indefinite amount of time. Interaction between cytotoxic T lymphocytes (CD8+) and MHC class I (13), which takes place both at the transcriptional level and in repeated infections caused by CL. The involvement of IFN- in the regulation of MHC class II. If an individual decides to grow active antigen-specific CD4+ T cells in response to a Leishmania infection, there is an increased likelihood of effective activation of macrophages. In mouse strains that are susceptible to the infection as well as resistant to it, the products that are created by activated cells as a reaction to Leishmania have an effect on the progression of the disease. an enzyme that is present within the cell and has the ability to eradicate it, and which can be located.

The IFN- response that a patient produces is likely to be their predominant immune response once they have fully recovered from cutaneous leishmaniasis. The production was not very high, and IL-4 was only sometimes found in the patients' supernatants of their peripheral blood mononuclear cells (PBMC). The purpose of the study, which was made more difficult to accomplish, was to identify whether the cells in cultures of Leishmania-activated PBMC had a CD4+ or CD8+ phenotype and what pattern of cytokine production they displayed. This was the goal of the research that was made more difficult. This was done in an effort to find out which of these two phenotypes the cells exhibited so that we could proceed accordingly. It is typical for both IFN- and IL-4 to be produced at the same time in these cultures; as a result, it is possible to single out the cells that are responsible for the production of IFN-. as CD3+ T cells, as well as IL-4 and IL-10, in the appropriate order. Only a very small percentage of CD8+ cells were revealed to have cytokines; nevertheless, CD4+ cells were discovered to contain the overwhelming bulk of these cytokines. During the course of our investigation into the concurrent synthesis of cytokines by T cells when they are grown in culture, we stumbled upon an unanticipated cleavage that involved both IFN and IL-4. This is because there is not a single type of cell that is capable of transporting both cytokines. As a consequence of this, we anticipated finding a cleavage. manufacturing of ce and all of its derivatives. As a consequence of this, the cells that generate cytokines can be classified into the following subgroups: (i) individuals that make IFN-, (ii) persons that generate IL-4, and (iii) individuals that generate both IFN- and IL-10. (15) The characteristics of the first group of cells are similar to those of type Th-1 cells, while the characteristics of the second group of cells are similar to those of type Th-2 cells. On the other hand, the group of cells that produce IFN- and IL-10 does not fit the traditional definition of Th0, Th-1, or Th-2 cells. These cells produce both of these cytokines. These cytokines are produced by the cells that are being discussed.

In addition to the pathways that L uses to replicate itself, an infection that L produces. main is responsible for activating a variety of pathways in the host cell that are crucial for primary infection. These pathways are activated when primary infection takes place. These pathways become active as a direct consequence of the initial infection. in order to increase the likelihood of its reproduction and occurrence in the wild. It is feasible for Leishmania major to infect a human

monocyte cell line in one of three different ways: either in the presence of interferon-gamma, in the absence of interferon-gamma, or in the presence of IFN-. This is done in order to evaluate and define the molecular processes that take place in the host cell as a reaction to Leishmania. These actions take place as a result of the infection caused by Leishmania. In order to investigate alon, a human oligonucleotide microarray with a high density was used. It is a well-established fact that L. major is to blame for the decreased phosphorylation of the IFN- receptor that is observed in cells that have been infected with Leishmania donovani. It has also been proved that this phenomenon occurs. There is a considerable and unfavorable effect on the expression of class II MHC molecules when Donovani amastigotes are present. This effect is caused by Donovani. It is critical to keep in mind that the Leishmania parasites are responsible for preventing the primary synthesis of IL-12 from taking place in the macrophages of the host. This stops the Canadian signaling from occurring, which, in a healthy immune-complementary host, would activate the synthesis of IFN-through the usage of T lymphocytes and natural killer cells as targets. This would trigger the production of IFN-in a healthy immune-complementary host.

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.8One vial containing 12 milliliters of streptavidin-HRP conjugate.

Figure (3.1): The kit that is used to measure serum interferon-gamma.

3.2.Preparation of reagents:

Equilibrate the kit components for 30 minutes at room temperature before use. Dilute 50 mL of wash solution (20 times) with 950 mL of distilled water mentioned on the vial label. Wait at least 30 minutes after thawing before dispensing and mix gently to avoid foaming, this will result in 250 IU/ml IFN-γ γ The solution. From the 250 IU/mL titrant and the appropriate diluent, prepare a new dilution series in plastic tubes before each test as described below:

Calibrator concentration	**IFN-γ**	**Diluent**
25 IU/ml	50 µL of 250 IU/mL	450 µl
6.25 IU/ml	100 µL of 25 IU/mL	300 µl
1.56 IU/ml	100 µL of 6.25 IU/mL	300 µl
0.39 IU/ml	100 µL of 1.56 IU/mL	300 µl
0 IU/ml		300 µl

3.2.1. Procedure:

Step 1-

1) Add 50 µl of calibrator or sample to each well.
2) Incubate for 2 hours at 18-25°C while shaking.
3) Wash the well.

Step 2-

1) Add 50 µl of biotinylated antibody and 100 µl of the streptavidin-HRP conjugate.
2) Incubate for 30 min at 18-25 °C with shaking.
3) Flush the wells.

Step 3-

1) Add 100 µl of the substrate.
2) Incubate for 20 min at 18-25 °C while shaking.
3) Add 50 µl of stop solution.
4) Read the absorbance at 450 nm.

3.2.1.3. consequences:

The sample results are calculated by interpolating from the calibration curve performed in the same test as given below:

IFN-Titration γ (IU/ml)	**absorption**	**Sample concentration**

0	19	7.4
0.39	49	5.8
1.56	131	1.6
6.25	506	0.1
25	1940	0.5

3.2.3. Determination of Serum Zinc:

Serum zinc was estimated by spectrophotometer using a zinc kit (LTA Sri-via Milano), as shown in Figure (3.2).

3.2.3. The machines and the equipment:

Cecil 1011 Spectrophotometer.

. Centrifuge from Hitachi 05p-21, Japan.

. Members Water Bath, Japan.

. Ordinary Sterilization Tube Avma Dispo, Z/5.

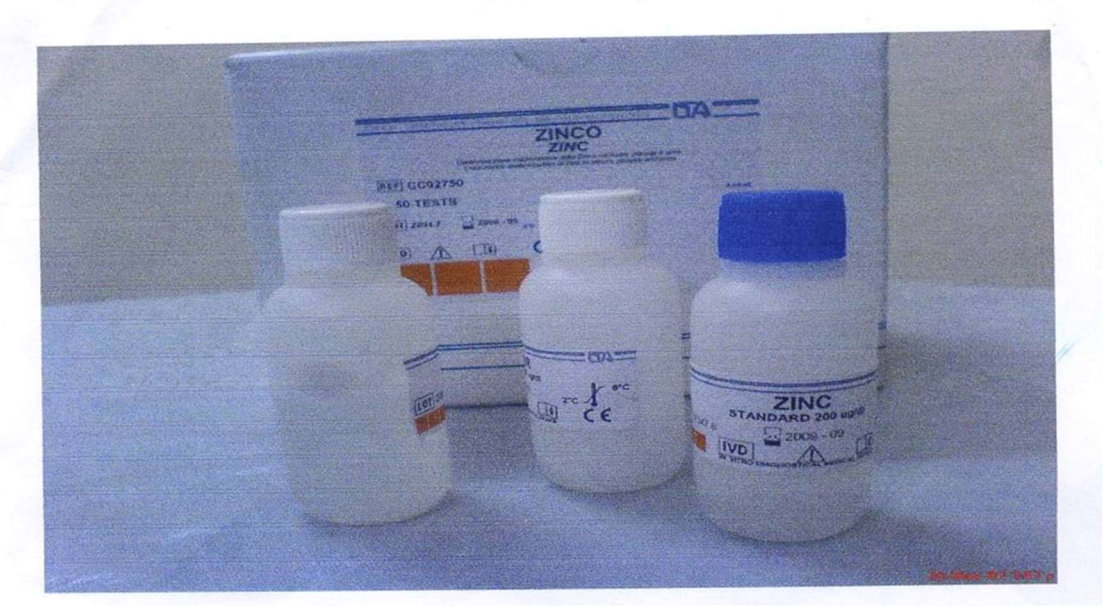
3.3.3. method:

Serum zinc is measured using a zinc kit. The zinc concentration in the serum samples of both patients and controls was measured by evaluating the color intensity resulting from the interaction of zinc in the samples with the presence of chromagen in the reagent forming a colored complex. The color intensity is proportional to the zinc concentration present in the sample. Color intensity is determined using a spectrophotometer.

3.4 Statistical Analysis:

All results were analyzed using:

1. mean average).
2. Standard error.
3. Standard deviation SD.
4. Student's test to compare the means of two groups.



Any p-value less than 0.05 was considered significant.

Figure (3.2): Kit used to measure zinc

4.1 Zinc level in serum of CL patients and control:

Figure (4.7) shows that the zinc concentration in 15-year-old patients was (9.67) µmol/L and in the control group it was (10.9) µmol/L. This relationship was significant ($P < 0.01$).

The results in Figure (4.8) showed that the serum zinc level of both patients and control groups over 15 years old was 9.9 µmol/L and 11.1 µmol/L, respectively. This relationship was statistically significant ($p < 0.01$).

The data in Table (4.6) showed that in CL patients 15 years old, the mean zinc concentration was 9.6 µmol / l, and in those patients over 15 years old, it was 9.7 µmol / l.

The mean zinc concentration in male patients was 10.0 µmol/L and in the male control, it was 11.6 µmol/L. The mean zinc concentration in female patients was 9.4 µmol/L, in contrast to the female control it was 10.8 µmol/L, as shown in Table (4.7). This relationship was statistically significant, (p-value < 0.01).

Age	case definition	n	Do you know?	Sexually transmitted diseases. deviation	P value (DF)
≤ 15 years	control	22	11.4 µmol/L	2.0	< 0.05 (44) *
	cases	25	9.6 µmol/L	1.8	
> 15 years	control	23	10.9 µmol/L	2.2	< 0.05 (43) *
	cases	26	9.7 µM/L	1.3	

Table (4.6) average zinc concentration in different age groups.

Sex	case definition	N	Do you know?	Sexually transmitted diseases. deviation	P value (DF)
Mention	control	19	11.6 µmol/L	1.9	< 0.05 (36) *
	cases	22	10.0 µL/L	1.5	
Feminine	control	26	10.8 µmol/L	2.2	< 0.05 (51) *
	cases	28	9.4 µM/L	1.5	

Table (4.7): Average concentration of zinc among different sex groups.

4.2

Interferon-gamma level in CL patients and control:

IFN-γ serum levelsin patients CLwase higher than those in the control group. In the age group less than 15 years, it was 0.81 l/ml and 0.53 l/ml, respectively. This relationship was statistically significant (p-value < 0.05) as shown in Figure (4.9). However, the serum IFN-γ level CClin patients were higher than the control at age >15 years, it was 0.97 IU/mL and 0.58 IU/mL, respectively. This relationship was also statistically significant (P value < 0.01) as shown in Figure (4.10).

Table (4.8) shows the average concentration of IFN-γ *γ* In CL patients younger than 15 years old, it was 0.8 IU/mL, while in patients over 15 years old, it was 1.0 IU/mL. mean IFN-γ concentration in male patients was 1.1 IU/ml, while it was 0.6 IU/ml in male control. It was observed that the mean IFN- *γ* The concentration in female patients was 0.7 IU/ml and in the female control I,t was 0.5 IU/ml, as shown in (Table 4.9). This result was statistically significant (p-value < 0.01).

Age	case definition	N	Do you know?	Sexually transmitted diseases. deviation	P value (DF)
≤ 15 years	control	23	0.5 IU/ml	0.3	< 0.05 (47) *
	cases	27	0.8 IU/ml	0.6	
> 15 years	control	25	0.6 IU/ml	0.4	< 0.05 (45) *
	cases	24	1.0 IU/ml	0.6	

Table (4.8): Mean IFN-γ concentration among different age groups.

Sex	case definition	N	Do you know?	Sexually transmitted diseases. deviation	P value (DF)
Mention	control	21	0.6 IU/ml	0.4	< 0.05 (40) *
	cases	23	1.1 IU/ml	0.7	
Feminine	control	27	0.5 IU/ml	0.3	< 0.05 (52) *
	cases	27	0.7 IU/ml	0.5	

Table (4.9): Mean IFN-γ concentration by sex.

Figure (4.10) shows the distribution of IFN-γ concentration in CL patients and control groups. showed that in more than 20% of CL patients the IFN-γ concentration was 0.5 IU/mL, and in less than 80% of them, it was IFN-2 IU/mL. This figure also shows that in more than 20% of the control the level of IFN-γ was 0.25 IU / ml, and in less than 80% of the IFN-γ, it was 1 IU / ml.

Chapter weave:-

5.1 Zinc concentration in the serum of CL patients:

Zinc is an essential element for all living things. In man, the growth and development of the body are strictly dependent on the element zinc. Zinc is a cofactor for more than 300 enzymes that affect the functions of various organs that have a secondary effect on the immune system. Direct effects of zinc on the production, maturation, and function of leukocytes. (29)

The data showed that the serum zinc concentration in all cutaneous leishmaniasis patients at different ages (<15 years and more than 15 years) was significantly reduced ($p < 0.01$). Cutaneous leishmaniasis is an infectious disease and people with zinc deficiency are more susceptible to infectious diseases. This result can be explained that CL patients may already have zinc deficiency and thus develop CL. Even the decrease in the serum zinc level of CL patients may be due to the defense mechanism or that Leishmania itself could be involved in the low serum zinc level through the proliferation and synthesis of Zn metalloenzyme glycoproteins (gp63), the entire surface of Leishmania consuming zinc ions from host cells Cells will replace this consumption of serum. (30) This is consistent with what was found by Murthy A, et al. Organisms. Regarding zinc concentration in CL patients, the result in this study is in agreement with the finding that there was a decrease in zinc concentrations and iron levels in theserum of CL patients.

This result is also in agreement with M. Farhadi. (30) who found that mean serum zinc concentration was significantly lower in CL patients because low serum zinc plays a role in exacerbating skin infection. It was also found that a low level of zinc in the blood correlates with the severity of the skin lesion. In addition, patients with zinc deficiency are very susceptible to skin infections such as staphylococcus, viral infection, and parasitic infection, so low zinc levels in the blood may be due to the defense mechanism during the acute phase of infection. Most microorganisms require Zn in a certain amount for basic cellular processes, during the acute phase response zinc is redistributed from plasma to liver and lymphocytes. It has been suggested that this is an adaptive response aimed at depriving invading pathogens of zinc.

Even so in the United States, analysis of serum zinc data from the Second National Health and Nutrition Examination Survey showed the lowest concentration of zinc in the serum of young children and the elderly, during aging there is a significant loss of both immune function and zinc status. Several researchers have tested the hypothesis that zinc supplementation can improve immune function in older adults. The daily intake should be adjusted according to the state of health since the stable state of zinc is regulated not only by absorption but also by fluctuations in zinc excretion related to the number of diseases and infections. ,Interestingly healthy elderly subjects have decreased serum zinc levels, which may be due to decreased absorption or increased excretion.

The serum zinc level was measured in the serum of CL patients and the control serum of both sexes in this work. It reveals that the mean serum zinc in male and female patients is slightly lower than in the control groups, so both sexes are susceptible to CL. This is in agreement with M. Thus, leukocyte endogenous mediators (interleukins), released from activated phagocytes, induce a decrease in serum zinc by redistributing zinc from the plasma to the liver. Low serum zinc levels appear to result from methalothionine (MT) synthesis in the liver and other tissues. The methalothionine binds 7 g of zinc atoms/mol and serum to pull zinc away from free pools, resulting

in lower serum zinc. Azad's thesis wasrevealed. (34) that in male and female patients aged >15 and <15 years, CD4+ significantly decreases compared to the control groups (P<0.01). The decrease in mean CD4+ may be related to zinc deficiency and the inability of CL patients to clear the infection.

The peripheral lymphoid organs and T lymphocytes were gradually depleted from the lymph nodes and spleen. and peripheral blood. Fernand J et al. agree (32) however, who found that the number of T lymphocytes was decreased in the zinc-deficient child. As explained by Ruhl, et al. They were included in our study to eliminate theinfection. The innate and specific parts of the immune system are affected by zinc, therefore, zinc is essential even in the early stages of the immune response. Zinc deficiency not only affects neutrophil recruitment but also reduces neutrophil chemotaxis.

Allen et al. (143) to Zn as a monocyte/macrophage activator, and the significant decrease in Zn in CL patients may be responsible for the patient's inability to clear the parasite despite elevated IFN-γ γ levels and several rounds of treatment. Zinc imbalance may be a sign of reduced Th1 response and immunodeficiency in leishmaniasis. Thus low zinc levels may be a cause rather than a consequence of CL. As seen above, the change of serum zinc is likely dependent on cytokines, especially IL-1, so serum Zn concentrations may have been altered by the same immune cells as the organism's host defense strategy during CL infection.

These results are consistent with those of Coto et al.32) and Wellinghausen et al (26) argue that zinc deficiency affects CD8+ T-lymphocyte proliferation, and zinc deficiency is associated with decreased T-cells. Proliferation after mitogen stimulation, even zinc deficiency in CL affected the phenotypic distribution of CD3+, CD4+, and CD8+ splenic T lymphocytes. Kocyigit et al. (162) reported that essential serum trace elements such as Zn and Cu may have been altered by the same immune cells as an organism's host defense strategy during CL infection. So the change of serum zinc is dependent on cytokines, especially IL-1 and TNF-α , although he could not quantify this immunomodulatory action, some observations have shown that the production of IL-1 and TNF-α It was caused by cutaneous leishmaniasis.

5.2 INF. concentration-γ In the serum of patients with CL:

Interferon-gamma-stimulated macrophages are more phagocytic, better able to kill intracellular pathogens, and have an increased ability to present antigens. Interferon-gamma has a role in activating macrophages to kill pathogens and protect the host cell from infection.

The results showed an elevated level of interferon-gamma in the blood serum of cutaneous leishmaniasis patients in all age groups. This result was agreed with Argemiro D. (33) As these patients had a strong Th-1 immune response andan intense inflammatory reaction. It cannot be excluded that a strong and uncontrolled inflammatory reaction is involved in the pathogenesis of skin ulcers.

Concerning reference CD4+ T lymphocytes, Th1 cells transactivate IL-2 and IFN-γ. γ and TNF-α While Th-2 locks in IL4, IL-6, and IL-10. Interferon-gamma is responsible for activating macrophages to produce nitric oxide to eliminate intracellular microorganisms such as amastigotes from Leishmania, while IL-10 is responsible for IFN-γ inactivation.

During the results of this work, the average level of IFN-γ γ In patients' CL increases in both males and females in contrast to the control. Argiro D. (168) revealed in his study that there are no differences in both females and males, he measured IFN-γ γ and TNF- α Serum levels in CL patients anddemonstrated that IFN-γ γ It is the main cytokine involved in the functioning of macrophages and with tumor necrosis factor stimulation of nitric oxide synthesis. It also showed that the CD4+/CD8+ ratio was significantly decreased in males and females and this affects the secretion of Th-1 and Th-2 cytokines, and thus there is an increase in IFN-γ γ level. (33)

This result is consistent with Azad's thesis.2 inches L patients with zinc deficiency. This is consistent with what Prasad found, (34) who demonstrated that cytotoxic T cells and helper T cells are affected by zinc deficiency and that zinc deficiency leads to an imbalance between Th-1 and Th-2 function and alters the secretion of typical Th-1 and Th-2 cytokines during zinc depletion. Moreover, this is consistent with that found by Shi NH. Which found that mild zinc deficiency produces an imbalance between humoral and humoral immunity. It has even been found that zinc depletion may affect the Th-1/Th-2 switch and this significantly determines the development of diseases.

Karamzin found A. (35) that the serum level of IL-10 and IFN-γ γ In CL patients were significantly higher than incontrol, indicating that Leishmania-specific T cells produce IL-10 and IFN-γ.It γ is enlarged as a result of infection. It was found that only one IFN-γ lymphokine leads to the elimination of amastigote by peritoneal macrophage secretions.

This finding is also consistent with that of Suazo N. (36), showing that macrophages were synchronously diminished, while IL-12 produced Langerhans cells and interferon gamma-producing natural killer cells and increased CD8+ lymphocytes. During the exogenous administration of interferon-gamma, the ability of the parasites to inhibit the oxidative impulse of the patient's monocytes was abolished.

6. Conclusions and Recommendations

6.1 Conclusions:-

1. All patients with cutaneous leishmaniasis have a low level of zinc in their serum.
2. Increased incidence of cutaneous leishmaniasis in areas where there are animals.
3. The sand fly bites the exposed parts of the body.
4. Most patients with cutaneous leishmaniasis have multiple lesions.

6.2. Recommendations:-

From the results of the current study, the following recommendations can be suggested:

1. Furthermore, he examined cytokine levels in CL patients such as IL-1, Il-2, and TNF- α and IL-4, IL-5, IL-6, IL-8, and IL-12 cytokines.
2. Moreover, study the trace elements such as iron, copper, selenium, cadmium, magnesium, and nickel in CL patients and their efficacy in immunity.
3. Moreover, a study on the effect of decreased serum IFN-γ. γ On the immune system of CL patients.

4. Oral zinc supplementation to enhance the immune system in zinc-deficient CL patients to eliminate the intracellular parasite and replace zinc deficiency.
5. Examining the effect of zinc deficiency in CL patients on natural killer cells, macrophages, neutrophils, synovial cells, and basophils.
6. Mesh windows.
7. IgM cutaneous leishmaniasis specific antibody screening, IgE IgG
8. Measurement of CD4+ and CD8+ in peripheral blood lymphocytes in all CL patients.

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