RELATIONSHIP BETWEEN PSORIASIS AND ‘SOME ENDOCRINE DISORDERS (HYPOTHYROIDISM, HYPERTHYROIDISM AND DIABETES MELLITUS)

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CHAPTER ONE
INTRODUCTION

1.1. Background

Autoimmune diseases are chronic conditions initiated by the loss of immunological tolerance to self—antigens. They constitute heterogeneous group of disorders, in which multiple alterations in the immune system result in a spectrum of syndromes that either target specific organs or affect the body systematically.[1]

Recent epidemiological studies have shown a possible shift of one autoimmune disease to another or the fact that more than one autoimmune disease may coexist in a single patient or in the same family. Numerous autoimmune diseases have been shown to co-exist frequently with thyroid autoimmune diseases.[2]

Psoriasis, a common papulosquamous disease of the skin, affects about 1-3% of the population, with a peak incidence in the third decade of life.[3]

The cause of psoriasis remains obscure, but a family history is found in 30% of patients and HLA-CW6 is most strongly associated with it. Despite the elucidation of numerous biochemical abnormalities affecting cyclic nucleotides, polyamines and arachidonic acid metabolism, immunological abnormalities of both humoral and cell mediate immunity and recently free radical generation abnormality, the pathogenesis of psoriasis has remained unclear; but some factors are known to be able to trigger, precipitate or aggravate the disease process, including drugs, severe sunlight and rarely metabolic disorders such as
hypocalcemia of primary or secondary type.[4]

Many studies have been done on psoriasis some of which were concerned with the pathogenesis of psoriasis, and others considered psoriasis as systemic disease.

1.2. AIM OF STUDY
This study aims to investigate the association between psoriasis and thyroid disorders (hypo and hyperthyroidism), diabetes mellitus, and family history relationship.

1.3. OBJECTIVES
• From the history, identify the percentage of diabetes mellitus cases, in psoriatic patients.
• Identify the family history relationship of psoriatic patients.
• Investigate the psoriatic patients for thyroid function tests, T3, T4, and TSH to identify the association between psoriasis and thyroid disorders.
• Classify the psoriatic patients, according to gender, age, types and duration of disease.

CHAPTER TWO
Literature Review
2.1. Psoriasis Definition
Psoriasis is a common skin disease characterized by thickened patches of inflamed, red skin covered with thick silvery scales. The elbows and knees are the most common areas affected by psoriasis. It will often appear in the same place on both sides of the body, the patches can range in size from smaller than a dime to larger than a hand.[5]

Normally, skin cells mature and shed after about a month. In psoriasis, the cell maturation speeds up, taking only three to four days. Because the lower layer of skin cells divides more rapidly than normal, dead cells accumulate in thicker patches on the skin's outermost layer (called the epidermis).[6]

2.2. Types of Psoriasis
Psoriasis appears in a variety of forms with distinct characteristics. Typically, an individual has only one type of psoriasis at a time. Generally, one type-of psoriasis will clear and another form of psoriasis will appear in response to a trigger.[7]

2.2.1. Plaque Psoriasis (psoriasis vulgaris)
Plaque psoriasis (psoriasis vulgaris) is the most prevalent form of the disease. About 80
percent of those who have psoriasis have this type. It is characterized by raised, inflamed, red
lesions covered by a silvery white scale, it is typically found on the elbows, knees, scalp and
lower back.[8]

2.2.2. Guttate Psoriasis
Guttate [GUH—tate] psoriasis is a form of psoriasis that often starts in childhood or young
adulthood. The word guttate is from the Latin word meaning "drop." This form of psoriasis
appears as small, red, individual spots on the skin. Guttate lesions usually appear on the trunk
and limbs. These spots are not usually as thick as plaque lesions.[9]

Guttate psoriasis often comes on quite suddenly. A variety of conditions can bring on an
attack of guttate psoriasis, including upper respiratory infections, streptococcal throat
infections, tonsillitis, stress, injury to the skin and the administration of certain drugs
including antimalarials and beta-blockers.[10]

2.2.3. Inverse Psoriasis
Inverse psoriasis is found in the armpits, groin, under the breasts, and in other skin folds
around the genitals and the buttocks. This type of psoriasis appears as bright-red lesions that
are smooth and shiny. Inverse psoriasis is subject to irritation from rubbing and sweating
because of its location in skin folds and tender areas. It can be more troublesome in
overweight people and those with deep skin folds.[11]

2.2.4. Pustular Psoriasis
Primarily seen in adults, pustular psoriasis is characterized by white blisters of noninfectious
pus (consisting of white blood cells) surrounded by red skin.[12]

Pustular psoriasis may be localized to certain areas of the body, such as the hands and feet, or
covering most of the body. It begins with the reddening of the skin followed by formation of
pustules and scaling.[13]

Pustular psoriasis may be triggered by internal medications, irritating topical agents,
overexposure to UV light, pregnancy, systemic steroids, infections, stress and sudden
withdrawal of systemic medications or potent topical steroids.[14]

2.2.5. Erythrodermic Psoriasis
Erythrodermic [eh-REETH-ro-der—mik] psoriasis is a particularly inflammatory form of
psoriasis that affects most of the body surface. It may occur in association with pustular psoriasis. It is characterized by periodic, widespread, fiery redness of the skin and the shedding of scales in sheets, rather than smaller flakes. The reddening and shedding of the skin are often accompanied by severe itching and pain, heart rate increase, and fluctuating body temperature.\textsuperscript{[15]}

People experiencing the symptoms of erythrodermic psoriasis flare should go see a doctor immediately. Erythrodermic psoriasis causes protein and fluid loss that can lead to severe illness. The condition may also bring on infection, pneumonia and congestive heart failure. People with severe cases of this condition often require hospitalization.\textsuperscript{[16]}

Known triggers of erythrodermic psoriasis include the abrupt withdrawal of a systemic psoriasis treatment including cortisone; allergic reaction to a drug resulting in the Koebner response; severe sunburns; infection; and medications such as lithium, anti-malarial drugs; and strong coal tar products.\textsuperscript{[17]}

2.3. Psoriasis Theories

Psoriasis Theories are the concepts which try to explain the reasons for psoriasis appearance. Psoriasis cannot be explained by any single theory. Each of the Psoriasis theories below is based on the clinical observations and the results of the laboratory tests.\textsuperscript{[18]}

The following psoriasis theories are presently the most reliable

2.3.1. Genetic Psoriasis Theory

Genetic psoriasis theory is based on multiple cases of family history of psoriasis. Psoriasis can often be found in up to 6 generations of one family genetic variants affect disease phenotype in both psoriasis and psoriasis arthritis. HLA—Cw*0602 is associated with early onset psoriasis, higher incidence of guttate or streptococcal-induced flares, Koebner's phenomenon, more severe course, and is more likely to remit with pregnancy. HLA-Cw*0602 is not associated with later onset of psoriasis, palmo-plantar psoriasis, nail or scalp involvement and is less frequent in patients with psoriasis arthritis.\textsuperscript{[19]}

In psoriasis arthritis, HLA—B27, Cw2, and DRw52 are associated with axial psoriasis arthritis, and HLA—B38 and B39 with polyarthritis. It has also been shown that HLA—BZ7 in the presence of HLA-DR7, HLA-B39 and HLA-DQw3 in the absence of HLA-DR7 are associated with progression of clinical damage, and that HLA-DR7, B22 alleles are
“protective.” HLA-DRBl rheumatoid arthritis shared epitope as well as IL-4 150V polymorphism have been shown to be associated with erosive psoriasis arthritis. Patients with psoriasis arthritis carrying both HLA- Cw6 and HLA-DRBl”07 alleles have a less severe course of arthritis.[20]

2.3.2. Autoimmune Psoriasis Theory

Autoimmune Psoriasis Theory is based on an assumption that certain antigens (foreign substances that can stimulate an immune response in the body) may trigger an Autoimmune Aggression in the body, and the Immune System starts attacking and tries to kill the body's own cells'.[21]

The Immune System is a sum total of cells and organs which protect the body from foreign invaders (i.e. infections etc.) The main organs of the Immune System include: thymus, spleen, and lymph nodes. The main cells of the Immune System include antibodies (defense proteins) and lymphocytes (a type of white blood cells) - NK-lymphocytes (NK-cells), B-lymphocytes (B-cells), and T-lymphocytes (T-cells). The Immune System recognizes an invader and gets rid of it with the aid of lymphocytes and antibodies. Normally the Immune System can tell the difference between the body proteins itself and the foreign proteins of bacteria or viruses. But sometimes the body's own proteins are recognized as foreign. In this case the Immune System starts attacking and tries to kill the body's own cells. This is known as an autoimmune aggression, autoimmune response or an autoimmune disorder.[22]

2.3.2.1. Immune Disorders and Psoriasis

According to the Immune Psoriasis Theory the immune disorders are the driving force in the development of psoriasis. Psoriasis can be defined as general immune-dependent dermatitis. According to the Immune Psoriasis Theory the following occurs: autoimmune aggression directed at epidermis (the outermost layer of skin) results in the Psoriasis Appearance. Certain antigens (foreign substances that can stimulate an immune response in the body) were discovered in the psoriatic lesions, while in the blood there were revealed their antibodies (defense proteins that bind to antigens in an attempt to neutralize them) in the people with psoriasis. These antigens and antibodies are absent in the skin and blood of people without psoriasis. This gives grounds to consider psoriasis to be connected with the autoimmune mechanisms.[23]
D.U.M. Hung et al. (1993, 1995) considered that psoriasis may "be started" by a superantigen (antigen that binds to and activates T cells), for example by the toxins secreted by some microbial staphylococci and streptococci.\textsuperscript{[24]}

2.3.3. Metabolic Psoriasis Theory

Metabolic Psoriasis Theory is based on the data testifying about various metabolism disorders in the people with psoriasis, changes in the DNA and RNA, the regression of psoriasis during low-fat diet etc.\textsuperscript{[25]}

Metabolism is the sum total of all the vital chemical processes that take place in a living cell or organism. In the metabolism certain substances are broken down and converted into energy while other necessary for life substances are synthesized.\textsuperscript{[26]}

Scientists note a slower metabolism in the people with psoriasis. There is noted a reduction in body temperature in the people with psoriasis, which also proves the slow metabolism.\textsuperscript{[27]}

Carbohydrate metabolism is disrupted in 60% of people with psoriasis. Approximately 25% of patients with psoriasis also have diabetes. Some scientists consider that carbohydrate metabolism disorders serve as the basis for Psoriasis Appearance, while others believe these disorders to be caused by psoriasis itself.\textsuperscript{[28]}

In the people with psoriasis there are observed the fluctuations of the content of micro cells, which participate in the oxidation-reduction processes.\textsuperscript{[29]}

Y. Kamei (1958) has revealed disorders of oxidation-reduction activity of the skin in the people with psoriasis. E. Neumann (1957) considered the increased oxidation-reduction activity of the epidermal cells (cells of the outer layer of the skin) to play the primary role in the development of psoriasis.\textsuperscript{[30]}

There are indications of a lowered level of oxygen in the blood in the people with psoriasis, which negatively affects the course of psoriasis. The concentration of free radicals in the skin of people with psoriasis exceeds their content in the skin in people without psoriasis by as much as 3 times on the average. This proportion becomes normal closer to the clinical recovery from psoriasis.\textsuperscript{[31]}

Accelerated epidermal cell development can be confirmed by increased synthesis of glycogen.
in the skin of people with psoriasis, and especially in the psoriatic lesions. The metabolism of vitamins with psoriasis is also disrupted, which decreases the adaptive abilities of the body. The content of Vitamin C is decreased in the blood, but it is increased in the skin; the content of the Vitamins A, B6, and B12 in the blood is reduced. Various shifts are also observed with the contents of copper, Zinc and iron.\textsuperscript{[32]}

There is also found liver function disorder in the people with psoriasis. Liver function disorder seems to play a specific role, but not the main role in the pathogenesis of psoriasis. In the progressive stage of psoriasis there is frequently noted an increased function of the thyroid and/or endocrine glands, there is noted the absence of fat and perspiration on the psoriatic plaques and near them; it is restored when the psoriatic lesions regress. There were discovered disorders of protein and of lipid metabolism in the people with psoriasis. The content of lipids and cholesterol in the people with psoriasis is increased. The increase in the lipids stimulates the overgrowth of layers of horny skin (keratosis). Good therapeutic effect of a fat free diet proves the presence of the abnormal levels of certain fats in the people with psoriasis. A low-calorie diet usually helps to improve the state of psoriasis.\textsuperscript{[33]}

\textbf{2.3.4. Hormones and Psoriasis Theory}

Hormones and psoriasis theory is based on the flare-ups of psoriasis during menstruation; an improvement in the flow of psoriasis, and even a complete recovery during pregnancy etc. Hormones and Psoriasis seem to be tightly connected. Psoriasis is characterized by an increased reproduction of the epidermal skin cells, which indicates the disorders of the regulatory endocrine system.\textsuperscript{[34]}

Endocrine System regulates the body organ's activity with the aid of the hormones. Hormones are produced in the endocrine glands, endocrine system produces various hormones, for example Steroid hormones (i.e. Glucocorticoids, Cortisone, Hydro Cortisone, Corticosterone, Prednisolone; Sex Hormones etc.). Together with the nervous system and the immune system, endocrine system regulates the growth and the development of an organism, sex differentiation, reproductive functions etc.\textsuperscript{[35]}

\textbf{2.3.4.1. Is Psoriasis Connected with the Endocrine Glands Disorders,}

In particular - the Thyroid and Adrenal Glands Disorders Thyroid gland is an endocrine gland that produces thyroid hormones to regulate the body's metabolism and growth. Deviations in the thyroid gland functions are found in many people with psoriasis. Adrenal gland is an
endocrine gland that produces the hormones adrenaline, noradrenaline, glucocorticoids (i.e. cortisone), sex hormones and others. Adrenal gland regulates metabolism, sexual function, water balance, heart rate, blood pressure, and stress'.[36]

In the majority of the people who had psoriasis for a long time, there is revealed a reduction in the glucocorticoid function of the outer region of the adrenal gland - the adrenal cortex, i.e. the production of the Steroid hormones is disrupted. In psoriasis treatment used are Topical Steroids which cause blood vessels in the epidermis to temporary constrict and thus to achieve an anti inflammatory effect with psoriasis. Topical Steroid hormones possess various side-effects.[37]

There are known cases of the appearance and flare—ups of psoriasis in women at the time of menstruation. It is also known that psoriasis may disappear during pregnancy and reappear during breast feeding. The above clearly indicates the connection of hormonal changes with psoriasis.[38]

However, a direct connection of any particular endocrine gland or hormone with psoriasis was not found. The presence of endocrine disorders in people with psoriasis does not allow asserting that these disorders are the direct cause for the appearance of psoriasis, because similar disorders are also observed with other illnesses.[39]

2.3.5. Nervous System Psoriasis Theory
Nervous System and Psoriasis theory is based on psoriasis appearance after stress and on the data that people with psoriasis frequently have functional disorders of the Nervous System.[40]

2.3.6. Infection and Psoriasis Theory
Infection and Psoriasis theory is based on the connection of psoriasis With a focal infection in the tonsils, the inflammation of the nose cavities and eardrum, the inflammation of the uterine appendages, the inflammation of the prostate gland etc.[40]

2.3.7. Virus and Psoriasis Theory
Virus and Psoriasis theory is based on an assumption that a certain virus (retrovirus) may be an agent that provokes psoriasis.[40]

2.3.8. Toxins and Psoriasis Theory
Toxins and Psoriasis theory is based on an assumption that toxins contained in certain foods
and medications can penetrate through the bowels and into the blood and lymph flow and then to be excreted.\textsuperscript{[40,42]} through skin causing the appearance of psoriatic lesions.

\subsection*{2.3.9. Antioxidant Psoriasis Theory}
Antioxidant Psoriasis theory is based on an assumption that the people with psoriasis are better protected from the reactive oxygen as an unfortunate forms than the people without psoriasis, which causes an inflammatory psoriatic reaction side-affect.\textsuperscript{[43]}

\subsection*{2.4. Is Psoriasis an Autoimmune Disease?}
Autoimmune disorders are diseases that occur when the body produces an inappropriate immune response against its own tissues. Sometimes the immune system will cease to recognize one or more of the body's normal constituents as "self" and will produce autoantibodies —antibodies that attack its own cells, tissues, and/or organs. This causes inflammation and damage and leads to autoimmune disorders.\textsuperscript{[43]}

The cause of autoimmune diseases is unknown, but it appears that there is an inherited predisposition in many cases. In a few types of autoimmune disease (such as rheumatic fever), a virus or infection with bacteria triggers an immune response and the antibodies or T-cells attack normal cells because some part of their structure resembles a part of the infecting microorganism.\textsuperscript{[44]}

Autoimmune disorders fall into two general types: those that damage many organs (systemic autoimmune diseases) and those where only a single organ or tissue is directly damaged by the autoimmune process (localized). However, the distinctions become blurred as the effect of localized autoimmune disorders frequently extends beyond the targeted tissues, indirectly affecting other body organs and systems.\textsuperscript{[45]}

In some cases, the antibodies may not be directed at a specific tissue or organ; for example, antiphospholipid antibodies can react with substances (phospholipids) that are the normal constituents of platelets and the outermost layer of cells (cell membranes), which can lead to the formation of blood clots within the blood vessels (thrombosis).\textsuperscript{[46]}

Symptoms of autoimmune disorders vary by the particular disorder but many include fatigue, dizziness, and low grade fever. Symptoms can also vary in severity over time. Acute guttate psoriasis is often self—limiting and reflects an abnormal immune reaction to streptococcal throat infection. Chronic plaque psoriasis, however, behaves like most autoimmune disease,
being characterized by a chronic but fluctuating HLA-linked inflammatory process. In contrast to other autoimmune diseases that are mostly linked to certain class II HLA alleles, psoriasis is the only known chronic inflammatory disease that has the strongest association with an HLA-C allele. Thus, over 60% of psoriasis patients carry the HLA-Cw6 allele, and the predominance of oligoclonal CD8+ T cells in lesional epidermis suggests that the pathogenic process is driven by autoantigen, that may be presented by HLA-Cw6 in those patients who carry this allele. The CD4+ T cells in stable lesions are also likely to be oligoclonal, further supporting the notion that chronic psoriasis is an antigen driven disease.\[47\]

It has been reported that patients with chronic plaque psoriasis can experience an exacerbation after streptococcal throat infection, and we have previously postulated that psoriasis is mediated by T cells that cross-react with epitopes which are common to streptococcal M proteins and those keratins that are up-regulated in psoriatic lesions.\[48\]

Streptococcal M proteins have extensive amino acid sequence homology to type I keratins, including keratins 14, 16 and 17.

Interestingly, these keratins are usually only expressed at low levels or not at all in normal skin but are up-regulated during inflammation or trauma.\[49\]

T cell responses against certain amino acid sequences that streptococcal M proteins share with these keratins have been shown to be increased in patients with active psoriasis but absent during disease remissions.\[50\]

Furthermore, CLA + CD8+ T cells in HLA-Cw*0602 positive psoriasis patients with an active disease showed IFN—γ responses against the homologous sequences present both in keratins and M proteins while nonpsoriatic HLA—Cw*0602 positive controls only responded to peptides from the M protein. This indicates that patients with active psoriasis have a recirculating subset of skin homing CD8+ T cells that react specifically to keratin peptides.\[51\]

2.5. Thyroid Gland
The thyroid gland is one of the largest endocrine glands. The thyroid gland is found in the neck, below the thyroid cartilage (which forms the laryngeal prominence, or "Adam's apple"). The isthmus (the bridge between the two lobes of the thyroid) is located inferior to the cricoid cartilage.\[52\]
The thyroid gland controls how quickly the body uses energy, makes proteins, and controls how sensitive the body is to other hormones. It participates in these processes by producing thyroid hormones, the principal ones being triiodothyronine (T3) and thyroxine which can sometimes be referred to as tetraiodothyronine (T4). These hormones regulate the rate of metabolism and affect the growth and rate of function of many other systems in the body. T3 and T4 are synthesized from other iodine and tyrosine. The thyroid also produces calcitonin, which plays a role in calcium homeostasis.\(^{[53]}\)

Hormonal output from the thyroid is regulated by thyroid-stimulating hormone (TSH) produced by the anterior pituitary, which itself is regulated by thyrotropin-releasing hormone (TRH) produced by the hypothalamus. The thyroid gets its name from the Greek word for “shield”, due to the shape of the related thyroid cartilage. The most common problems of the thyroid gland consist of an overactive thyroid gland, referred to as hyperthyroidism, and an underactive thyroid gland, referred to as hypothyroidism.\(^{[54]}\)

2.5.1. Thyroid Gland Physiology

The primary function of the thyroid is production of the hormones triiodothyronine (T3), thyroxine (T4), and calcitonin. Up to 80% of the T4 is converted to T3 by peripheral organs such as the liver, kidney, and spleen. T3 is several times more powerful than T4, which is largely a prohormone, perhaps four or even ten times more active.\(^{[55]}\)

2.5.1.1. T3 and T4 Production and Action

Thyroxine (T4) is synthesized 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 the hydrogen peroxide generated 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.\(^{[56]}\)

Upon stimulation by the thyroid-stimulating hormone (TSH), the follicular cells reabsorb Tg and cleave the iodinated tyrosines from Tg in lysosomes, forming T4 and T3 (in T3, one iodine atom is absent compared to T4), and releasing them into the blood. Deiodinase enzymes convert T4 to T3 ‘Thyroid hormone secreted from the gland is about 80-90% T4 and about 10-20% T3’.\(^{[57]}\)

Cells of the developing brain are a major target for the thyroid hormones T3 and T4. Thyroid hormones play a particularly crucial role in brain maturation during fetal development. A
transport protein that seems to be important for T4 transport across the blood—brain barrier (OATP1C1) has been identified. A second transport protein (MCT8) is important for T3 transport across brain cell membranes.\[^{[58]}\]

Non-genomic actions of T4 are those that are not initiated by liganding of the hormone to intranuclear thyroid receptor. These may begin at the plasma membrane or within cytoplasm. Plasma membrane-initiated actions begin at a receptor on the integrin alphaV beta3 that activates ERK1/2. This binding culminates in local membrane actions on ion transport systems such as the Na(+)/H(+) exchanger or complex cellular events including cell proliferation. These integrins are concentrated on cells of the vasculature and on some types of tumor cells, which in part explains the proangiogenic effects of iodothyronines and proliferative actions of thyroid hormone on some cancers including gliomas. T4 also acts on the mitochondrial genome via imported isoforms of nuclear thyroid receptors to affect several mitochondrial transcription factors. Regulation of V actin polymerization by T4 is critical to cell migration in neurons and glial cells and is important to brain development.\[^{[59]}\]

T3 can activate phosphatidylinositol 3-kinase by a mechanism that may be cytoplasmic in origin or may begin at integrin alpha V beta3. In the blood, T4 and T3 are partially bound to thyroxine-binding globulin (TBG), transthyretin, and albumin. Only a very small fraction of the circulating hormone is free (unbound) - T4 0.03% and T3 0.3%. Only the free fraction has hormonal activity. As with the steroid hormones and retinoic acid, thyroid hormones cross the cell membrane and bind to intracellular receptors (0:1, (12, 0, and [32], which act alone, in pairs or together with the retinoid X-receptor as transcription factors to modulate DNA transcription.\[^{[60]}\]

\[2.5.1.2. \text{T3 and T4 Regulation}\]

The production of thyroxine and triiodothyronine is regulated by thyroid—stimulating hormone (TSH), released by the anterior pituitary. The thyroid and thyrotropes form a negative feedback loop: TSH production is suppressed when the T4 levels are high. The TSH production itself is modulated by thyrotropin—releasing hormone (TRH), which is produced by the hypothalamus and secreted at an increased rate in situations such as cold exposure (to stimulate thermogenesis). TSH production is blunted by somatostatin (SRIH), rising levels of glucocorticoids and sex hormones (estrogen and testosterone), and excessively high blood iodide concentration.\[^{[61]}\]
An additional hormone produced by the thyroid contributes to the regulation of blood calcium levels. Parafollicular cells produce calcitonin in response to hypercalcemia. Calcitonin stimulates movement of calcium into bone, in opposition to the effects of parathyroid hormone (PTH). However, calcitonin seems far less essential than PTH, as calcium metabolism remains clinically normal after removal of the thyroid (thyroidectomy), but not the parathyroids.\[62\]

2.5.2. Disorders of Thyroid
Thyroid disorders include hyperthyroidism (abnormally increased activity), hypothyroidism (abnormally decreased activity) and thyroid nodules, which are generally benign thyroid neoplasms, but may be thyroid cancers. All these disorders may give rise to goiter, that is, an enlarged thyroid.\[63\]

2.5.2.1. Hyperthyroidism
Hyperthyroidism, or overactive thyroid, is the overproduction of the thyroid hormones T3 and T4, and is most commonly caused by the development of Graves' disease, an autoimmune disease in which antibodies are produced which stimulate the thyroid to secrete excessive quantities of thyroid hormones. The disease can result in the formation of a toxic goiter as a result of thyroid growth in response to a lack of negative feedback mechanisms. It presents with symptoms such as a thyroid goiter, protruding eyes (exophthalmos), palpitations, excess sweating, diarrhea, weight loss, muscle weakness and unusual sensitivity to heat. The appetite is often increased.\[64\]

Beta blockers are used to decrease symptoms of hyperthyroidism such as increased heart rate, tremors, anxiety and heart palpitations, and anti-thyroid drugs are used to decrease the production of thyroid hormones, in particular, in the case of Graves' disease. These medications take several months to take full effect and have side-effects such as Skin rash or a drop in white blood cell count, which decreases the ability of the body to fight off infections. These drugs involve frequent dosing (often one pill every 8 hours) and often require frequent doctor visits and blood tests to monitor the treatment, and may sometimes lose effectiveness over time.\[65\]

Due to the side-effects and inconvenience of such drug regimens, some patients choose to undergo radioactive iodine-131 treatment. Radioactive iodine is administered in order to destroy a portion of or the entire thyroid gland, since the radioactive iodine is selectively
taken up by the gland and gradually destroys the cells of the gland. Alternatively, the gland may be partially or entirely removed surgically, though iodine treatment is usually preferred since the surgery is invasive and carries a risk of damage to the parathyroid glands or the nerves controlling the vocal cords. If the entire thyroid gland is removed, hypothyroidism results.\[66\]

2.5.2.2. Hypothyroidism

Hypothyroidism is the underproduction of the thyroid hormones T3 and T4. Hypothyroid disorders may occur as a result of congenital thyroid abnormalities, autoimmune disorders such as Hashimoto's thyroiditis, iodine deficiency (more likely in poorer countries) or the removal of the thyroid following surgery to treat severe hyperthyroidism and/or thyroid cancer. Typical symptoms are abnormal weight gain, tiredness, baldness, cold intolerance, and bradycardia. Hypothyroidism is treated with hormone replacement therapy, such as levothyroxine, which is typically required for the rest of the patient's life. Thyroid hormone treatment is given under the care of a physician and may take a few weeks to become effective.\[67\]

Negative feedback mechanisms result in growth of the thyroid gland when thyroid hormones are being produced in sufficiently low quantities as a means of increasing the thyroid output; however, where the hypothyroidism is caused by iodine insufficiency, the thyroid is unable to produce T3 and T4 and as a result, the thyroid may continue to grow to form a nontoxic goiter. It is termed non-toxic as it does not produce toxic quantities of thyroid hormones, despite its size.

2.5.2.3. Initial Hyperthyroidism Followed by Hypothyroidism

This is the overproduction of T3 and T4 followed by the underproduction of T3 and T4. There are two types: Hashimoto's thyroiditis and postpartum thyroiditis.\[68\]

Hashimoto's thyroiditis or Hashimoto's Disease is an autoimmune disorder whereby the body's own immune system reacts with the thyroid tissues in an attempt to destroy it. At the beginning, the gland may be overactive, and then becomes underactive as the gland is damaged resulting in too little thyroid hormone production or hypothyroidism. Some patients may experience "swings" in hormone levels that can progress rapidly from hyper— to hypothyroid (sometimes mistaken as severe moodswings, or even being bipolar, before the proper clinical diagnosis is made). Some patients may experience these "swings" over a
longer period of time, over days or weeks or even months. Hashimoto's is more common in females than males, usually appearing after the age of 30, and tends to run in families meaning it can be seen as a genetic disease. Also more common in individuals with Hashimoto's Thyroiditis are type 1 diabetes and celiac disease. \[^{69}\]

Postpartum thyroiditis occurs in some females following the birth of a child. After delivery, the gland becomes inflamed and the condition initially presents with overactivity of the gland followed by underactivity. In some cases, the gland may recover with time and resume its functions. In others it may not. The etiology is not always known, but can sometimes be attributed to mitochondriality, such as Hashimoto's Thyroiditis or Graves' Disease. \[^{70}\]

2.5.2.4. Cancers

In most cases, the thyroid cancer presents as a painless mass in the neck. It is very unusual for the thyroid cancers to present with symptoms, unless it has been neglected. One may be able to feel a hard nodule in the neck. Diagnosis is made using a needle biopsy and various radiological studies. \[^{71}\]

2.5.2.4.1. Non-Cancerous Nodules

Many individuals may find the presence of thyroid nodules in the neck. The majority of these thyroid nodules are benign (non cancerous). The presence of a thyroid nodule does not mean that one has thyroid disease. Most thyroid nodules do not cause any symptoms, and most are discovered on an incidental examination. Doctors usually perform a needle aspiration biopsy of the thyroid to determine the status of the nodules. If the nodule is found to be non—cancerous, no other treatment is required. If the nodule is suspicious then surgery is recommended. \[^{72}\]

2.5.2.4.2. Congenital Anomalies

A persistent thyroglossal duct or cyst is the most common clinically significant congenital anomaly of the thyroid gland. A persistent sinus tract may remain as a vestigial remnant of the tubular development of the thyroid gland. Parts of this tube may be obliterated, leaving small segments to form cysts. These occur at any age and might not become evident until adult life. Mucinous, clear secretions may collect within these cysts to form either spherical masses or fusiform swellings, rarely larger than 2 to 3 cm in diameter. These are present in the midline of the neck anterior to the trachea. Segments of the duct and cysts that occur high in the neck are lined by stratified squamous epithelium, which is essentially identical to that
covering the posterior portion of the tongue in the region of the foreamen cecum. The anomalies that occur in the lower neck more proximal to the thyroid gland are lined by epithelium resembling the thyroidal acinar epithelium. Characteristically, next to the lining epithelium, there is an intense lymphocytic infiltrate. Superimposed infection may convert these lesions into abscess cavities, and rarely, give rise to cancers.\cite{73}

2.5.3. Other Disorders

E! Limited research shows that seasonal allergies may trigger episodes of hypo- or hyperthyroidism. D A ectopic thyroid is an entire or parts of the thyroid located in another part of the body than what is the usual case.\cite{73}

2.5.3.1. Significance of Iodine

Gland can become considerably enlarged, a condition called endemic goiter. Pregnant women on a diet that is severely deficient of iodine can give birth to infants who can present with thyroid hormone deficiency (congenital hypothyroidism), manifesting in problems of physical growth and development as well as brain development (a condition referred to as endemic cretinism). In many developed countries, newborns are routinely tested for congenital hypothyroidism as part of newborn screening. Children With congenital hypothyroidism are treated supplementally with levothyroxine, which facilitates normal growth and development.\cite{74}

Thyroxine is critical to the regulation of metabolism and growth throughout the animal kingdom. Among amphibians, for example, administering a thyroid-blocking agent such as propylthiouracil(PTU) can prevent tadpoles from metamorphosing into frogs; in contrast, administering thyroxine will trigger metamorphosis.\cite{75}

Because the thyroid concentrates this element, it also concentrates the various radioactive isotopes of iodine produced by nuclear fission. In the event of large accidental releases of such material into the environment, the uptake of radioactive iodine isotopes by the thyroid can, in theory, be blocked by saturating the uptake mechanism with a large surplus of non-radioactive iodine, taken in the form of potassium iodide tablets. One consequence of the Chernobyl disaster was an increase in thyroid cancers in children in the years following the accident.\cite{76}
The use of iodised salt is an efficient way to add iodine to the diet. It has eliminated endemic cretinism in most developed countries, and some governments have made the iodination of flour, cooking oil, and salt mandatory. Potassium iodide and sodium iodide are typically used forms of supplemental iodine. As with most substances, either too much or too little can cause problems. Recent studies on some populations are showing that excess iodine intake could cause an increased prevalence of autoimmune thyroid disease, resulting in permanent hypothyroidism.\textsuperscript{[77]}

### 2.6. Comorbid Conditions in Psoriasis

Psoriasis is newly defined as a systemic disease. Common co-morbidities associated with psoriasis include diabetes, hypertension, and metabolic syndromes. Psoriasis can have a significant impact on a patient's quality of life and is associated with loss of productivity, depression, and an increased prevalence of malignancy.\textsuperscript{1} Pro-inflammatory cytokines such as tumour necrosis factor—alpha (TNF-\(\alpha\)), and other factors like pro—inflammatory T-helper type 1 cytokines that are overproduced in patients with psoriasis likely contributes to the increased risk for development of metabolic syndrome.\textsuperscript{[78]}

In terms of the other diseases associated with psoriasis, Crohn’s disease is another condition that is not common but its prevalence is certainly increased in patients with psoriasis.\textsuperscript{[79]}

Depression or anxiety is another common problem in patients with psoriasis as is genitourinary disease. 20% of hospitalised patients with psoriasis have some genitourinary complaints.\textsuperscript{[80]}

Patients should adopt a healthy lifestyle so as not to contribute any move to risk ‘hctor's. 'l'm'ming psoriasis and the associated co-morbid cmutious awssivel'v from the beginning will definitely improve the quality m'lit'e ot'the patient.\textsuperscript{[81]}

### 2.7. Benefits of Psoriasis Therapy on Comorbid Conditions

Since many comorbid conditions have inflammatory mechanisms in common with psoriasis' drugs targeting inflammation and/or suppressing the immune response are often effective in treating both psoriasis and related comorbidities. A number of treatments have shown some efficacy in heming both psoriasis and psoriatic arthritis including methotrexate, cyclosporine, lefunomide, etanercept and infliximab. 'Tumor necrosis factor (TNF) inhibitors etanercept and infliximab have demonstrated halting of joint degradation.\textsuperscript{[82]}
2.8. 'Ili’pe 2 diabetes. psoriasis and thiazolidinediones

Thiazolidinediones, synthetic ligands for the peroxisome proliferator— activity receptor — gamma (PPAR—gamma) receptor, are insuline — sensitizing drugs licensed for use in selected patients with type 2 diabetes mellitus. The potential therapeutic applications of the thiazolidinediones extend to other clinical specialties such as dermatology. Rosiglitazone and Pioglitazone are being evaluated for the treatment of psoriasis. Type 2 diabetes and psoriasis may coexist, prompting speculation that dual benefits might accrue for patients with both conditions.\[83\]

A recent open pilot study suggest that oral pioglitazone may be beneficial for moderate chronic plaque psoriasis. However, changes in antidiabetic medication must be made in the knowledge of the cautions and contraindications to oral agents as well as the impact on metabolic control. Further study are required before the use of thiazolidinediones for psoriasis can be advocated.\[84\]

CHAPTER THREE
PATIENTS AND METHODS

3.1. Study Design
This is a cross section study designed to illustrate the relationship between psoriasis and thyroid disorders by doing the thyroid function tests on psoriasis and control group.

3.2 Patient Selection
Sixty patients had psoriasis consulting the outpatient dermatology clinic of Tikrit General Hospital in Tikrit city and sixty cases of normal persons (control group). Carried out from January to August 2012.

3.3. Inclusion Criteria
1. Patient agreement
2. Age range from 16 to 65 year, depending on Tilo henseler, who dividing psoriasis into type I and type II, which demonstrate distinct characteristics. Firstly the disease presents in different decades of life, in type I before the age of 40 years and later in type II. Secondly, contrasting frequencies of HLA alleles are found: type I patients express predominantly HLA-Cw6, — B57, and—DR7, whereas in type 11 patients HLA-CwZ is overrepresented. Finally, familial inheritance is found in type I but not in type II psoriasis.\[85\]
3. known case of psoriasis and was diagnosed by dermatologist.
4.3. Exclusion Criteria
Exclusion criteria were psoriatics or controls with known thyroid impairment, those using thyroid hormones, anti-thyroid drugs or other drugs affecting thyroid function, such as lithium, iodine, steroids, dopamine, anticonvulsant drugs and interferon.

3.5. Clinical History
The patients’ disease history recording include name, age, sex, address, occupation, site, duration, family history, drug history, and associated endocrine diseases.

3.6. Diagnosis
The diagnosis of psoriasis is made clinically, by dermatologist.

3.7. Investigations
Investigations of thyroid function tests includes, total triiodothyronine (TT3), thyroxine (T4), and measurement of thyroid stimulating hormone (TSH). Overt hypothyroidism was defined as elevated TSH and low T4, subclinical hypothyroidism as elevated TSH and normal T4, overt hyperthyroidism as low TSH and elevated T4 and subclinical hyperthyroidism as low TSH and normal T4.[86]

3.7.1. Triiodothyronine (T3)
For quantitative measurement of total triiodothyronine (TT3) in human serum ST AIA-PACK TT3 is used on TOSOH AIA System Analyzers.[87]

3.7.1.1. Summary and Explanation of Test
Triiodothyronine (T3) and thyroid hormone (thyroxine; T4) regulate a variety of biochemical processes throughout the body, the majority of T3 is produced enzymatically by monodeiodination of T4 in the peripheral tissues, rather than from the direct secretion from the thyroid gland. Approximately one third of all T4 secreted is deiodinated to yield T3.

Senon T3 measurement can a valuable component of a thyroid function screening panel in diagnosing certain disorders of thyroid function in addition to conditions caused by iodide deficiency. Assay for T3 are valuable in early detection of hyperthyroidism and for monitoring the efficacy of treatment for thyroid disorders. A normal T3 value in the presence of an elevated T4 level may also help to rule out hyperthyroidism.[88]

3.7.1.2. Principle of the Assay
The ST AIA-PACK TT3 is a competitive enzyme immunoassay which is performed entirely
within the AIA-PACK test cups. Triiodothyronine, which is displaced from its binding protein by AN S (8-anilino-1- naphthalene sulfonic acid), and free T3 present in the test sample compete with enzyme-labeled T3 for a limited number of binding sites on a T3.

Specific antibody immobilized on magnetic beads. The beads are washed to remove the unbound enzyme-labeled T3 and are then incubated with a fluorogenic substrate, 4-methylumbelliferyl phosphate (4-MUP). The amount of enzyme-labeled T3 that binds to the beads is inversely proportional to the T3 concentration in the test sample. A standard curve using a range of known standard concentrations is prepared and unknown T3 concentration are calculated using the curve.

3.7.1.3. Specimen Collection and Handling

Serum or heparinized plasma is required for the assay. EDTA and citrated plasma should not be used. If using serum, a venous blood sample is collected aseptically without additives. Store at 18-25°C until a clot has formed (usually 15-45 minutes), then centrifuge to obtain the serum specimen for assay.

If using heparinized plasma, a venous blood sample is collected aseptically with designed additive. Centrifuge and separate plasma from the packed cells as soon as possible.

Specimens types should not be used interchangeably during serial monitoring of an individual patient. Measured concentration may vary slightly between sample types in certain patients.

Samples may be stored at 2-8°C: for up to 24 hours prior to analysis. If the analysis cannot be done within 24 hours, the sample should be stored frozen at -20°C: or below for up to 60 days.

Repeated freeze—thaw cycles should be avoided. Turbid serum samples or samples containing particular matter should be centrifuged prior to testing. Prior to assay, bring frozen samples to 18-25°C: slowly and mix gently.

The sample required for analysis is ZSpL.[90]

3.7.1.4. Reference range

The interval given here was determined in serum samples from 573 apparently healthy Asian individuals. Reference interval =0.79-1.58ng/mL (1.22-2.43nmol/L).
3.7.1.5. Conversion Factors

T3 concentration in this application are in units of ng/mL. conversion to SI units of nmol/l may be made using the following equation: nmol T3/L = ng T3/mL x 1.54.\(^\text{[91]}\)

3.7.2. Thyroxine (T4)

For quantitative measurement of thyroxine (T4) in human serum ST AIA-PACK T4 is used on TOSOH AIA System Analysers.\(^\text{[87]}\)

3.7.2.1. Summary and Explanation of Test

Evaluation of thyroid status is complex. The primary function of thyroid gland is the secretion of thyroxine (T4) or triiodothyronine (T3). Abnormal secretion of T4 and/or T3 may lead either to hyper- or hypo- thyroidism. The synthesis and release of T4 and T3 are in response to a hypothalamic-pituitary signal, thyroid stimulating hormone (TSH), which is released from the anterior and is principle regulator of thyroid activity. The release of TSH is controlled by thyrotropin releasing hormone (TRH) from the hypothalamus. This combined system regulating the release of thyroid hormone is the hypothalamic-pituitary axis. In the circulation, T4 is 99.97% protein bound (0.03% free) while T3 is 99.7% bound (0.3% free). Thyroxine binding globulin (TBG) is the primary binding protein. To a lesser extent, thyroxine binding prealbumin (TBPA) and albumin can also bind T4. Only unbound (free) forms exert the physiological action. T4 is largely converted to T3 in peripheral tissues by monodeiodination. Total T4 rises and falls with the TBG level in euthyroid individuals. An erroneous interpretation of thyroid function may be obtained if a condition which changes the TBG concentration exists. Certain drugs compete with T4 for binding to TBG, which results in decreased levels of total T4 through the negative feedback of thyroid hormone concentration on TSH secretion.\(^\text{[92]}\)

3.7.2.2. Principle of the Assay

The ST AIA—PACK T4 is a competitive enzyme immunoassay which is performed entirely within the AIA-PACK test cups. Thyroxine, WhiCh is displaced from its binding protein by ANS (8-anilino-1-naphthalene sulfonic acid), and free T4 present in the test sample compete with the enzyme-labeled thyroxine for a limited number of binding site on a thyroxine-specific antibody immobilized on magnetic beads. The beads are washed to removed the unbound enzyme labeled thyroxine and are the incubated with a fluorogenic substrate, 4-methylumbelliferyl phosphate (4MUP). The amount of enzyme-labeled thyroxine that binds to the heads is inversely proportional to the thyroxine concentration in the test sample. A
standard curve using a range of known standard concentration is constructed and unknown thyroxine concentrations are calculated using this curve.\cite{88}

### 3.7.2.3. Specimen Collection and Handling

- Serum or heparinized plasma is required for the assay. EDTA and citrated plasma should not be used.
- If using serum, a venous blood sample is collected aseptically without additives. Store at 18-256: until a clot has formed (usually 15-45 minutes), then centrifuge to obtain the serum specimen for assay.
- If using heparinized plasma, a venous blood sample is collected aseptically with designated additive. Centrifuge and separate plasma from the packed cells as soon as possible.
- Specimen types should not be used interchangeably during serial monitoring of an individual patient. Measured concentration may vary slightly between sample types in certain patients.
- Samples may be stored at 2-8\(^\circ\)C for up to 24 hours prior to analysis. If the analysis cannot be done within 24 hours, the sample should be stored frozen at _20\(^\circ\)C or below for up to 60 days.
- Repeated freeze-thaw cycles should be avoided. Turbid serum samples containing particular matter should be centrifuged prior to testing. Prior to assay, bring frozen samples to 18-256 slowly and mix gently.
- The sample required for analysis is 10uL.\cite{90}

### 3.7.2.4. Reference Range

The interval given here was determined in serum samples from 760 apparently healthy Asian individuals. Reference interval = 4.9-11.0ttg/dL (63.21-141.9nmol/L).\cite{91}

### 3.7.2.5. Conversion Factors

Thyroxine concentration in this application are in units of pg/dL. Conversion to SI units of nmol/L may be made using the following equation: nmol T4/L = pg T4/dL x 12.9.\cite{92}

### 3.7.3. Thyroid Stimulating Hormone (TSH or thyrotropin)

For quantitative measurement of thyroid stimulating hormone (TSH) in human serum ST AIA—PACK TSH is used on TOSOH AIA system Analysers.\cite{87}
3.7.3.1. Summary and Explanation of Test

Thyroid stimulating hormone is a glycoprotein hormone secreted by anterior pituitary gland. When feedback suppression of the pituitary is reduced by a reduced production of thyroid hormones (T4 and T3), TSH rise in an attempt to increase thyroid hormone production. This rise occur while the patient is still a symptomatic and thus is an early and very sensitive indication of hypothyroidism. TSH is also controlled by the hypothalamic peptide, thyrotropin releasing hormone (TRH).

Accurate determination of serum TSH is the most useful and sensitive test for primary hypothyroidism, where serum thyroid hormone concentration are depressed and serum TSH concentration are significantly elevated. Serum TSH determinations may also be used to differentiate between pituitary (secondary) and hypothalamic (tertiary) hypothyroidisms. Through the use of monoclonal antibody technology which provides the necessary specificity and sensitivity, the usefulness of TSH determination in the diagnosis of hyperthyroidism distinguished from euthyroidism has been well established.\[88\]

3.7.3.2. Specimen Collection and Handling

- Serum or heparinized plasma is required for the assay. EDTA and citrated plasma should not be used.
- If using serum, a venous blood sample is collected aseptically without additive. Store at 18-256 until a clot has formed (usually 15-45 minutes), then centrifuge to obtain the serum specimen for assay.
- If using heparinized plasma, a venous blood sample is collected aseptically with designed additive. Centrifuge and separate plasma from the packed cells as soon as possible.
- Specimen types should not be used interchangeably during serial monitoring of an individual patient. Measured concentration may vary slightly between sample types in certain patients.
- Samples may be stored at 2-86 for up to 24 hours prior to analysis. If the analysis cannot be done within 24 hours. The sample should be stored frozen at -20\(\degree\)C or below for up to 60 days.
- Repeated freeze-thaw cycles should be avoided. Turbid serum samples or samples containing particular matter should be centrifuged prior to testing. Prior to assay, bring frozen samples to 18-256: slowly and mix gently.
- The sample required for analysis is 10011L.\[89\]
The interval given here was determined in serum samples from 497 apparently healthy Asian individuals.

3.7.3.4. Conversion Factors
TSH concentration in this application are in units of iLIU/ml. conversion to SI units of quU/L may be made using the following equation: mIU TSH/L = pIU TSH/mL x 1.0.

3.8. Statistical Analysis
Statistical assessment was done by using the SPSS 19.0 for windows. Unpaired t-test was used when comparing mean values between group. Chi-square test was used when comparing differences.

CHAPTER FOUR
RESULTS
4.1. Psoriasis and Control Groups.
This study is included 60 patients with psoriasis and 60 controls. The mean age of the case patients was 36.4 years (SD:1:11.6) and that of the controls was 33.01(SD i124). In the case group, there were 34 (56.6%) and 26 women (43.4%). In the control group there were 30 men (50%) and 30 women (50%).

The proportions of hypothyroidism and hyperthyroidism were increased in patients with psoriasis as compared to the control group (table 1).

Table 1: No. and percentages of hypothyroidism and hyperthyroidism in psoriasis and control groups.
The number of hypothyroidisms cases were increase from 1 (1.66%) in control group to 3 (5%) in psoriasis group (significant association), also there is a significant association between psoriasis and control group in the increase number of hyperthyroidism from zero(0%) in control group to 2 (3.33%) in psoriasis group.

**Thyroid function tests of psoriasis and control groups as follows.**

T3 values mean were decreased in psoriasis group (1.727±0.690) compared to T3 values mean of control group (1.871±0.275), but there is no significant association as in table 2.

**Table 2: T3 Values in Psoriasis and Control Groups.**

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Mean of T3 mmol/l</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>60</td>
<td>1.7278</td>
<td>.690488</td>
<td>.089142</td>
<td>Not significant</td>
</tr>
<tr>
<td>B</td>
<td>60</td>
<td>1.87167</td>
<td>.275614</td>
<td>.035582</td>
<td></td>
</tr>
</tbody>
</table>

\(A: \text{psoriasis group} \quad \text{B: control group}\)

T4 values mean was decreased in patient with psoriasis as compared to control group as follows (84.5 ± 63:20.26) and (91.78±87) respectively, which appear strong significant association as in table 3.

**Table 3: T4 Values in Psoriasis and Control Groups.**

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Mean of T4 mmol/l</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>T4</td>
<td>A</td>
<td>84.56677</td>
<td>20.159001</td>
<td>2.602516</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>91.78333</td>
<td>8.717975</td>
<td>1.125486</td>
<td></td>
</tr>
</tbody>
</table>

\(A: \text{psoriasis group, B: control group}\)

TSH level was increased in psoriasis group, comparing to control group (2.834.181), and (2.02±0.67) respectively, showing no significant association as in table 4.
4.2. Psoriasis Group

In addition to thyroid function tests level, the analysis include the percentage of diabetes mellitus in psoriasis patients, and the +ve family history of psoriasis within the family depending on clinical history, the number of diabetes mellitus in psoriasis group was 11(18.3%), there was 12 (20%) of positive family history within the psoriasis group(figure 1).

4.2.1. Gender in Psoriasis Group

In psoriasis group the distribution of data according to gender as follows: the male number 34(56.6%), female number 26 (43.4%), the mean of age was 34.82±10.6 for male and 37.1±12.5 for female, there was no significant difference in the number of diabetes mellitus between male and female, and there were a significant association in the number of positive family history between male and female 8 (66.6%) and 4 (33.4%) respectively.

There was a significant differences in the number and percentage of hypothyroidism 2 (66.6), in male and 1 (33.4) in female, but there was no significant differences between male and female in hyperthyroidism as shown in table 5, figure 2,3.

Table 5: Distribution of Hypothyroidism, Hyperthyroidism, Diabetes Mellitus and +ve Family History of Psoriasis according to Gender.
According to T3 values mean there was no significant differences between male and female psoriasis patients instead of decrease level of T3 in females as shown in table 6.

**Table 6: T3 Values in Psoriasis Group According to Gender.**

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Mean of T3 mmol/l</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>34</td>
<td>1.8553</td>
<td>.58305</td>
<td>.09999</td>
<td>Not significant</td>
</tr>
<tr>
<td>B</td>
<td>26</td>
<td>1.7723</td>
<td>.71449</td>
<td>.14012</td>
<td></td>
</tr>
</tbody>
</table>

A: male   B: female

There was a slightly decrease in the level of T4 among females but there was no significant differences in T4 values mean as in table 7.

**Table 7: T4 Values in Psoriasis Group According to Gender.**

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Mean of T4 mmol/l</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>34</td>
<td>85.5000</td>
<td>18.76853</td>
<td>3.21878</td>
<td>Not significant</td>
</tr>
<tr>
<td>B</td>
<td>26</td>
<td>83.5000</td>
<td>22.14182</td>
<td>4.34237</td>
<td></td>
</tr>
</tbody>
</table>

A: male group   B: female group

TSH level in males and females among psoriasis patients show decreased among females but there was no significant differences as in table 8.

**Table 8: TSH Values in Psoriasis Group According to Gender.**

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Mean of TSH mmol/l</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>34</td>
<td>3.7176</td>
<td>7.44976</td>
<td>1.27762</td>
<td>Not significant</td>
</tr>
<tr>
<td>B</td>
<td>26</td>
<td>3.1538</td>
<td>2.11666</td>
<td>.41511</td>
<td></td>
</tr>
</tbody>
</table>

A: male group   B: female group
4.2.2. Age Groups in Psoriasis Patients

There were two age groups among psoriasis patients, first group 16-40 year, and second group 41-65 year, the number of diabetes mellitus was 4 (36.3) in first group, and 7 (63.64) in second group and there is a significant differences between age groups.

The all cases of hypothyroidism distributed within the second age group, and there was a significant differences between age groups (figure 4,5).

There was a significant differences between age groups in the percentage of positive family history, 9 (75%), in first group and 3(25%) in the second age group. Table 9.

Table 9: Distribution of Hypothyroidism, Hyperthyroidism, Diabetes Mellitus and +ve Family History of Psoriasis according to Age.

<table>
<thead>
<tr>
<th>Age group</th>
<th>No. and percent</th>
<th>No. and percent of diabetes mellitus</th>
<th>No. and percent of +ve family history</th>
<th>No. and percent of hypothyroidism</th>
<th>No. and percent of hyperthyroidism</th>
</tr>
</thead>
<tbody>
<tr>
<td>16-40 year</td>
<td>37 61.6%</td>
<td>4 36.3%</td>
<td>9 75%</td>
<td>Zero 0%</td>
<td>2 100%</td>
</tr>
<tr>
<td>41-65 year</td>
<td>23 38.4%</td>
<td>7 63.64%</td>
<td>3 25%</td>
<td>Zero 0%</td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td></td>
</tr>
</tbody>
</table>

Between two age groups within psoriasis patients, there was a slight decrease in the T3 values mean among the second (older) age group, but there was no significant differences as shown in table 10.

Table 10: T3 Values in Psoriasis Group According to Age Group.

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Mean of T3 (mmol/l)</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A 16-40 year</td>
<td>37</td>
<td>1.8719</td>
<td>.68726</td>
<td>.11298</td>
<td>Not significant</td>
</tr>
<tr>
<td>B 41-65 year</td>
<td>23</td>
<td>1.7043</td>
<td>.55471</td>
<td>.11567</td>
<td></td>
</tr>
</tbody>
</table>

T4 values mean was decreased among first (younger) age group, but there was no significant differences between two age groups, table 11.
Table 11: T4 Values in Psoriasis Group According to Age.

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Mean of T4nmol/l</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A 16-40 year</td>
<td>37</td>
<td>83.9730</td>
<td>21.67370</td>
<td>3.56313</td>
<td>Not significant</td>
</tr>
<tr>
<td>B 41-65 year</td>
<td>23</td>
<td>85.5217</td>
<td>17.87805</td>
<td>3.72783</td>
<td></td>
</tr>
</tbody>
</table>

TSH values mean show no significant differences among two groups as in table 12.

Table 12: TSH Values in Psoriasis Group According to Age.

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Mean of TSH mmol/l</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A 16-40 year</td>
<td>37</td>
<td>2.7081</td>
<td>1.84846</td>
<td>.30388</td>
<td>Not significant</td>
</tr>
<tr>
<td>B 41-65 year</td>
<td>23</td>
<td>2.8609</td>
<td>1.85958</td>
<td>.38775</td>
<td></td>
</tr>
</tbody>
</table>

4.2.3. Type of Psoriasis in Psoriasis Patients

The psoriasis patients divided into psoriasis vulgaris group and other types groups, vulgaris type was 28 (46.6), and other types group was 32 (53.4). The mean age of psoriasis vulgaris was 37.7521:11.37 and for other types group was 35.2121:11.94.

There as a significant differences in the number of diabetes mellitus within vulgaris and other types of psoriasis 7 (63.6%) and 4(35.4) respectively. The number of positive family history was significantly differences 9 (75%) in vulgaris group and 3 (25%) in other types group.

Number and percentage of hypothyroidism among vulgaris group was 2 (66.6), and was significantly differences from other types of psoriasis (163.4), there was strong significant differences among two groups in the number and percentage of hyperthyroidism 2 (100%) in vulgaris group and zero in other types table 13, (figure 6,7).
Table 13: Distribution of Hypothyroidism, Hyperthyroidism, Diabetes Mellitus and +ve Family History of Psoriasis according to Type of Psoriasis.

<table>
<thead>
<tr>
<th>Types of psoriasis</th>
<th>Age</th>
<th>No. and percent</th>
<th>No. and percent of diabetes mellitus</th>
<th>No.and percent of +ve family history</th>
<th>No. and percent of hypothyroidism</th>
<th>No. and percent of hyperthyroidism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psoriasis vulgaris</td>
<td>37.75±11.371</td>
<td>28 46.6%</td>
<td>7 63.6%</td>
<td>9 75%</td>
<td>2 66.66%</td>
<td>2 100%</td>
</tr>
<tr>
<td>Other types</td>
<td>35.218±11.94</td>
<td>32 53.4%</td>
<td>4 36.4%</td>
<td>3 25%</td>
<td>1 33.33%</td>
<td>0 0%</td>
</tr>
<tr>
<td>P value</td>
<td></td>
<td>&lt;0.05</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td></td>
</tr>
</tbody>
</table>

T3 values mean among other types of psoriasis was decreased compared to vulgaris psoriasis type but there was no significant differences, table 14.

Table 14: T3 Values in Psoriasis Group According to Type of Psoriasis.

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Mean of T3 mmol/l</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A psoriasis vulgaris</td>
<td>28</td>
<td>1.8957</td>
<td>.60326</td>
<td>.11401</td>
<td>Not significant</td>
</tr>
<tr>
<td>B Other types</td>
<td>32</td>
<td>1.7306</td>
<td>.67054</td>
<td>.11854</td>
<td></td>
</tr>
</tbody>
</table>

T4 values mean was decreased among other types group of psoriasis 80.5 and 89.2 in psoriasis vulgaris, but this differences not significant as in table 15.

Table 15: T4 Values in Psoriasis Group According to Type of Psoriasis.

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Mean of T4 mmol/l</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A psoriasis vulgaris</td>
<td>28</td>
<td>89.2143</td>
<td>20.00992</td>
<td>3.78152</td>
<td>Not significant</td>
</tr>
<tr>
<td>B Other types</td>
<td>32</td>
<td>80.5000</td>
<td>19.70099</td>
<td>3.48268</td>
<td></td>
</tr>
</tbody>
</table>

TSH values mean was decreased in psoriasis vulgaris group than other types group 2.4 and 3.2 respectively, but the differences is not significant, table 16.
Table 16: TSH Values in Psoriasis Group According to T3pe of Psoriasis.

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Mean of TSH mmol/l</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A psoriasis vulgaris</td>
<td>28</td>
<td>2.4025</td>
<td>1.66863</td>
<td>.31534</td>
<td>Not significant</td>
</tr>
<tr>
<td>B Other types</td>
<td>32</td>
<td>3.2103</td>
<td>1.83106</td>
<td>.33253</td>
<td></td>
</tr>
</tbody>
</table>

4.2.4. Psoriatic Groups According to Duration of Disease

Psoriasis patients were divided according to duration of psoriasis into less than 10 year duration group (A), and more than 10 year duration group (B). In group A the number was 24(40%), group B 36(60%), there was a strong significant differences between two groups in diabetes mellitus number, the total diabetics number were in group B(>10 year duration).

The number of positive family history was 4(33.4) in group A, and 8(66.66) in group B(>10 year duration), and there was signifith differences.

The number and percentage of hypothyroidism was significantly different among two groups 3 (100%) in group B and zero in group A.

The hyperthyroidism number and percentage was 2(100%) in group A, and zero in group B, table 17, figure (8,9).

Table 17: Distribution of Hypothyroidism, Hyperthyroidism, Diabetes Mellitus and +ve Family History of Psoriasis according to Duration.

<table>
<thead>
<tr>
<th>Psoriasis duration</th>
<th>No. and percent</th>
<th>No. and percent of diabetes mellitus</th>
<th>No. and percent of +ve Family history</th>
<th>No. and percent of hypothyroidism</th>
<th>No. and percent of hyperthyroidism</th>
</tr>
</thead>
<tbody>
<tr>
<td>A &lt;10 year</td>
<td>24</td>
<td>Zero</td>
<td>4</td>
<td>Zero</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>40%</td>
<td>0%</td>
<td>33.4%</td>
<td>0%</td>
<td>100%</td>
</tr>
<tr>
<td>B &gt;10 year</td>
<td>36</td>
<td>11</td>
<td>8</td>
<td>3</td>
<td>Zero</td>
</tr>
<tr>
<td></td>
<td>60%</td>
<td>100%</td>
<td>66.6%</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.01</td>
<td>&lt;0.05</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

T3 values mean was decreased in group A (<10 year duration), compared with group B (1.63 and 1.9) respectively, but this decreased was nbt significantly, table 18.
Table 18: T3 Values in Psoriasis Group According to Duration of Psoriasis.

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Mean of T3 mmol/l</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A &lt;10 year duration</td>
<td>24</td>
<td>1.6358</td>
<td>.51109</td>
<td>.10433</td>
<td>Not significant</td>
</tr>
<tr>
<td>B &gt;10 year duration</td>
<td>36</td>
<td>1.9222</td>
<td>.69657</td>
<td>.11609</td>
<td></td>
</tr>
</tbody>
</table>

T4 values mean was decreased in group A (<10 year duration), compared with group B (>10 year duration), 82.04 and 86.25 respectively, that is not significantly differences, table 19.

Table 19: T4 Values in Psoriasis Group According to Duration of Psoriasis.

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Mean of T4 mmol/l</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A &lt;10 year duration</td>
<td>24</td>
<td>82.0417</td>
<td>19.79565</td>
<td>4.04077</td>
<td>Not significant</td>
</tr>
<tr>
<td>B &gt;10 year duration</td>
<td>36</td>
<td>86.2500</td>
<td>20.50000</td>
<td>3.41667</td>
<td></td>
</tr>
</tbody>
</table>

TSH values mean was decreased in group B compared to group A (2.62 and 3.13 respectively), but there was no significantly differences, table 20.

Table 20: TSH Values in Psoriasis Group According to Duration of Psoriasis.

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Mean of TSH mmol/l</th>
<th>Std. Deviation</th>
<th>Std. Error Mean</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A &lt;10 year duration</td>
<td>24</td>
<td>3.1354</td>
<td>1.65825</td>
<td>.33849</td>
<td>Not significant</td>
</tr>
<tr>
<td>B &gt;10 year duration</td>
<td>36</td>
<td>2.6264</td>
<td>1.90854</td>
<td>.31809</td>
<td></td>
</tr>
</tbody>
</table>
CHAPTER FIVE
DISCUSSION
The etiopathogenesis of psoriasis still remains obscure although many developments and recorded in the treatment and pathogenesis of psoriasis. Propylthiouracil, an anti-thyroid preparation, was successfully used both in local, and systemic treatment of psoriasis. Although the mechanism of action was unclear, it was suggested that this drug might have a regulatory effect on the T cells in the psoriasis plague. Propylthiouracil increased the number of total and suppressor/cytotoxic T cells and reduced activated lymphocytes in psoriatic plaques. Other anti-thyroid agents, such as methimazole, and thiamazole have also been used successfully in the treatment of psoriasis. This means that thyroid hormones may have unknown effects on the disease.

5.1. Psoriatic and Control Groups
In this study which included, 60 psoriatic patients and 60 control, the proportion of hypothyroidism and hyperthyroidism were increased compared to the control group. There was 3 (5%) hypothyroidism cases, and 2 (3.3%) hyperthyroidism cases, which is significantly different from this percentage in control group (table 1), (figure 1).

According to Dr. Ray Peat and others, low thyroid function is associated with many skin problems, including psoriasis. When thyroid function is low, prolactin increases, and Dr. Peat associates excess prolactin with psoriasis. Why? Prolactin increases cell division and sebum formation. Sunlight decreases prolactin formation whereas darkness and stress increase it. This may be the connection between sunlight and the alleviation of psoriasis.

In this study the serum T3 and T4 were decreased and TSH was increased in psoriatic patients compared to control group, but only serum T4, was significantly reduced in psoriatic group (table 2, 3, and 4 respectively). This decrease in serum T4 level did not correlate with gender, age of the patients, types of psoriasis, and duration of disease.

Hoath SB et al. explain that thyroid hormone receptors are expressed in human skin and are thought to be involved in the regulation of epidermal proliferation and differentiation. Thyroid hormones cause an increase in epidermal growth factor (EGF). EGF play an important role in cell proliferation. In psoriasis, increased histochemical expression of EGF receptors has been reported in the epidermis. This altered process of EGF receptor production may be involved in the onset of psoriasis.
According to this theory we can explained the 3.3% of hyperthyroidism in psoriatic patients. Also, another suggestion may be that increased T4 levels result from psoriasis. Increased level of T4 in non-thyroid illness have been reported. About 80% of the extrathyroidal T3 pool is produced from T4 by monodeiodination with 5-deiodinase enzyme in peripheral tissues. The activity of the 5-deiodinase enzyme may diminish in some patients with nonthyroidal disease.\textsuperscript{[97]} 5-deiodinase enzyme activity is regulated by proinflammatory cytokines such as interleukin, and tumor necrosis factor (TNF).\textsuperscript{[32,98]} Cytokines like TNF are directly involved in psoriasis. The reason for the increased T4 levels in psoriasis may be related to the increase in some cytokines in psoriasis.\textsuperscript{[36]}

According to this explanation T4, must be increased in psoriatic patients, and the decrease T4 level in our study can explained as a result of the usage of anti-thyroid drugs in the treatment of psoriasis.

In the present study, and from the history of psoriatic patient the percentage of diabetes mellitus was 18.6 (11 from 60 psoriatic patients). Cohen A. D. et al.,\textsuperscript{[99]} improved that diabetes mellitus percentage in psoriasis was 13.6, when they demonstrates that patients with psoriasis have a significant association with each of the components of the metabolic syndrome.

This different in two studies can be explain by the number of cases was taken, and the nature of community and life style.

The high percentages of positive family history in psoriatic patients (20%, 12 from 60 psoriatic patients), can be explained by psoriatic genetic theory. It was suggested by several studies that psoriasis clusters in families. In the study of Lomholt on the fame islands, 91% had at least one affected first or second degree relative.

Farber and Nall\textsuperscript{[101]} found that 36% of 5,600 respondents with psoriasis had an affected family member. Similarly, Kavli et al., could show the prevalence of psoriasis increases with the number of relatives with the same disease.

\textbf{5.2. Psoriatic Groups According to Gender}

In the present study the psoriatic patients were divided according to gender, age, types and duration of psoriasis.
According to the gender there is a significant increased in the number of hypothyroidism among females compared to number in males, Akhtar et al. has reported 1.3% hypothyroidism in males and 2.75% in female, that explain the higher percentage of hypothyroidism in females psoriatic patients. There was no significant different in hyperthyroidism distribution according to gender (table 5, figure 2,33) There was no significant differences of thyroid function tests levels and number of diabetes mellitus cases according to gender.

Pitchappan RM et al., they found that a female psoriasics most often show a younger age of onset than males.

Lindegard B., demonstrate that psoriasis associated diseases, found more often in female than in male psoriasis.

Krasteva at el., Also established a higher incidence of diabetes in psoriasis patients, but in contrast to the findings of Lindegard, no gender relationship was observed in regard to diabetes and urticaria.

5.3. Psoriatic Groups According to Age

In the present study the psoriatic patients according to age was divided into younger and older groups (table 9, figure 4,5), there was a significant increase in the number of hyperthyroidism among younger group, which can be explained by Hoath SB, and Safer JD et al. about the role of thyroid hormones in the etiopathogenesis of psoriasis.[95,96] Also younger group of psoriasis demonstrates a significant association with positive family history, which agreed by Farbar and Nall.

The older group of psoriasis (more than 40 year), there was a significant association between age and hypothyroidism, which may explained by the theory of long period treatment of psoriasis with anti-thyroid drugs. The number of diabetes mellitus was significantly increased in older psoriatic patients can be explained as a result of increase the percent of type 2 diabetes mellitus in older age group(m), there is a recognized association between diabetes and thyroid disease, which has long been reported, Feely and others studied the relation between diabetes mellitus and thyroid dysfunction.

There were no significant correlation in T3, T4, and TSH levels according to age groups of psoriasis.
5.4. Psoriatic Groups According to Psoriasis Type

In the present study the psoriatic patients dividing into psoriasis vulgaris group and other types group of psoriasis (table 13, figure 6,7), there were a significant increased in diabetes mellitus distribution among psoriatic vulgaris group of psoriasis, this can be explained by Nini et al., they observed an increase in I-ILA-B27 in minimal psoriasis, in A2 in guttate psoriasis and in B41 inverted psoriasis, therefore psoriasis comorbidity appear according to these factors.

There was a significant association between psoriasis and hypo and hyperthyroidism in psoriasis vulgaris type, which can be explained as psoriasis vulgaris is the common type of psoriasis, for that reason more comorbidities can appear at this type of psoriasis.

5.5. Psoriatic Groups According to Duration

According to duration, psoriatic patients was divided into two groups, less and more than 10 year duration (table 17, figure 8 and 9). There was a significant correlation between psoriasis and comorbidities (hypothyroidism, hyperthyroidism, and diabetes mellitus) in group of more than 10 year duration of psoriasis, previous studies was explain the occurrence of psoriasis comorbidies associated directly with the duration of psoriasis.

CHAPTER SIX
CONCLUSION AND RECOMMENDATIONS

6.1. Conclusions

From the results of the present study, it can be concluded that:

- Psoriatic patients had higher percentage of diabetes mellitus.
- The study showed that, many cases of psoriasis had positive family history.
- Positive correlation between psoriasis and thyroid disorders.
- Triiodothyronine (T3) and thyroxine (T4) level was decreased in psoriatic patient compared to control group.
- Risk of psoriasis comorbidities were increased in older psoriatic age groups. The duration of psoriasis had positive correlation with psoriasis comorbidities.
- Psoriasis vulgaris is a common type of psoriasis.

6.2. Recommendations

Further studies are recommended as follows: Free and total triiodothyronine (T3) thyroxine (T4) should be measured. Thyroid antibodies (antiperoxidase antibodies and
antithyroglobuline antibodies) should be measured in the screening for thyroid autoimmune diseases. Ultrasonography and fine needle aspiration make the screening for thyroid disorders more accurate.

CONCLUSIONS
From the results of the present study, it can be concluded that: Psoriatic patients had higher percentage of diabetes mellitus, the study showed that, many cases of psoriasis had positive family history of psoriasis, there was a positive correlation between psoriasis and thyroid disorders. Triiodothyronine (T3) and thyroxine (T4) level was decreased in psoriatic patient compared to control group. Risk of psoriasis comorbidities were increased in older psoriatic age groups, the duration of psoriasis had positive correlation with psoriasis comorbidities.

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<table>
<thead>
<tr>
<th>No.</th>
<th>Author(s)</th>
<th>Title</th>
</tr>
</thead>
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<tr>
<td>88.</td>
<td>Browing, M. C. K. ct</td>
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<tr>
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<td></td>
</tr>
</tbody>
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