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CLINICAL AND HEMATOLOGICAL ESTIMATIONS FOR PSORIASIS SEVERITY THAT CORRELATED WITH CCHCR1 GENE SEQUENCING POLYMORPHISM FOR PATIENTS WITH PSORIASIS ARTHRITIS

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AHMED MOHAMMED FADHIL JAWAD AL-MUKHTAR

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By Ahmed Mohammed Fadhil Jawad AL-MUKHTAR

January 2024

We certify that we have read this dissertation and that, in our opinion, it is fully adequate in scope and quality as a thesis for the degree of Doctor of Philosophy.

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ABSTRACT

CLINICAL AND HEMATOLOGICAL ESTIMATIONS FOR PSORIASIS SEVERITY THAT CORRELATED WITH CCHCR1 GENE SEQUENCING POLYMORPHISM FOR PATIENTS WITH PSORIASIS ARTHRITIS

Ahmed Mohammed Fadhil Jawad AL-MUKHTAR

Doctor of Philosophy in Chemistry

Advisor: Prof. Dr. Şevki ADEM

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January 2024

Most of the prevalent chronic autoimmune and inflammatory diseases is a psoriasis arthritis (PsA), that is a mostly with a multiple idiopathic cause. Our present study was gaining a positive significance changes between the serum biochemical and the hematological parameters for all group subject's. We enrolled at this our present case control study, for two groups (50 patients and 40 healthy control). Clinical and biochemical parameters were represented by a Vitamin D3, Vitamin K2, s. uric acid, Adiponectin, Tumor Necrosis Factor – α, CRP, GSH/GSSG ratio, that done by more than one technique like ELISA, HPLC, spectrophotometric and ELFA. All of these evaluations with a clear change between the patients and control healthy groups. As well as the genetic parameter results of a (CCHCR1 Gene) that's revealed also with a clear and significant polymorphism for the (rs3130453) SNP for a patient's group that show statistically, that done by a PCR (REFLIP) type. Apparently affected and elevation levels of serum uric acid, adiponectin, TNF– α, CRP, ESR and GSSG parameters that been increases for the PsA group also were found a normal level in healthy group. As well as a decrease in the levels of serum Vitamin D3, Vitamin K2 and GSH for a PsA group and also been normal levels in the second group. Due to our revealed and present study results, after matching oxidative stress will be concluded finally elevated and GSH/GSSG ratio found low for patients' group. The poor controlling for the PsA diagnosed cases also may contributed with the family risk and triggering genes factors, for disease (PsA) pathogenesis and exacerbations.

2024, 97 pages

Keywords: Vitamin D, Vitamin K2, ESR, CRP, CCHCR1 gene, GSH, GSSG

ÖZET

PSORIASIS ARTRITLI HASTALARDA CCHCR1 GEN DIZILEME POLIMORFIZMI ILE İLIŞKILI PSORIASIS ŞIDDETI IÇIN KLINIK VE HEMATOLOJIK TAHMIN

Ahmed Mohammed Fadhil Jawad AL-MUKHTAR
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Yaygın kronik otoimmün ve inflamatuar hastalıkların çoğu, çoğunlukla birden fazla idiyopatik nedeni olan sedef artritidir (PsA). Mevcut çalışmamız tüm grup deneklerinde serum biyokimyasal ve hematolojik parametreler arasında olumlu bir anlamlı değişiklik elde ediyordu. Bu mevcut vaka kontrol çalışmamıza iki grup (50 hasta ve 40 sağlıklı kontrol) için kaydolduk. Klinik ve biyokimyasal parametreler D3 Vitamini, K2 Vitamini, s ile temsil edildi. ürik asit, Adiponektin, Tümör Nekroz Faktörü – α, CRP, GSH/GSSG oranı, ELISA, HPLC, spektrofotometrik ve ELFA gibi birden fazla teknikle yapılır. Tüm bu değerlendirmelerde hasta ve kontrol sağlıklı grupları arasında belirgin bir değişiklik görülmektedir. Ayrıca bir hasta grubuna ait (rs3130453) SNP'sinde açık ve anlamlı bir polimorfizm ile ortaya çıkan (CCHCR1 Geni) genetik parametre sonuçları, PCR (REFLIP) tipi ile yapılan istatistiksel olarak da gösterilmiştir. PsA grubunda artış gösteren serum ürik asit, adiponektin, TNF-α, CRP, ESR ve GSSG parametrelerinin belirgin olarak etkilendiği ve yükselme düzeyleri sağlıklı grupta da normal düzeyde bulundu. Bir PsA grubunda serum D3 Vitamini, K2 Vitamini ve GSH düzeylerinde azalmanın yanı sıra, ikinci grupta da normal düzeylerde bulundu. Ortaya çıkan ve mevcut çalışma sonuçlarımız eşleştirildikten sonra hasta grubunda oksidatif stresin nihayet yükseldiği ve GSH/GSSG oranının düşük olduğu sonucuna varılacaktır. PsA tanısı konulan vakaların zayıf kontrolü, hastalık (PsA) patogenezi ve alevlenmeleri için aile riskine ve tetikleyici gen faktörlerine de katkıda bulunabilir.

2024, 97 sayfa

Anahtar Kelimeler: Vitamin D, Vitamin K2, ESR, CRP, CCHCR1 gene, GSH, GSSG

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Ahmed Mohammed Fadhil Jawad AL-MUKHTAR
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CONTENTS

LIST OF SYMBOLS

µL	Microliter
ng	Nonogram
L	Liter
-	Minus
%	Percent
*	Star
/	Divide
+	Plus
<	Less-than
=	Equal
>	More-than
dL	Deciliter
g	Gram
mg	Milligram
mL	Milliliter
ºC	Degrees celsius

LIST OF ABBREVIATIONS

CCHCR1	Coiled-coil alpha-helical rod protein 1
CRP	C-reactive protein
ESR	Erythrocyte sedimentation rate
GSH	Glutathione
GSSG	Glutathione disulfide
MHC	Major histocompatibility complex
PCPs	Primary care physicians
PsA	Psoriasis arthritis
TNF-α	Tumor necrosis factor alpha

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1. INTRODUCTION

Thick, scaly areas of abundantly causes for infected skin. While there is can not be a cure for ever from this disorder, so the psoriasis treatment can help to manage symptoms of disease severity. Doctors or dermatology specialists may prescribe special creams or ointments for psoriasis (Myo Clinic 2022b, Klaus Wolff *et al.* 2013, Almukhtar 2016).

Psoriasis is a chronic, noncommunicable, painful, disfiguring and disabling disease for which there is no final cure and with great negative impact on patient's quality of life. It can also occur at any age, and is mostly common seen in the mean of age group 50–69 (Evaluation 2012). The most reported prevalence of the psoriasis in many countries were ranges between 0.09% (S. *et al.* 1996) and 11.4% (Danielsen *et al.* 2013).

Prevalence of the Iraqi psoriasis patients were been approximately 1.5–2% of population (Almukhtar 2016). Psoriasis also has been a significant impact on patients quality of life and in surveys, patients feel that the current treatments, although often effective, do not provide a satisfactory long-term solution (Jeffrey *et al.* 2010).

Psoriasis is a polygenic and represented a skin disorder caused by an immune-mediated. As well as a various of environmental factors like trauma, infections and medications, may facilitated the disease in predisposed individuals. The characteristic lesion is a sharply demarcated erythematous plaque with micaceous scale, and the plaques may be localized or widespread in distribution (Jeffrey *et al.* 2010).

The chronic inflammation and apparently redness scales around are fairly common. Typical psoriatic scales that mostly seen are whitish-silver and may be develop in thick patches for many patients with red patches. The darker skin and a tone that they can also appear more as purplish so dark brown with grey scales. Sometimes, these patches will crack and bleed (Klaus Wolff *et al.*2013).

Disorder of the psoriasis was results of the speed and over skin production hyperproliferations or increase the process of hyperproliferation of keratinocytes. Typically, skin cells in state with deep grow in your skin and slowly rise to the surface, so the typical life cycle of a skin cell is 1 month. In patients with a chronic plaque of psoriasis this production process apparently occur duo to a few period days. This rapid overproduction mostly leads to the build-up of skin cells (Klaus Wolff *et al.* 2013).

Arthritis is a one of the swelling types and the tenderness. Mostly one or more than one joints with a main symptom of arthritis are joint pain and stiffness, which typically worsen with age. Most commonly types of arthritis are osteoarthritis and rheumatoid arthritis in rheumatoid arthritis (Myo Clinic 2022).

The crystals of a uric acid which form in too much uric concentrations in blood circulation can cause gout in most time chances. Infections and the underlying diseases such as psoriasis or lupus, can cause other types of arthritis (Myo Clinic 2022).

Psoriasis arthritis is one of the forms of arthritis disorders that affects some of patient's peoples who suffer from psoriasis, a skin condition that results in red skin areas covered in silvery scales. Before being diagnosed with psoriatic arthritis, the majority of patients first develop psoriasis. However, for some people, joint issues start concurrently with or before skin patches occur (Myoclinic 2022).

The primary indicators and symptoms of psoriatic arthritis include joint pain, stiffness, and edema. They can range in severity from mild to severe and affect any area of the body, including your fingertips and spine. Periods of remission can alternate with flare-ups of the disease in both psoriasis and psoriatic arthritis. (Myoclinic 2022).

About and Between 1.3% (Bedi. *et al.* 1995) 34.7% (Pariser *et al.* 2015) of individuals persons and patients with disorder of psoriasis were develop to chronic, inflammatory arthritis psoriatic arthritis that mostly leads to joint deformations and disability.

1.1 Aims of This Study

- Examination and determination the genetic levels of the PsA pathogenesis by the polymorphism of a [CCHCR1 gene], and detection the mutation of the [rs 3130453] SNP.
- Serum determination of the clinical scavenging agents' levels of a vitamin D3, vitamin K2 for the PsA and healthy groups.
- Estimations cytokines level to detect the disease severity for PsA and healthy groups adiponectin, TNF-α, as well as serum uric acid and the C-reactive protein.
- GSH and GSSG determination for investigation the oxidative stress state for the two groups.
- Creation a correlation between the genetic results with the clinical levels for PsA group for investigation a pathogenesis triggering.

2. LITERATURE REVIEW

2.1 The Psoriasis Generally

Psoriasis is an auto immune and mediated disease with an unclear cause that is characterized by many clear inflammation sources, that caused by a dysfunction of the immune system, that by away lead to causes inflammation in the body. There may be in mostly with a visible sign of inflammation. A raised plaques different skin types and scales on the skin (Klaus *et al.* 2013).

Over activity of the immune system may be a speeds up skin cell growth. Normally the skin cells were in a completely grow and shed in a month. Psoriasis affected with skin cells like the keratinocytes and the dendric cells this is only in three or four days. Plaques and scales may appear on any part of the body, although they are commonly found on the elbows, knees, and scalp (Jeffrey *et al.* 2010).

The first degree of an immunological disorders and disturbances with the predominance of blood cells type (Th1) duo to the over response and over synthesis of proinflammatory like a cytokines especially in this obvious combination with the genetic predispositions lead to a clear pathogenic vicious circle with the inception and maintenance of the chronic inflammation and abnormal epidermal proliferation that shwed in Figure 2.1), (Anna *et al.* 2015).

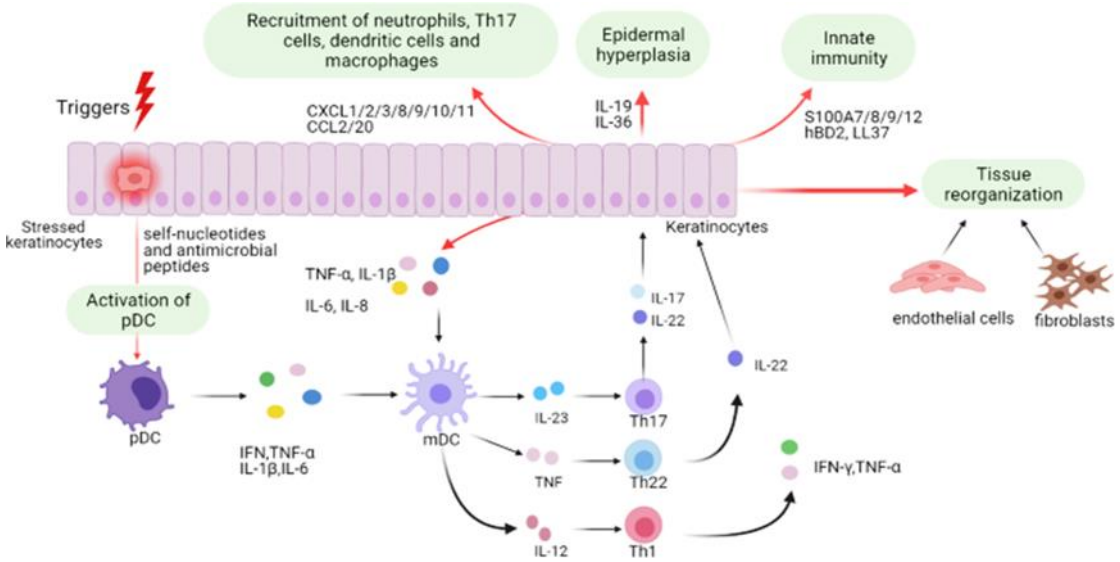

Figure 2.1 Show the role of T1 and T17 in psoriasis pathogenesis

2.2 Types and Classification of Psoriasis

- The Psoriasis vulgaris class: like Acute guttate, Chronic stable plaque, Palmoplantar, Inverse (Klaus *et al.* 2013).
- The Psoriatic erythroderma class: like Psoriatic Arthritis (Klaus *et al*. 2013).

2.3 Psoriasis Pathogenesis

The most noticeable anomalies in psoriasis are changes in the keratinocytes' cell kinetics, specifically a shortening of the cell cycle that causes an increase in epidermal cell and CD8+ T cell production 28 times normal, which is the predominant T cell population in lesions. Psoriatic lesions are thought to be maintained by a continuing autoreactive immune response (Jeffrey *et al* 2010, Klaus *et al*. 2013).

Trigger elements, such as the bodily trauma One of the main things that causes lesions is rubbing and scratching. Psoriasis flare-ups are linked to stress, which has been shown to be as high as 40% in adults and greater in children. Psoriasiform drug eruptions and flare-ups can be brought on by medications such as β-adrenergic blockers, oral lithium,

systemic glucocorticoids, antimalarial medications, and interferon. Consuming alcohol is one potential trigger (Klaus *et al.* 2013).

Plaque makes up over 90% of PS, with the other four forms being pustular, erythrodermic, guttate, and inverse PS. Traditionally, plaque-type PS causes itchy plaques with white scaling on top (Rendon. *et al.* 2019, Boehncke *et al.* 2015, Griffiths *et al.* 2007).

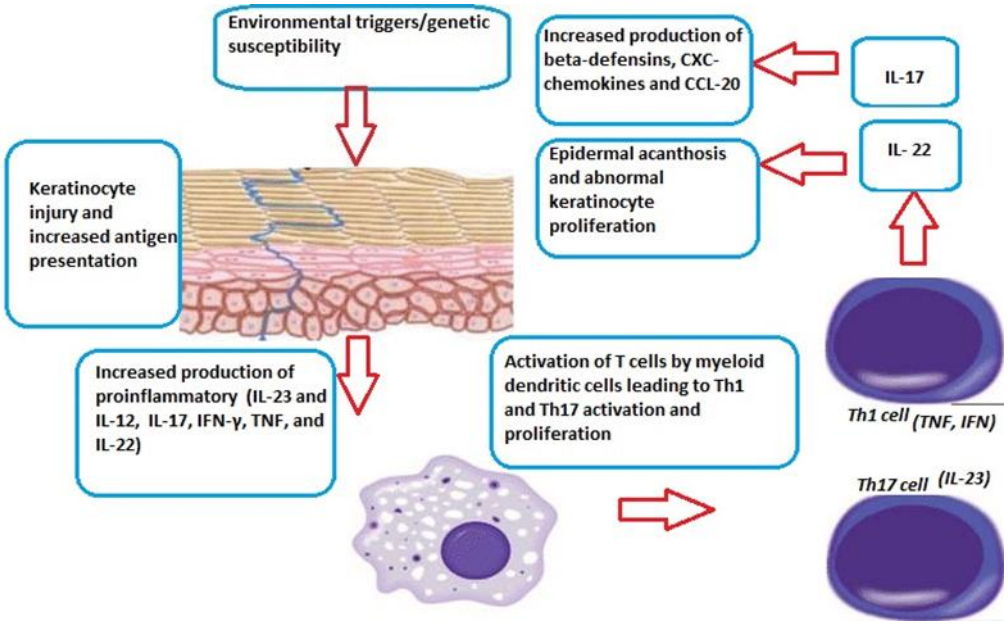

Figure 2.2 Shows the pathogenesis mechanism of PsA progress

2.4 Psoriasis Epidemiology

The frequency. roughly 1.5% to 2% of people living in Western nations. Three to five million people in the US suffer with psoriasis. Most people have localized psoriasis, however about 300,000 people have widespread psoriasis (Jeffrey *et al.* 2010).

Equal sex incidence for infected males and females. As well as race so psoriasis seen low for the incidence and showed a little prevalence in West Africans people , Japanese, also very low incidence or absence in North and South American Indians lands (Jeffrey *et al.* 2010).

Iraqi dermatology clinic recorded that 1.5-3 % patients who visit hospitals with dermatologic problems diagnose with psoriasis as well as also psoriasis arthritis, volgaris chronic plaque psoriasis (Almukhtar 2016).

2.5 Psoriasis Arthritis

Psoriatic arthritis can also develop in psoriasis patients. PsA symptoms include pain, stiffness, and edema in the joints and surrounding tissues. Particularly in its milder forms, PsA frequently remains undetected. Nonetheless, early PsA treatment is crucial to preventing irreversible joint injury (Augusti *et al.* 2015).

Children may be impacted by psoriatic arthritis disease, which can manifest and begin at any age. Ages 30 to 50 are when the illness most frequently manifests. Many begin about ten years after the onset of psoriasis, while some get PsA earlier or don't even realize they have psoriasis at all (AlMease *et al.* 2013, Klaus Wolf *et al.* 2013).

2.5.1 The prevalent symptoms of psoriasis arthritis

Psoriasis arthritis can develop rapidly and severely, but it usually progresses slowly with modest symptoms. Some patients with PsA may experience joint pain, such as following a fracture or other trauma. Genes that initiate development may also be linked to a primary factor such as heredity. One or more of the genes that cause a propensity to psoriasis are inherited by at least 10% of the general population (AlMease *et al.* 2013, Darren *et al.* 2019).

2.5.2 Psoriasis arthritis most common clinical symptoms

The most apparently clinical symptoms of th PsA is a fatigue with a tenderness, pain of joints and swelling over tendons. As well as a swollen fingers and toes that seen in sometimes resemble sausages. So the stiffness and throbbing also swelling tenderness in one or more joints also be present (AlMease *et al.* 2013).

2.5.3 Epidemiology of psoriasis arthritis

Because of the ongoing evolution of our understanding of psoriatic arthritis (PsA), epidemiological investigations of PsA provide significant challenges. The different nations report varying incidence and prevalence rates, indicating the influence of both genetic and environmental variables on the epidemiology of PsA. The wide range and variety of PsA epidemiology can also be attributed to differences in ethnicity, age and gender, a lack of a clear case definition, and small sample sizes (Husni *et al.* 2018).

In order to improve early detection and management of PsA and, ultimately, improve overall patient outcomes and quality of life, primary care physicians (PCPs), dermatologists, and rheumatologists should exercise a high degree of skepticism when treating patients who already have psoriasis (Husni *et al.* 2018).

2.5.4 Pathogenesis of the psoriasis arthritis

Patients who have psoriasis may develop psoriatic arthritis (PsA), a chronic inflammatory arthritis. Some view it as a component of the diverse range of illnesses that are collectively referred to as spondyloarthritis (SpA). At least a few subtypes fall under the SpA category, including the axial and oligoarticular subtypes. There is little knowledge about the aetiology and pathophysiology (de Vlam *et al.* 2018).

To integrate skin and joint manifestations and distinguish PsA from other rheumatic illnesses including osteoarthritis and rheumatoid arthritis, an enthesitis-based model was put out. PsA develops as a result of interactions between environmental variables, immunological response, and gene regulation. Psoriasis is almost a "condicio sine qua non" for the development of PsA, as evidenced by the fact that over 80% of PsA patients also have psoriasis (de Vlam *et al.* 2018).

2.5.5 Mechanisms of bone destruction and proliferation of psoriasis arthritis

A chronic inflammatory joint condition that can impact the axial and peripheral skeletons is psoriatic arthritis. Psoriatic arthritis exhibits a highly variable clinical appearance, with various subtypes having been identified. One of the most common complications of psoriatic arthritis is structural damage to the joint. Joint inflammation and the resulting damage it causes might vary widely in intensity (Lories *et al.* 2018).

The last ten years have seen a progressive rise in our understanding of the molecular and cellular mechanisms behind the skeletal alterations associated with psoriatic arthritis; however, translational confirmation of notions utilizing patient-derived materials remains a work in progress. It is currently unknown how current therapy approaches that target important inflammatory mediators will affect ankylosis and the production of new bone in the medium and long term, but they seem to have a positive effect on joint degradation. New avenues for therapeutic interventions become available when the significance of important growth factors in the latter process is recognized (Lories *et al.* 2018).

2.5.6 Mechanisms immunology and cytokines pathway

Psoriatic arthritis immunopathology is currently the focus of much research. These results highlight important mechanisms where this form of inflammatory arthritis differs from others.. Innate immune cells found in the skin may be activated by direct environmental stimuli, which could then start a chronic adaptive immune response (Kirkham *et al.* 2018).

Although there are less native innate immune cells in the joint, recent research indicates that IL-17-producing cells may be important in immunopathology. The newly available data that has been compiled here will offer crucial theories for the study of pathogenic pathways. Variations in the function of non-immune cells, such as dendritic cells' IL-12 or IL-23 production, may also be important response mediators. Skin keratinocytes and

joint fibroblasts may play a crucial role in mediating the generation of cytokines and effector function (Kirkham *et al.* 2018)

2.5.7 Biomarkers of psoriatic arthritis

Patients with psoriasis may develop psoriatic arthritis, an inflammatory musculoskeletal condition. The skin, axial and peripheral joints, and periarticular structures are also affected by the disease's symptoms. Psoriatic arthritis presents with a wide range of symptoms, making diagnosis and treatment difficult. But prompt diagnosis and suitable treatment afterward lessen disease activity, shield joints from injury, and enhance long-term results (Oikonomopoulou *et al.* 2018).

Biomarkers for disease activity and progression are expected to help with clinical patient management that is both affordable and efficient. The disease-related components of skin and articular tissues, biological fluids like blood and synovial fluid, and cell populations linked to arthritis are all being studied as potential biomarkers for psoriatic arthritis. As biomarkers for diagnosis, activity, and outcome, imaging, such as MRI and ultrasound, is also being studied. Many of these markers show promise for the future treatment of psoriatic arthritis patients, despite the difficulties in using these new markers in the clinic (Oikonomopoulou *et al.* 2018).

- The vitamin D_3

One of the essential fat-soluble vitamins, vitamin D (also known as ergocalciferol-D2 or cholecalciferol-D3), stimulates and aids in the body's absorption of calcium and phosphorus. A healthy diet rich in calcium, phosphorus, and vitamin D is essential for the development and maintenance of strong bones. Rickets and osteomalacia are two bone diseases that vitamin D is used to treat and prevent (Crook 2016) .

The body produces vitamin D when skin is exposed to sunshine. Age, dark skin, and sunscreen protection gear may all prevent you from getting enough vitamin D from the

sun. Osteoporosis, commonly known as bone loss, is treated or prevented using vitamin D and calcium. In addition, low calcium or phosphate levels brought on by conditions including hypoparathyroidism, pseudohypoparathyroidism, and familial hypophosphatemia are treated with vitamin D in addition to other drugs. It can be utilized to maintain normal bone growth and calcium levels in kidney disease patients. Breastfed babies are given vitamin D drops or other supplements because breast milk typically has low amounts of vitamin D (Carl *et al.* 2012).

An essential investigative criterion for general wellness is vitamin D3. It aids in the body's retention of phosphorus and calcium, both of which are necessary for bone growth. However, it may also aid in reducing inflammation, as it is believed that a vitamin D3 deficiency is a major contributing factor to the development of psoriatic arthritis. According to research, vitamin D may assist in reducing inflammation in a number of ways that may contribute to PsA (Ratini 2022).

- It suppresses the production of three inflammatory chemicals made by your body: IL-2, IL-6, and interferon gamma.
- It promotes suppressor T-cell activity. This is a type of immune cell that prevents your immune system from going into overdrive.
- It ramps down the production of natural killer cells, which have been associated with PsA.

- Vitamin K2

In the past, vitamin K was identified in 1929 as a necessary nutrient for the process of blood coagulation, or blood clotting as defined by science. The initial discovery was named "Koagulationsvitamin" and published in a German scientific journal. That is the source of the K in vitamin K (Jones 2023).

There are various subtypes of vitamin K2, which isoprenoid chain length-variable, and is the primary form of storage in mammals. The quantity of isoprenoid residues on the

side chains of these vitamin K2 homologues, known as menaquinones, is what gives them away. Menaquinones are referred to as MK-n, where K is for vitamin K, N is the number of isoprenoid side chain residues, and M is for menaquinone (Premysl *et al.* 2021).

By the inhibiting a generation of signals that trigger inflammation, vitamin K2 reduces inflammation. Other research has examined vitamin K2 in rheumatoid arthritis, another inflammatory-driven illness (Li *et al.* 2009, Meghji *et al.* 1995).

Supplementing with vitamin K2 reduced the total inflammatory results on blood tests in these investigations. Studies particularly examining the effects of vitamin K on psoriasis are still lacking. The best way to combine vitamin K2 with vitamin D is still up for debate (Abdel-Rahman *et al.* 2015, Ebina *et al.* 2013).

Overall, despite the paucity of research, vitamin K may be helpful in the management of PsA. To properly comprehend its function in the illness and to ascertain the best type and dosage of vitamin K for the therapy of PsA, more research is necessary. Before taking vitamin K for PsA or any other ailment, like with any supplement, it's crucial to speak with a doctor (Simes *et al.* 2020).

- Tumor necrosis factor alpha

The cytokine tumor necrosis factor alpha (TNF-α) affects different types of cells in pleiotropic ways. It is known to play a role in the etiology of some inflammatory and autoimmune disorders and has been identified as a key regulator of inflammatory responses. TNF-α is a homotrimer protein with 157 amino acids that is primarily produced by natural killer cells, T lymphocytes, and activated macrophages (Bradley *et al.* 2008, Horiuchi *et al.* 2010, Dan-in Jang *et al.*2021).

TNFα is a major player in the pathophysiology of psoriasis because it causes dendritic and Langerhan's cells to mature, encourages leucocyte migration, and increases the

production of other proinflammatory cytokines. In contrast to PsA, TNFα stimulates osteoclast formation and activation as well as the manufacture of bone-degrading enzymes, which results in inflammation and joint and bone damage (Giampiero. *et al.* 2012, Fantuzzi *et al.*2008)

The function of TNF-α in psoriatic and rheumatoid arthritis. Th1 cells and macrophages release TNF-α primarily. TNF-α stimulates synovial fibroblasts in RA, leading to an excess of MMP and cathepsin synthesis. Subsequently, there is a breakdown of collagen and proteoglycan, which leads to the erosion of joints, degradation of bone and cartilage. In RA, osteoclasts cause angiogenesis and synovial hyperplasia. TNF-α and IL-23 are secreted abundantly by activated dendritic cell macrophages in psoriatic arthritis. Th17 cells, which release IL-17, undergo T cell differentiation in response to IL-23. Psoriasis is caused by keratinocytes being activated by blood levels of TNF-_ and IL-17. Additionally, TNF-α stimulates osteoclasts, resulting in synovial fibroblasts and joint erosion (Dan-in Jang *et al.* 2021).

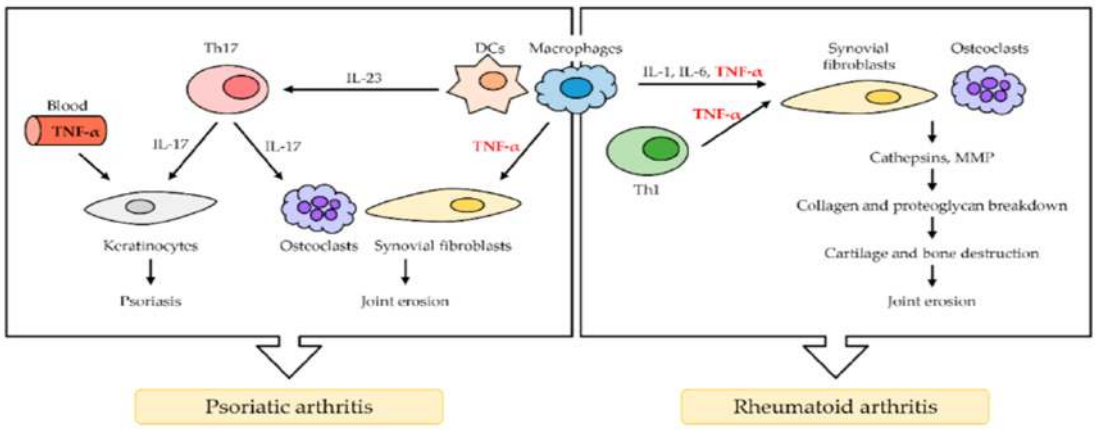

Figure 2.3 Shows a main role of the TNF-α cytokine in a pathogenesis of rheumatoid arthritis with psoriasis arthritis

- Adiponectin

The numerous chemical events that occur inside the body during metabolic processes liberate calories from meals, convert them into energy, and distribute that energy to all body cells (Clinic 2022).

Adiponectin is an adipokine protein and cytokine that is also sometimes referred to as a hormone. It influences multiple metabolic processes and is most recognized for its anti-inflammatory and insulin-sensitizing properties. Adipocytes are cells in white adipose tissue that store energy and are largely responsible for producing and releasing adiponectin. The majority of fat in the body is found in white adipose tissue. Subcutaneous fat is found beneath the skin, visceral fat surrounds internal organs, and marrowfat is found in bones (Achari *et al.* 2017, Clinic 2022).

Adiponectin's primary function involves a number of metabolic and cellular processes. Insulin sensitization and anti-inflammatory actions are its two primary roles. It has also been established that adiponectin controls innate immunity. This role of adiponectin is consistent with recent findings suggesting dermal adipocytes play a role in the skin's natural defense against infection (Shibata. *et al.* 2015, Luo *et al.* 2016).

Serum samples are the primary method used to test the adiponectin content in psoriasis patients. This measure indicates the systemic level of this adipokine, and it was discovered that PsA patients had much greater levels of this adipokine than psoriatic patients without arthritis (Eder *et al.* 2013).

When psoriasis severity (PASI) score is associated with serum adiponectin levels, the latter rise. When determining the severity and potential for complications of psoriasis, leptin may be helpful. Furthermore, these findings supported the link between psoriasis, obesity, and leptin (Baran *et al.* 2015).

In comparison to normal skin, psoriatic lesions showed downregulated expression of the Adiponectin protein in both the dermis and epidermis. By reducing the expression of cytokines linked to psoriasis (Il17a, Il1b, Il6, and Tnfa), topically applied P5 mitigated the severity of imiquimod-induced psoriatic dermatitis. When P5 was applied, the percentage of γδT cells that produced interleukin-17A was considerably decreased (Joong *et al.* 2022).

Serum adiponectin expressions that are out of balance will exacerbate psoriasis and encourage the development of atherosclerosis. The increased release of inflammatory substances and the disturbance of lipid metabolism could be linked to the mechanism. Psoriasis patients' serum adiponectin levels can be used to gauge the severity of their condition and identify vascular lesions early on. Controlling the equilibrium of adiponectin levels is crucial in preventing the worsening of psoriasis and slowing its progression towards cardiovascular disease (Haoxiang *et al.*2022).

- The C-reactive protein (CRP)

Tillett and Francis made the discovery of C-reactive protein (CRP) in 1930. The material in the serum of patients experiencing acute inflammation was originally found to react with the "c" carbohydrate antigen of the pneumococcus capsule, hence the name CRP (Nehring *et al.* 2022).

Psoriatic arthritis patients may have high levels of C-reactive protein (CRP), a significant and non-specific marker of both acute and chronic inflammation (PsA). CRP testing, however, can be used in several ways while managing PsA. Further research is required to determine the appropriate role of CRP testing in the diagnosis and treatment of PsA, given the lack of a more effective serum biomarker of inflammation (Ogdie *et al.* 2022a).

Even in cases where CRP is normal, most people with psoriatic arthritis have detectable systemic inflammation. The corresponding marker pattern is determined by how the psoriatic illness manifests in terms of skin, entheseal, and joint involvement (Maria *et al.* 2020).

- The uric acid

One typical waste product of the body is uric acid. It develops from the breakdown of substances known as purines. The human body naturally contains purines. They can

also be present in a variety of foods, including wine, seafood, and liver. They may also develop within the body as a result of DNA deterioration. The body eliminates purines by urination or bowel movements, which result from purines being converted to uric acid in the blood. However, uric acid can accumulate in the blood if the kidneys aren't functioning properly or if the body produces too much of it. Consuming an excessive amount of meals high in purines or using medications such as niacin, aspirin, and diuretics can also raise your blood levels of uric acid. Uric acid crystals may then develop and gather in the joints. This results in excruciating inflammation. Gout is the name for this ailment. Kidney stones might also result from it (Crook 2016).

Uric acid is believed to be a consequence of systemic inflammation and fast skin cell turnover in psoriasis and psoriatic arthritis. Uric acid crystals that resemble needles accumulate in the gout patient's joints and surrounding tissue, frequently the big toe. This accumulation can result in abrupt flare-ups of excruciating pain and edema. (Arithritis 2023).

In comparison to normal persons or controls, psoriatic patients had hyperuricemia that was around twice as high. After controlling for related baseline variables such age, sex, BMI, and other metabolic syndrome characteristics, psoriasis was a significantly positive predictor of hyperuricemia. Strong evidence suggests that hyperuricemia and psoriasis are related in their own right. According to earlier research, hyperuricemia may be directly caused by psoriasis Figure 2.4 was shows the role of a uric acid in PsA pathogenesis (Gui *et al.* 2018).

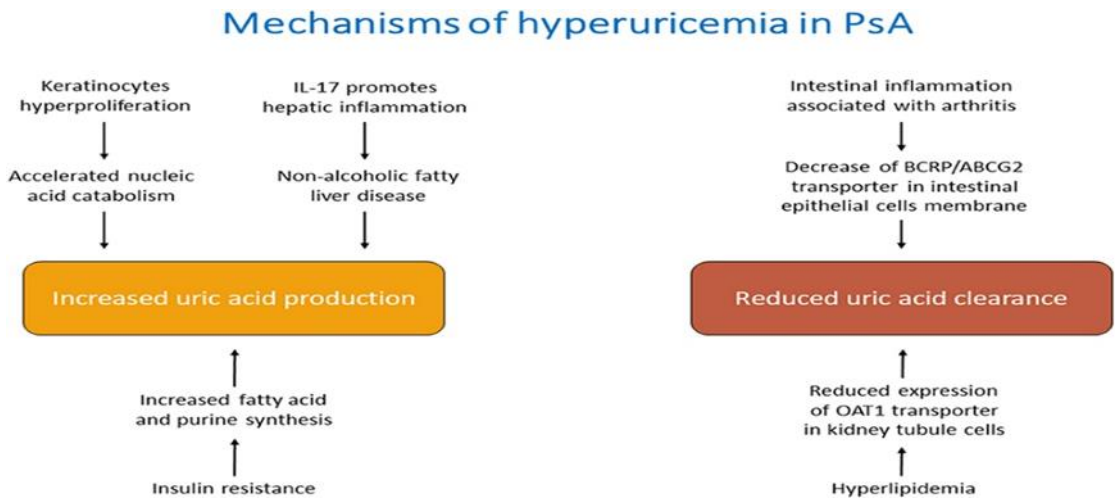

Figure 2.4 Shows the role of uric acid in PsA patients

- GSH

Glutathione (GSH) γ-L-glutamyl-L-cysteinyl-glycine or γ-glutamylcysteinylglycine is that the most significant non-protein thiol available in human and animal cells additionally as in plant, and microorganism. It is probable that the speed of GSH synthesis and consequently, the GSH level are considerably influenced by the supply of intracellular cysteine. Cysteine molecule includes a sulfur-containing portion, that provides GSH molecule its biochemical activity (Almukhtar 2016).

One of the most prevalent thiol antioxidants in living cells is glutathione, or GSH. Reduced cellular GSH levels or reduced catalytic activity of glutamate cysteine ligase (GCL), the enzyme that synthesizes GSH, are linked to a number of age- and chronically-related disorders. Under oxidative stress circumstances, γ-glutamylcysteine (GGC), a precursor to glutathione (GSH), can restore reduced GSH levels by avoiding the regulation of GSH biosynthesis and acting as the limiting substrate (Nady Braidy *et al.* 2019).

The ratio of reduced glutathione to oxidized glutathione within cells is a measure of cellular oxidative stress where increased GSSG-to-GSH ratio is indicative of greater oxidative stress (Fiorella *et al.* 2001).

Patients with psoriasis are known to have elevated levels of free radicals and aberrant GSH enzyme activity. Other tissues may be impacted by this rise in oxidative stress, which is quantifiable systemically. For instance, there is a correlation between the severity of psoriasis and alterations in hemogram as well as red blood cell fragility (Rocha *et al.* 2004, Yldirim *et al.*2003, Seifert *et al.* 2007).

Psoriasis has been shown to be linked both locally4 and systemically to increased oxidative stress and decreased glutathione (GSH) levels. It has been demonstrated that obese psoriasis patients had higher levels of oxidized GSH and lower plasma adiponectin, which are linked to increased oxidative stress and systemic inflammation (Prussick *et al.* 2013).

- GSSG

Two glutathione molecules combine to form glutathione disulfide (GSSG). Glutathione reductase is the enzyme that catalyzes this process. Glutathione disulfide is produced when peroxides like hydrogen peroxide (H_2O_2) and organic hydroperoxides are reduced by antioxidant enzymes such glutathione peroxidases and peroxiredoxins Equation (2.1) (Meister *et al.* 1988, Meister *et al.* 1983, Deneke *et al.* 1989).

$$2GSH + ROOH \rightarrow GSSG + ROH + H_2O \quad (2.1)$$

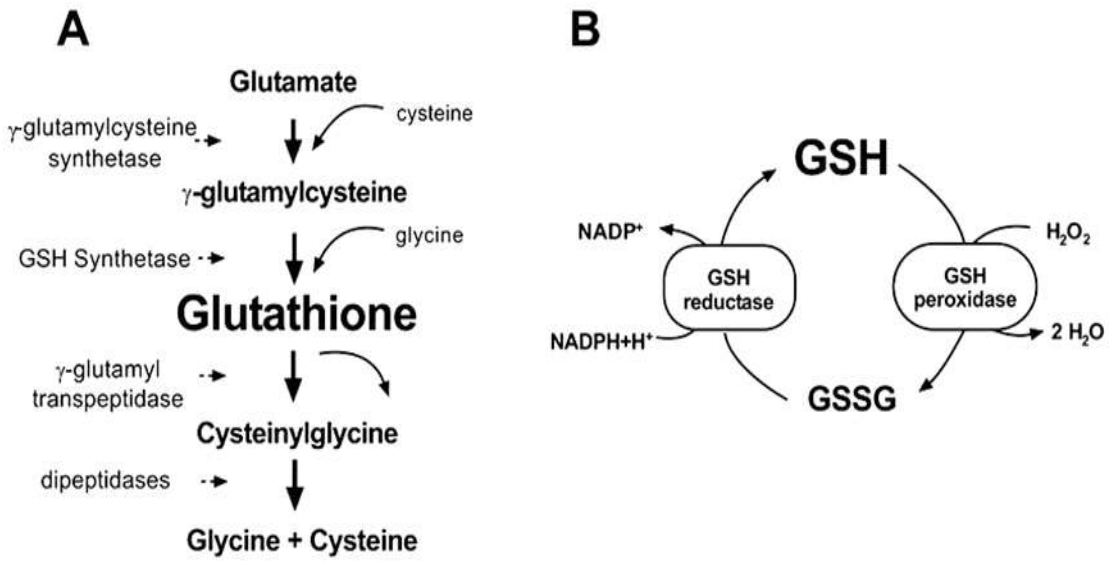

Figure 2.5 Shows the mechanism of action for glutathione enzyme and the shifting between (GSH&GSSG)

2.5.8 Genetics of psoriatic arthritis

Psoriatic arthritis (PsA) develops in 20–30% of persons with psoriasis (Pso). To stop structural deterioration, Psoriasis patients who are (at risk of) developing PsA must be identified. We thoroughly searched five bibliographic databases (Mulder *et al.* 2021).

Psoriasis arthritis (PsA) is a skin and joint autoimmune condition that lasts a long time. Numerous genes, including the CCHCR1 gene, have been linked to the complicated genetic foundation of PsA (Tiwari *et al.* 2023).

Numerous genes, particularly those related to inflammation and the immune system including TNF-α, IL23R, and HLA-B27, have been linked to the development of PsA. Specifically, PsA development and other inflammatory arthritis have been closely linked to the HLA-B27 gene (Nograles *et al.* 2009).

Other genes that have been linked to PsA include those involved in the regulation of bone metabolism and joint development, such as TRAF3IP2 and RUNX2. Variants in

these genes may lead to abnormal bone remodeling and the development of joint damage in PsA (Szczerkowska *et al.* 2020).

In addition to these specific genes as well as the genome of wide is association studies GWAS have identified a number of other the genetic region that may be mostly associat with the development of PsA. These include regions on chromosomes 1, 2, 4, 5, 6, 8, 9, 10, 11, 12, 13, 14, 16, 19, and X (Stuart *et al.* 2015).

All things considered, PsA's genetics are complicated and little known. The precise mechanisms underlying the genetic risk factors for PsA are still being studied, despite the fact that there is evidence of a hereditary component to the disease (Laborde *et al.* 2022).

In line with the clinical heterogeneity of psoriatic arthritis (PsA), the psoriatic phenotype is also diverse. Research has repeatedly shown that there is a significant genetic component to PsA and that the illness etiology involves a complicated interaction between environmental, immunological, and genetic variables. Examine the genetics of PsA, taking into account both non-MHC loci and the major histocompatibility complex (MHC) area (Winchester *et al.* 2018).

Research has found genetic markers associated with PsA. A genetic marker is a DNA sequence that is physically located exactly on a chromosome. The protein structures called chromosomes hold the genetic material required to create progeny. The heritability of particular genes or situations may be tracked with the use of genetic markers. They might also be useful in estimating a person's risk of contracting an illness. Previous research indicates that a sizable fraction of PsA's heritability may be attributed to single nucleotide polymorphisms (SNPs) in the HLA region of chromosomes (Stella Bard. 2021).

- The CCHCR1 gene

The CCHCR1 (Coiled-coil alpha-helical rod protein 1) This gene, which is found on chromosome 6p21.3, controls the proliferation and differentiation of skin cells. It has been discovered that the CCHCR1 gene is linked to the likelihood of acquiring psoriasis and PsA. It is around 63 kilobases long and has 10 exons that code for a 939-amino acid protein (NCBI 2023).

The protein produced by the CCHCR1 gene contains several domains, including a coiled-coil domain and a zinc finger domain. These domains are thought to be important for protein-protein interactions and binding to DNA (Sharifi *et al.* 2017).

The CCHCR1 protein contains several domains, including a coiled-coil domain and a zinc finger domain, they are assumed to play a role in binding to DNA and protein-protein interactions. Although the exact purpose of the CCHCR1 protein is unknown, it is thought to be involved in immune response regulation as well as cellular signaling pathways (Ying *et al.* 2022).

3. MATERIALS AND METHODS

The main purpose these clinical and genetic investigation and examination were done to learn more about the issues of psoriasis arthritis and give more clear idea for inflammatory disease diagnosis, pathogenesis and progression. The main objectives that will be shown in the present study were given a relationship between the clinical parameters and the genetic mutations for the PsA progression and the extent of the relationship between them. The gadgets utilized in this investigation are mentioned in the materials for this chapter. The collection of samples and techniques for keeping them safe until the last results are known are also briefly covered in the procedures section.

3.1 Materials of This Study

All the materials and chemicals that used in the present study as supplied without further purification are listed in Table 3.1.

Table 3.1 Lists the unpurified materials and compounds utilised in this study

No	The Chemicals	Purity	Company and Country
1	Acetonitrile for HPLC mobile phase	99.99%	Sig.Aldrich Germany
2	Binding Buffer TGP-2	99.9%	Germany
3	CRP Detection Buffer (fluorescence conjugate)	99%	Belgium
4	CRP Strip (Cartridges)	99%	Belgium
5	Distilled water	98%	England
6	Elution Buffer EL-3	99.9%	Germany
7	Ethanol	99.9%	France
8	Lysis Buffer TCBL-1 a	99.9%	Germany
9	Manual	99.9%	Germany
10	Methanol absolute HPLC	99%	France
11	Mini spin columns	99.9%	Germany
12	Mini spin columns	99.9%	Germany
13	[Neocuproine] 2,9-dimethyl-1,10 phenanthroline	98.9%	England
14	O-Pthaldiealdehyde (OPA)	99%	U.S.A
15	Oxidized Glutathion (GSSG) Standard	99.9%	USA
16	Proteinase K (20 mg/ml)	99.9%	Germany
17	R1, Uric Acid, Enzyme	99%	France
18	R2, Uric Acid, Buffer	99%	France
19	R3, Uric Acid, Standard	99%	France
20	Reduced Glutathione (GSH) Standard	98%	USA
21	Sodium Citrate Solution (ESR)	98%	China
22	Wash Buffer TE-4 concentrate c	99.9%	Germany
23	Wash Buffer TGI-3 concentrate b	99.9%	Germany
24	Agarose	99.9%	China
25	DNA ladder100 bp and 1 kbp	99.9%	Korea
26	Loading dye (bromophenol blue)	99.9%	USA
27	PCR Master Mix Kit	99.9%	Korea
28	Sybr safe	99.9%	USA
29	Tris Borate EDTA buffer	99.9%	USA

3.2 Instruments and Equipment of This Study

All the instruments and equipments that used in the present study as supplied without further purification are listed in Table 3.2.

Table 3.2 Lists all the devices and equipment used in this investigation as provided unpurified

No	The Instruments and Glasses	Company and Country
1	Beaker 50 ml	Lab (Germany)
2	Centrifuge	Eppendorf (Germany)
3	Cylinder 1000 ml	Lab (Germany)
4	The Disposable Test Tube of (10 mL)	China
5	The Distillator	England
6	Tubes of EDTA Type	AFCO (Jordan)
7	Reader and Washer of ELISA Instruments	USA
8	Mini Tube of Eppendorf (1.5 ml)	China
9	ESR Westergren pipette	China
10	Filter paper	Whitman No.1 (England)
11	Gel tube	AFCO (Jordan)
12	High Performance Liquid Chromatography (HPLC)	UFLC Shimadzu (Japan)
13	Incubator	Fisher (USA)
14	İchroma Incubator	BELGIUM
15	İchroma Reader	BELGIUM
16	JK-201BD Oscillator Shaker	Germany
17	Micro syringe filter	Anow (China)
18	Micropipette 100-1000 µl	Slamed (Germany)
19	Micropipette 10-100 µl	Slamed (Germany)
20	Micropipette 20-200 µl	Slamed (Germany)
21	Micropipette tips	Biobasic (Canada)
22	Multichannel micropipette 10-250 µl	Slamed (Germany)
23	Orbital shaker	Esco (Japan)
24	Oven	Memart (Germany)
25	Sensitive balance	Hearson (England)
26	Spectrophotometer	Sartorius (Germany)
27	Volumetric flask 100ml	Aple (Japan)
28	Water path	Lab (Germany)
29	Weight and height measuring device	Lab Companion (Korea)
30	Eppendorf tube (1.5ml)	China
31	Gel electrophoresis	Korea
32	Hood	China
33	Incubator	Germany
34	Kahn tube	China
35	Autoclave	Japan
36	Cooling Centrifuge	USA
37	Deep Freeze	Korea
38	Optizen (Nanodrop)	Korea
39	Test tube with Separating gel	Jordan
40	Thermocycler	Korea
41	UV trans-illuminator	UK
42	Vortex (Electronic)	Germany
34	Water bath	Germany

3.3 Chemicals and Kits of This Study

Table 3.3 is contains a list of all the chemicals and kits used in this study as supplied, unpurified.

Table 3.3 Lists all unpurified substances and kits utilised in this investigation

No	The Chemicals	Purity	Company and Country
1	ELISA Kit for Apeponectine	99.9%	USA
2	ELISA Kit for Human TNF-α	99.9%	USA
3	ELISA Kit for Vitamin K2	99.9%	AFG Bioscinces, USA
4	Fluorescence Immunoassay for CRP	98.0%	Belgium
5	Manual Spectronic Kit for Uric Acid	98.0%	BIOLABO, France
6	Pure Column DNA Extraction Kit	99.9%	Germany
7	Rapid ESR Kit	99.0%	Chaina
8	TOSOH ST	99.9%	JAPAN

3.4 Subjects of This Study (Patients and Control) Groups

Subjects enrolled present study were collected due to many factors that will be showed in details.

3.4.1 Subjects exclusion and inclusion criteria

The inclusion criteria were included for many patients (50) of cases with past diagnosed psoriasis arthritis. So, the selections done only for the chronic patients who recurrent visit the dermatologic and rheumatology clinics of Hospital.

Exclusion of participants (patient and healthy control) were done for the suffered from any other chronic diseases like the chronic heart disease and diabetes.

Excluded from the current study were participants who were pregnant, smokers, taking any medication other than psoriasis treatment, and patients who had received treatment during the previous two weeks to one month.

Subjects who represented the control health group, were collected without any problems and chronic diseases.

3.4.2 Patients selected group

In all, fifty patients psoriasis arthritis were included in the research. There were numbers divided into to 30 males and 20 females. Patients were attended to Rheumatology and Dermatology Clinics of Merjan Medical Teaching Hospital in Hilla City.

All of patients that enrolled in this present study with chronic PsA for several months or years and received various topical and systemic treatments like potent topical steroids, methotrexate, negotiator. But at the time of the study done patients were stopped the treatments intake, either because of no response or poor complaints. Some of cases were newly diagnosed as PsA

The data of PsA all patients were enrolled in this present study were, taken such as their family history, age, sex, residences, and the duration of psoriasis and then progression to PsA and associated symptoms like itching and swelling were reported in the screening sheet abbreviated with all joints. Also, the type of medication that received by the patients and the duration of treatments were reported.

3.4.3 Healthy control selected group

In this study, forty participants (20 men and 20 females) who looked to be in good health were matched in terms of age and sex with patients. There were no skin issues or dermatological diseases when the subjects were chosen.

3.4.4 Study design and selection of sample size

This present study was designed as a case and a control study. As ell as the sample size is calculated according to standard formula called Daniel sample size formula equation.

$n= Z^2P(1-P)/d^2$, (Almukhtar 2016).

3.4.5 Date and place of study

The added time frame was November 2022 June 2024. The work was conducted in the Central Laboratory of Merjan Medical Teaching City Hospital in Babylon, Hilla City, Iraq, in the Departments of Dermatology, Rhumatology, and The Biochemistry Section.

3.5 The Specific and Physical Measurements:

There were many of main and specific measurements examination done for patients and the healthy control groups that calculated by mathematical equations.

3.5.1 The body mass index (BMI)

A precise mathematical equation was applied to calculate the body mass index for both the patients and the control group. The weight in kilograms was divided by the square height in meters.

$$\text{Body Mass Index (BMI)} = \frac{\textbf{Weight (Kilograms)}}{\textbf{Height (Meters)}^2}$$ (Almukhtar 2016)

3.5.2 Psoriasis severity index (PASI) score detection disease severity

The three main features of chronic PsA lesions—their redness, thickness, and scariness—offer a way to gauge the disease's severity. One approach for assessing the

severity of psoriasis, a chronic skin illness, is the PASI score. The thickness and redness of the scales, the quantity of skin involvement, and the percentage of body surface area impacted by psoriasis are all factors considered in the score (Fredriksson 2023).

The area impacted by the scoring method was used to classify the clinical severity of psoriasis. (PASI) score >20% is deemed a severe form; a score between 10 and 20 percent is defined as moderate; a score below 10 percent is considered a mild form (Salgado *et al.* 2021).

- Skin sections

The body was divided into four sections according to its parts and the skin was divided according to this parts by the percent method:

- 40% of total body skin in the lower limbs.
- 30% of total body skin in the body trunk area.
- 20% of total body skin in the in upper limbs.
- 10% of total body skin in the head .

- Area

The each of these surfaces area of infected the skin with psoriasis plaques in each part of the body should be calculated in a percentage.

- The criteria of a severity

The degree of psoriasis was determined by a number of factors, such as scaling, erythema, itching, and plaque thickness. The area impacted scoring method was used to classify the clinical severity of psoriasis. Where een the [0 is with non disease, 1 in mild state of disese, 2 in a moderate, 3 at a sever state adn the 4 in the maximum.

3.5.3 (PSAJAI) the PsA joint activity index detection severity

In order to create models that best distinguished active drug from placebo.The models were primarily based on statistical considerations and some clinical input. Data and the present PsA response criteria were assessed, and logistic regression models based on the component parts of these response criteria were examined. The 30% response criteria of the American College of Rheumatology were modeled by the PsAJAI (PHILIP *et al.* 2011). PsAJAI was calculated by the electronic PsA calculator (App 2021).

3.6 The Detemination Techniques Methods

There were many important and developed techniques method for the clinical, hematological and genetic parametrs evaluations like TOSOH, ELISA, HPLC, Spectrophotometric, ESR and PCR methods. These technique will be show beloow breaifly.

3.6.1 Clinical biochemical measurements

There were more than one and many techniques that used in the present study, so there were showen below breafly with their details.

- The determination of serum vitamin D concentrations by TOSOH technique

The Tosoh technique's competitive antigen-coated plate, ST AIA-PACK 25-OH While analyzing 25-OH Vitamins D2 and D3 in equimolar quantities, vitamin D correlates well with gold standard methodologies. (WICK, 2015).

- The quantitative determination of serum vitamin K2 by ELISA technique

Principle:

The kit assays the amount of human vitamin K2 (VK2) in serum for human samples quantitatively. It coats microtiter plates with purified VK2 antibody, creates solid-phase antibody, and then adds VK2 to wells. After fully washing. Combine VK2 antibody with labeled HRP to form antibody-antigen-enzymeantibody complex. Next, the O.D. of the samples is compared to the standard curve to determine the concentration of VK2 in the samples (Lasemi 2019).

The preparations of reagent:

- That done by diluted a [20ml] of Concentrate washing bufer [30ml] into the a deionized water to prepare [600ml] of wash bufer.
- The STD solution should be diluted the standard Pipette 50l standard diluent in each tube. Pipette 100l standard [13.5 nmol/L] in the fifth tube.
- The undiluted Standard serves by, a high STD [13.5 nmol/L]. Samples was also diluented serves as the zero standard blank well [0 nmol/L].

Assay procedure:

- STDs was pipette 50l to testing standard in a first marked wells pipette sample that also diluent 40l to testing sample well, then added for test it.
- A samples with a dilution 5-fold, putting and pipette the samples to labeled wells.
- Incubation was done with the cover with the adhesive strip provided, incubate for [30 min] at [37 C].
- Configurate a liquid that dilute wash solution 30-fold with distilled water.
- Washing was done by, uncover the adhesive strip, discard liquid pipette washing buffer to every well, still for [30sec] then drain and proess was repeated for 5 times.
- The enzyme was added Pipette HRP-Conjugate reagent 50l to each well, except blank well.
- Incubate this operation with 4 cycles.
- Washing operation with 6 cycles.

- Color of the pipette Chromogen Solution A [50ul] and Chromogen Solution B 50ul was added to each well, and then avoid the light preservation.
- Leave the plate for [15 min] at [37 C].
- Stop solution of the reaction was added by Pipette Stop Solution 50l to each well, stop the reaction (the blue change to yellow).
- Calculations was done by the taking blank well as zero. Thte Reading of a concenrtrationsby the absorbances of all samples at [450nm] after the stop solution by [15min].

- The quantitative determination of serum TNF-α levels by ELISA technique

The Sandwich-ELISA idea is used in the ELISA kit concept. An antibody specific to human TNF-α has been pre-coated on the micro ELISA plate included in this kit. The micro ELISA plate wells are filled with Standards and Samples, then the particular antibody is added. Next, each micro plate well receives a sequential addition of a biotinylated detection antibody specific for Human TNF-α and an Avidin-Horseradish Peroxidase (HRP) conjugate before being incubated (Mandy Alhajj *et al.* 2023).

Sample collection:

Serums of all participants were allowed at room temperature or overnight at [2 to 8℃] before centrifugation for [20 min] at [1000G] at [2 to 8℃]. Collect the supernatant to carry out and used for this assay.

The preparations of the reagents:

1. All of the study reagents was brout to at room temperature [18-25C] before use.

2. the washing bufer was diluted by a [30mL]. concentrated and compleded to [720mL] of deionized water.

3. The standard of a working solution sould be Centrifugated by [10.000 G], for [1 min]. And thene added [1.0 mL] of all the references of STDs as well as the samples with the diluent. Reconstitutions ofa working solution of [500pg/mL]. Taken to create the serial dilutions that started by a [500, 250, 125, 62.500, 31.250, 15.630, 7.81, 0 pg/mL].

4. The working solution that contain a detection Ab, required an amount was taken before the experiment done [100µL for every well]. The concentrated solution Ab should be centrifugated at [800G] for [1 min].

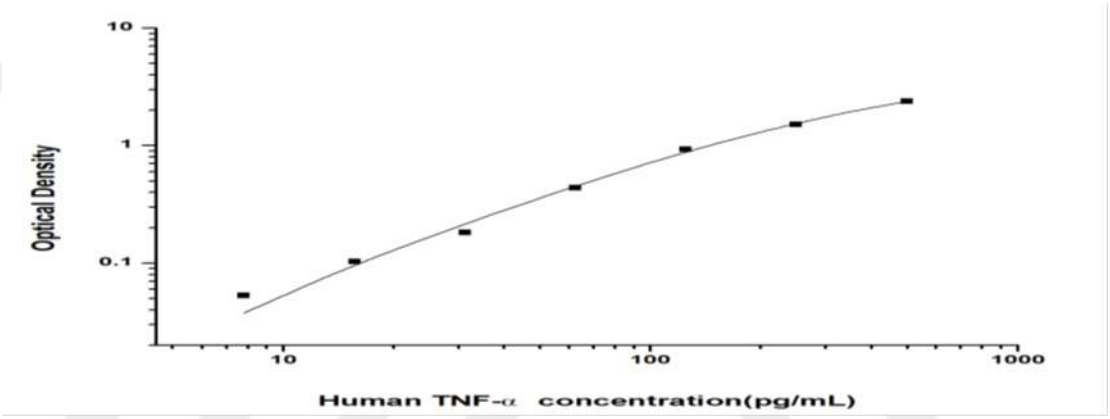

Figure 3.1 Shows ELISA kit standard curve of serum human TNF-α

Assay procedure:

1. A[100 µL] was added of a diluted standard. The blank and sample for the each dilution of standard, blank and sample into the appropriate and labeled wells. The cover of the plate was applied with the sealer provided in the kit. Incubate for [90 min] at [37°C].

2. A [100 µL] of decant liquid or solution was added from for each well .The cover of the plate was applied with a new sealer. Incubation for 1 hour at [37°C].

3. A [350 µL] decant wash solution was added for each well. Repeat this wash step 3 times.

4. A [100 µL] was added of the HRP conjugate or a working solution to each labeled wells. The cover of the plate was applied the plate with a new sealer. Incubate for [30 min] at [37°C].

5. The decant of the solution from each labeled well added, this step was repeat of wash process was done for 5 times as conducted in step 3.

6. A [90 µL] was added of substrate reagent for each labled wells. The cover of the plate was applied the plate with a new sealer. Incubate for about [15 min] at [37°C].

7. A [50 µL] was added of stop solution for each well.

8. Reader of the ELISA was determine at the optical density with a micro-plate reader set to [450 nm].

- The quantitative determination of serum adeponectine levels by ELISA technique

Each micro plate well receives a consecutive addition of the Horseradish Peroxidase (HRP) conjugate, which is then incubated. The free conjugated components are then removed by washing (Mandy Alhajj *et al.* 2023).

Sample preperation:

Blood sample was allowed as well as the serum samples for [2 hours] at room temperature or from the overnight at room temperature for thiong.

Reagents preparations:

1. Reagents was brought in room at a temperature [18 – 30 C].

2. The washing Bufer [30mL] concentrated was copleted to [720mL] of deionized water.

3. The STD. Of working solution was centrifugation [10.000G] for [1 min]. [1.0 mL] of erference was added to the standard and the sample diluent. The main serial dilutions was needed in a gradient [0 ug/mL 20, 40, 60, 80, 100 and 120].

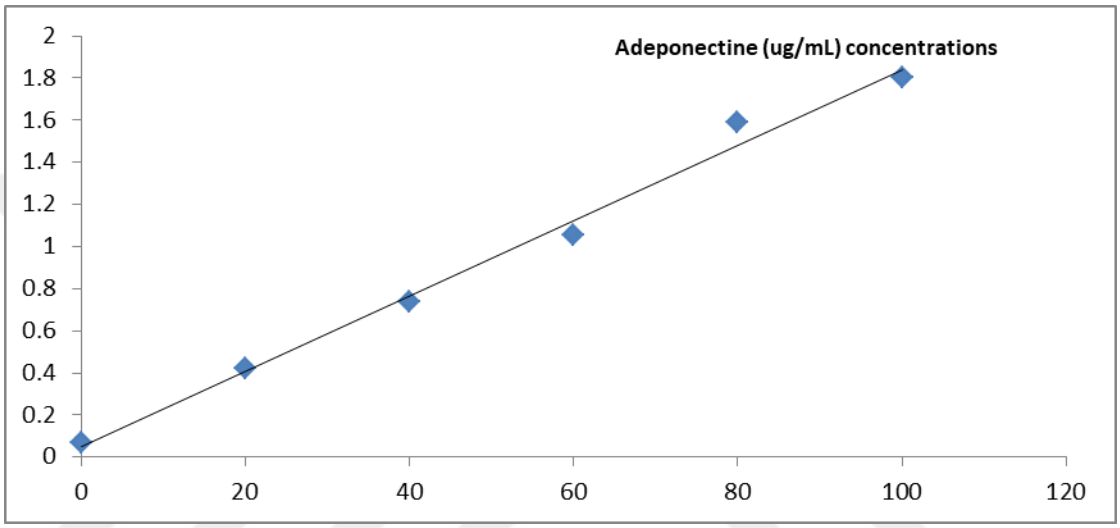

Figure 3.2 Shows ELISA kit standard curve of serum human adeponectine

Assay procedure:

1. The blank and sample were added a 50µL for the each dilution of standard. The cover of the plate was applied with the sealer provided in the kit. The incubate done [90 min] at [37°C].

2. For each well [350µL] was added a washing bufer for each labbeled well. this washing step was repeat for a 3 times.

3. A [100µL] was added of HRP conjugate of a working solution for the each labbeled well. [30 min]. incubation at [37°C].

4. 5 times of washing step shuld be repeated as conducted in step 2.

5. A [90µL] was added of the substrate solution each labbeled well. Incubation for about [15 min] at [37°C]. The protect the plate from light was done.

6. A [50µL] was added of stop solution to each well. The adding stop solution should be done in the same order as the substrate solution.

7. The reading process was determine on the of each well at once with a micro plate reader set to [450 nm].

- The determination of plasma CRP levels by fluorescence ımmunoassay technique

This test's basic methodology is sandwich immunodetection. In order to capture the other immobilized antibodies that fixed on the test strip, the detector antibodies, which were in a buffer, attach to the antigens that we screened in the sample and form antigen-antibody complexes. These then migrate onto nitrocellulose matrix (Pepys *et al.* 2003).

The linearity of kit:

The high concentration range was [300 mg/L] and its also was diluted with the low pool con. [2.5 mg/L] to the final percentag 100%, 75%, 50%, 25%, 10%, 5% and 0%. The coefficient of linear regression was R=0.997.

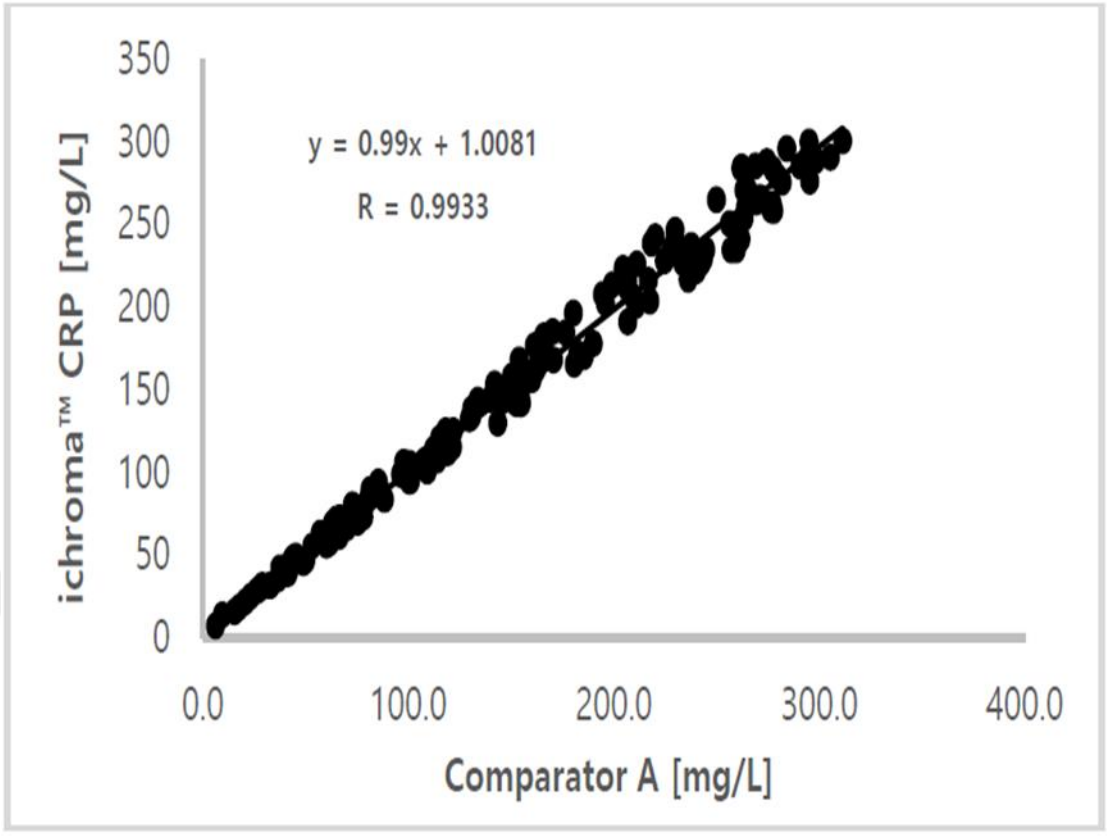

Figure 3.3 Shows a standard curve of kit lenarity for serum human CRP

Procedure:

- A [10 µL] of the plasma patients' sample was drawer as a specimen with a sample collector.
- The assembling of a sample collector and the detection buffer shoulb be done for mixing the plasma with a ragent.
- The Mixture shakes for 10 times or more until the sample out of the sample collector by inversion.
- After the collector cap was removing off from the assembled tube. Only two drops of reagent were discarded into the tap derange
- Two drops only of the mixture were uploaded onto the sample well of the testing cartridge.
- The cartridge was leaving the at room temperature for [3min] before inserting the device into the holder.

- The sample was loaded cartridge immediately when the incubation time is over.
- The cartridge was inserts into the holder of the instrument for ichrom tests for reading the results.

- The determination of serum GSH and GSSG concentrations by HPLC technique

Principle:

The two forms of glutathione (GSH and GSSG) in bodily fluids, such as serum, can be identified using the HPLC method and the drivatization principle. At pH 12, orthophthalaldehyde (OPA) degrades glutathione. This assay makes advantage of the high specificity and high selectivity HPLC technological advances with a fluorescence detector for many different substances, which involves glutathione. (Francesco. *et al. 2021)* (Almukhtar, 2016) (Liu S. *et al.* 1996) .

The Shimadzu 10AV-LC model HPLC system, originally outfitted with the binary delivery nozzle model LC-10AV, was employed in this investigation. GSSG oxidized glutathione with OPA complex, and GSH or glutathione was detected using a fluorescence detector. The concentrations of GSH and GSSG were indicated by the eluted peaks in comparison to the standard peak. Five minutes after the run began, the first GSH peak emerged. Thus, within [20 min] of the elution, the GSSG was observable. (Yap LP. *et al.* 2010).

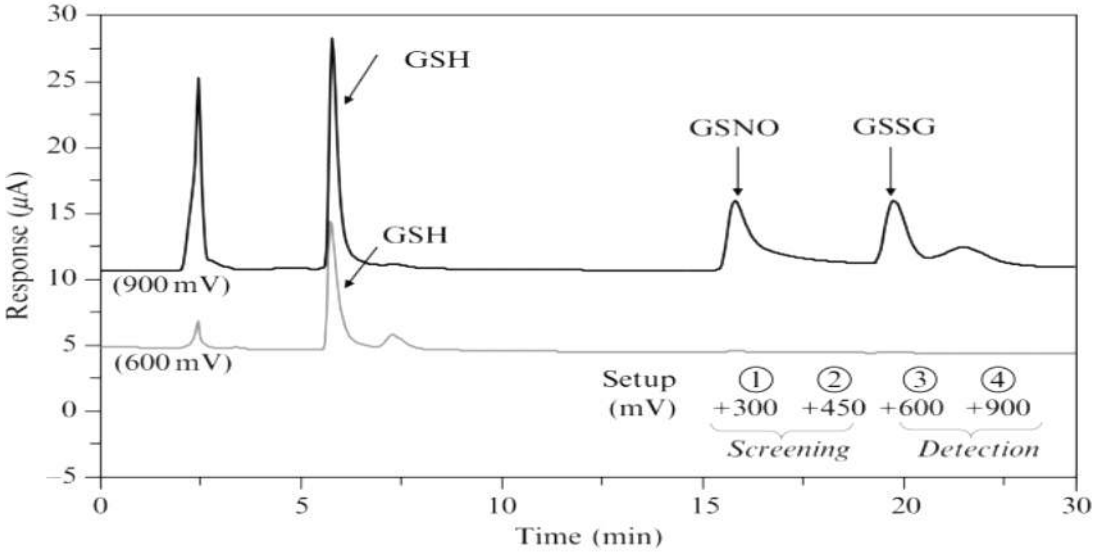

Figure 3.4 Shows the chromatogram of GSH & GSSG standards that eluted in HPLC and shows in screen. GSH in 5 minuts was appear as well as in 20 minuts show a GSSG

Preparations of reagents and procedure:

1- Standard solutions:

By weighing out the minimum amount needed of [0.5 mg] and dissolving it in [500 mL] of HPLC-grade methanol to the appropriate concentrations, a standard solution of GSH was created. Consequently, the GSH standard's eluted peak appears five minutes after the run begins.

2- Ortho-phthalaldehyde (OPA) solution:

Preparation of OPA: A weight of [0.50 mg] of OPA was dissolved in absolute methanol, and adjusted by NH4OH (5N) to pH=12 and brought to a final volume of [5 mL].

3-Mobile phase:

Acetonitrile was used as mobile phase by completed it to distilled water as [60:40ml] for example under pump pressure [2ml/min] it was the flow rate of GSH eluted.

4- Sample treatment:

- A volume of [100 µL] of serum was added to [50µL] of OPA .
- A volume of sample was completed with a 1ml of distilled water to get the dilution factor (1:10 fold).
- The diluted sample was filtered by mille syringe filter.
- After [1min] of mixing by mixer, [20 µL] of sample was taken and injected into the HPLC injector.
- A volume of [2 ml/min] of mobile phase was the flow rate that used for eluted GSH.

The calculation of results:

The area under on a peak of the enzyme is used for calculating the concentration of a GSH as show in the following formula:

Concentration of GSH [µg/mL]=[area of the sample/area of the standard]×[Standard Conc.]×[Dilution factor] (Carroll *et al.* 2016).

- The determination of serum uric concentrations by spectrophotometric technique

The selective oxidation of uric acid by uricase, which changes its substrate into allantoin, leads to the enzymatic determination of uric acid. Uricase reacts with uric acid to generate hydrogen peroxide, carbon dioxide, and allantoin. Quinoneimine, a red-colored compound, is produced when hydrogen peroxide and a chromogen (amino-antipyrine and dichloro-hydroxybenzene sulfonate) react in the presence of peroxidase. Quantification is possible due to these compounds' distinct absorbance at 293 nm (Burtis *et al.* 1999).

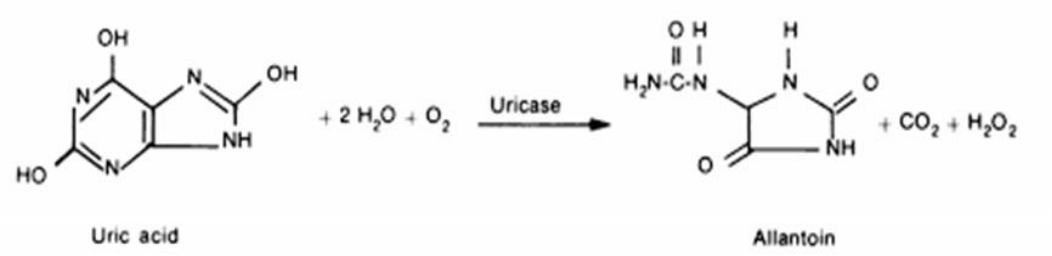

Figure 3.5 Shows the shifting of uric acid to allantoin

Reagents:

R1: The Enzymeof uricase:

- Potassium hexacyanoferrate (II) [42µmol/L]
- Peroxidase >[450 U/L]
- Amino-antipyrine [0,150 mmol/L]
- Uricase >[120 U/L]

R2: The Buffer:

- Dichlorohydroxybenzene Sulfonate [2 mmol/L]
- Tris pH [8.0] at [25°C] by a [50 mmol/L]
- Preservative

R3: The Standard [STD]:

- Uric acid [10 mg/dL] [595 µmol/L]

Procedure:

- Reagent [1000 µL] took up by can tube.
- Control Specimen [25 µL] Serum.

- Mix the let stands for a 5 minutes at [25°C].
- The absorbance was recorded at 505 [495-505nm] range of spectrum.
- Blank should be against by a reagent.

3.6.2 The determination of the ESR degree by precepetation sedementation technique

The principle of test:

A nonspecific test called the Erythrocyte Sedimentation Rate (ESR) is used to determine if an illness is actively present or absent. The differing densities of the red corpuscles, or red blood cells, and their medium cause the RBCs to settle. An elevated ESR is typically caused by an increase in plasma proteins, or acute phase globulins, and is less frequently caused by intrinsic RBC features (Wintrobe 30). The Modified Westergren Method is used to measure ESR in mm/hr (Tishkowski 2023).

Procedure:

- The blood sample was transferred from the anticoagulated whole blood collecting test specific tube to a vertical test tube contain a [0.25ml] of a sodium citrate.
- A mixed blood and [sodium citrate] sample was allowed to stand in the vertical tube and top rubber for [1 hour], and then taken a grade number will be the result (Tishkowski 2023).

3.6.3 The genetic modification determination for CCHCR1 gene

There were more than one or many techniques that used in the prevalent diagnosis in the world and mainly for researches for the genetic study levels like PCR, Real time PCR and the Sequencing. So, some of there were techniques applied in the present study and then show below briefly with their details.

- The detection of CCHCR1 gene by real time PCR technique

The enzymatic replication of DNA forms the foundation of the PCR process. Primer-mediated enzymes are used in PCR to amp up a brief DNA fragment. DNA polymerase creates new DNA strands that are complementary to the DNA template. The only nucleotide that the DNA polymerase can add to the pre-existing 3'-OH group is one. For this reason, a primer is needed. Consequently, more nucleotides are added to the DNA polymerase's 3' prime end (BYJUS 2022) .

The main components of PCR test:

Components of PCR constitutes the following:

- DNA Template: was been the DNA of an interest from the patients sample.
- DNA Polymerase: [Taq. Polymerase] was used. It is thermostable and does not denature at very high temperatures.
- Oligonucleotide Primer: where been the short stretches of a single stranded DNA complementary to the [3’ ends] of sense and anti - sense strands.
- Deoxyribonucleotide triphosphate: These detected as a provider of the PCR cycling.
- Buffer System: The dual magnesium and a potassium were provided an optimum conditions, that the DNA needed for a denaturation and renaturation. It is also important for fidelity, polymerase activity, and stability.

- DNA extraction (ORIGENE 2023):

- Before starting: Concentrates are Wash Buffer TE-4 and Wash Buffer TGI-3. The advised amounts of ethanol (Wash Buffer TE-4) and isopropanol (Wash Buffer TGI-3) were added (10%) before using for the first time, as per the bottle regulations.
- Warm up an incubator to [55 °C] (see to step 1 of the protocol) and a second one to [70 °C] (refer to step 3). Elution Buffer EL-3 should be heated at 70 °C.

Procedure:

- [200µl] as added of lysising bufer [TCBL-1 + 20 µl] and Proteinase K Solution [20mg/ml] to the sample. Vortex was done at maximum speed for [1 min].
- Incubation of the tube at [55 C] at the shaker with heating for [60 min].
- [200µl] was added also of the binding bufer [TGP-2] for a lysate, after then vortex done for [10sec] and the incubate of mixture solution at [70C] for [10 min].
- Centrifugation the tube [10000G] for a [5min], and then transfer the DNA containing supernatant for a new sterilized tube.
- [200µl] of ethanol was added to the DNA solution, vortex for [10 sec].
- Provided a [2ml] new collection tube, by applying of the [600µl] sample to the column. Centrifuge the tube at [7400G] for [1 min].
- Discard flow through. Place the column back into the same tube. Collection tubes are reused to reduce plastic waste.
- [500 µl] was added of a Wash Buffer TGI-3 (add isopropanol before use, as indicated on the bottle) to the column and centrifuge at [7400G] for [1 minute].
- Discard flow through. Place the column back into the collection tube.
- [500µl] was added of washing bufer column and centrifuge at [7400G] for [1min].
- The step 10 was repeated for a one time, with [2 min] at [10000 rpm].
- The column was placed in a [1.5ml], called a new receiver tub, incubate at [70C] for [2 to 5 min] to remove residues of alcohol. [50-100µl] was added elution [70°C] to the column and incubate for [2 min] at room temperature.
- Centrifugation was done at[7400G] for [1min]. finally, the eluate was collected and proceed with a gel electrophoresis and PCR

- The estimation of DNA concentrations and purity by absorbance

When extracting DNA, the final step is to use Nano-drop to measure the purity and concentration of the extracted material. The measurement of absorbance was done at [260nm] (García *et al.* 2020).

- The agarose gel electrophoresis

Electrophoresis can be defined as the flow of charged molecules, primarily proteins and nucleic acids, via an electric field. The average migration, or mobility, of the molecules across the electric field, which is dependent upon the temperature, viscosity, ionic strength, size, shape, and strength of the field (Sonagra 2022).

- The preparations of gel electrophoresis

The preparation for a [100ml] of a [0.8%] agarose solution mostly nedeed for:

- A weight of [0.8 gm] of powdered material was calculated and placed into a conical flask. [100ml].
- Magnatic stirr was applied the pawdered, [50°C] then [0.5mg/ml].The sybr of a green was added.
- To make wells for loading samples, a comb was inserted into the cast, and the agarose was left to solidify for at least 30 minutes at room temperature.
- After carefully removing the comb, the tray was put in an electrophoresis tank such that the slab gel would be fully submerged in buffer (TBE buffer) for the electrophoresis process.

- The loading of study samples

[2µl] of [5X] loading buffer was added for every [8µl] of DNA sample that was extracted. After a quick mixing, the mixture was moved to the wells. In gel analysis, [10µl] of DNA was used. Ladder loaded parallel to the sample and used as a size marker. Electrophoresis was performed at [70 volts]. Also followed by [50 volts] at ambient temperature (Zhang *et al.* 2008).

- The reconstituting study and diluting primers reagents

Primers were typically sent in a state known as lyophilization. A lyophilized primer's units were expressed as mass in picomoles. Reconstituting the primer in sterile Tris-EDTA buffer (TE buffer) is the process of making a stock of primers.In order to create a master stock that would be utilized once more to create a working stock,.The following steps were followed for reconstituting and diluting the primers:

- Tube was spined from the down before opening the cap.
- The requred amount of TE-buffer or DW was added according to Oligos manufacturer to acquire a [100 picomoles/ µl] that called master stock.
- Primer were by vortex re-suspended properl.
- [10µl] of master stock was transferred in to a [0.2 ml] by eppendorf tube, with [90 µl] of sterile TE buffer to acquire a [10 picomoles/ µl].
- Working stock were stored at [-20C].
- PCR working solution then stored [-20C].

- Determination of the gene CCHCR1 genotyping (ORIGENE 2023)

The SNP represents by the transversion in exon 4, with 445 bp. This was amplified from DNA as 1.1-kb PCR product using primers .

Forward Sequence: GCAGATAGCCTCTGCTGAAGAG

Reverse Sequence: GGACAGCATAGCTGAGTCGGTT

This was done by master mix Exon (Korea), and its' in the Table 3.4 that was showing the materials.

Table 3.4 The used master mix components

Component	Concentration
Taq DNA Polymerase	[1 U]
Each: dNTP (dATP, dCTP, dGTP, dTTP)	[250µM]
Tris-HCl [pH 9.0]	[10 mM]
KCl	[30 mM]
$MgCl_2$	[1.5 mM]
Stabilizer and tracking dye	

Table 3.5 The amplified conditions of CCHCR1 genotyping

Stage	Temp.(C°)	Time	Function	Cycles
One	95	5 min.	Initial denaturation	1
Two	95	45 sec.	DNA denaturation	35
	48	1 min.	Primer annealing	
	72	1.30 min.	Template elongation	
Three	72	10 min	Final elongation	1
Four	8	-	Incubation	Hold

- The polymerase chain reaction restriction fragment length polymorphism

Based on restriction endonuclease cleavage, approach to single nucleotide polymorphism. The area around the restriction enzyme site was amplified using PCR, and the result was digested using the proper enzyme for genotyping (Hashim *et al.* 2019).

The PCR-RFLP procedure involved preparing a volume of [10 µl] for each of the PCR products and 5 units of the restriction enzyme XbaI, which was obtained from the bacterium Xanthomonas badrii, at [37C] degrees Celsius. that show in Figure 3.6, (Biolabs 2016).

Figure 3.6 Shows the XbaI enzyme nitrogenous bases restrictions

Approximately 1 hours in the buffer advised by the manufacturer. The elongated or enlarged DNA fragments was electrophoresed on 1.2% agarose (Krüger 1983).

3.7 Statistical Analysis

Software Package for Social Science (SPSS-22.0 version) was used for data analysis and conclusion in this study, which will be presented in chapter (4). The mean and standard deviation (SD) of the data were displayed. The ANOVA (t-test) and linear regression analysis, which have been employed to evaluate the significant difference between the groups, were utilized to test the normality of continuous variables. Genetic analysis was done using Chi-square ($\chi 2$) test to evaluate odd ratio (OR), that done by using the odd ration calculator by (MedCal) (Altman1991 2023). As well as the accepted of P.Values that detected less than of (0.05) was considered significant. Correlations of the curent study were done by the Excel Office Software Version 2010.

4. RESULTS

The PsA it's one of most problems that with a modern medical focus and the studies are looking for the available finding a solution for a final or immediately cure and control due to show the main causes, risks and how can treated. The early detection and identifying of the disease causes can help to show a type of pathogenesis and the following up on patients during treatment. We have studied the genetic level of a disease pathogenesis and its effect. As well as the most important demographic, physiological, haematological, clinical and the biochemical variables parameters, who's with there's changes in increase or decrease and the presence of the first place can causing a first step of the disease processing. Our present study results will be start to explained the physical parameters like the age, BMI and PASI score for the twin's groups of PsA patients and the healthy control groups, and then after shown the clinical, haematological and the genotyping polymorphism results.

4.1 The Results of Demographic and Physicals Parameters for The Patients and Healthy Control Groups

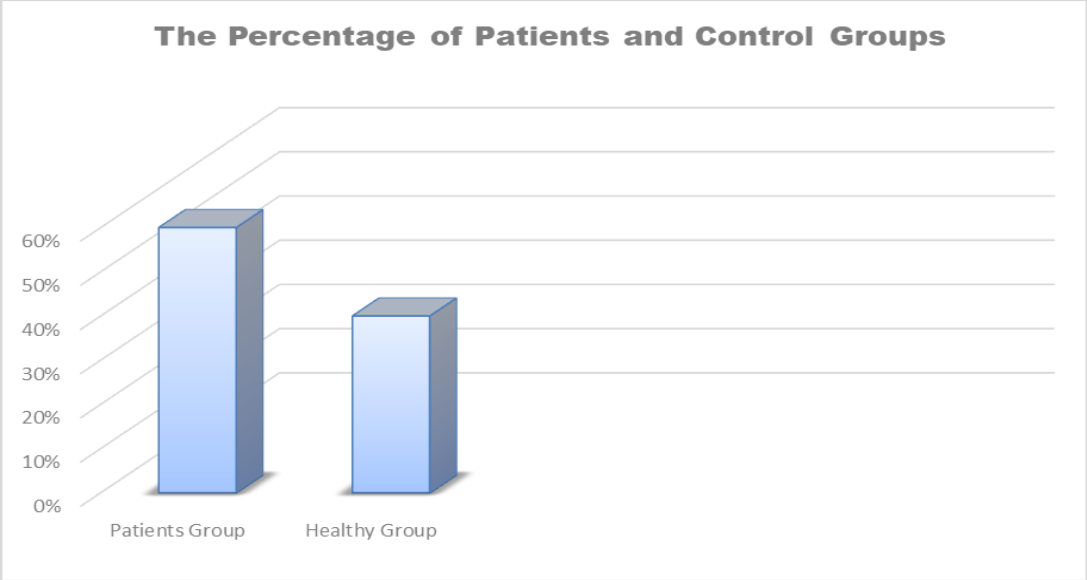

Figure 4.1 Shows distribution of the all study subjects, patients group that represented a (60%), as well as the healthy control which composed an (40%) of a total numbers of the subjects that enrolled in this present study

4.1.1 Results of patients and healthy control groups age for the present study

Participants that enrolled in the present were categorized into two groups (patients and control). A fifty adult persons with a chronic and diagnosed PsA, were taken selected due the mentioned criteria in chapter two of this study (subjects). A forty apparently healthy adults were dependent as control group without any chronic and autoimmune diseases. Mean of the age with the ± SD (standard deviation) of all participants of PsA patients and healthy groups (males and females) were calculated and showed Table 4.1. The difference was non-significant between the matched groups because the all subjects were approximate in age years.

Table 4.1 The number and age of all patient and control groups

The Study Parameter		S.	Mean	Standards DEV.	Standards of Error	Study Confidence Interval 95% Results		P. Value
						Mean of Low level	Mean of Uper level	
Age	Patients	50	40.5	±5	1.32	33.47	54.78	Up to 1
	Control	40	42.6	±5	1.44	34.21	51.36	

4.1.2 Results of patients and healthy control groups BMI for the present study

Results that revealed of the present study were also with non-significant increase or decrease in the BMI (body mass index) for a both PsA patients and the control groups when a comparsim done between them and the groups were matched for this result, this shown in Table 4.2.

Table 4.2 Numbers and the BMI for PsA patients and healthy control

The study parameter		S.	Mean	Standards DEV.	Standards of Error	Study Confidence Interval 95% Results		S.
						Mean of Low level	Mean of Uper level	
BMI	Patients	50	25.18	± 4.05795	.57388	24.0327	26.3393	Up to 1
	Control	40	25.06	± 3.98610	.63026	23.7902	26.3398	

4.1.3 Results of the PASI score degree for patients of the present study

The results and values of (PASI) for patients group with PsA were done and showed in Table 4.3. Also the correlation or a comparison of PASI score between patient and the healthy control groups were showed a non-significant with P.Value Up to 0.05 and been up to 1.

Table 4.3 Numbers and the PASI score for PsA patients

The Study Parameter		S.	Mean	Standards DEV.	Standards of Error	Study Confidence Interval 95% Results		P. value
						Mean of Low level	Mean of Uper level	
PASI Score	Patients	50	27.87	± 5.41295	.76551	26.3337	29.4103	0.05
	Control	40	0	0	0	0	0	0

4.1.4 Results of the (PSAJAI) score degree for patients of the present study

Table 4.4 Numbers and the PSAJAI Score for PsA patients

The Study Parameter		S.	Mean	Standards DEV.	Standards of Error	Study Confidence Interval 95% Results		P. value
						Mean of Low level	Mean of Uper level	
PSAJAI Score	Patients	50	152	± 25.41295	.76551	123	185	0.05
	Control	40	0	0	0	0	0	0

4.2 Clinical Biochemistry and Hematological Examinations

4.2.1 Results of serum vitamin D concentration (ng/ml) for the PsA patients and healthy control groups

The mean concentrations of Vitamin D results for the patient and control groups was apperantly a significantly decreased in patients of PsA when correlated with those matched groups of healthy control, so in the second group were been normal, these results as shown in Table 4.5.

Table 4.5 Means of vitamin D Con. for PsA patients and the control groups

The Study Parameter		S.	Mean	Standards DEV.	Standards of Error	Study Confidence Interval 95% Results		P. value
						Mean of Low level	Mean of Uper level	
Vit. D	Patients	50	12.30	± 5.47899	.77485	10.7449	13.8591	0.05
	Control	40	53.07	± 9.94795	1.20536	28.6167	59.5383	

4.2.2 Results of serum vitamin K2 concentration (ng/ml) for the PsA patients and healthy control groups

The results of a Vitamin K2 with a mean concentrations for the patient and control groups was apperantly and significantly decreased in patients than those of matched groups of healthy control. Some of the PsA patients treated with vitamin k2 and the CRP parameter been negative for this section of patients, so in the second group (control) were been normal, these results as shown in Table 4.6.

Table 4.6 The vitamin K2 Con. for PsA patients and the control groups

The Study Parameter		S.	Mean	Standards DEV.	Standards of Error	Study Confidence Interval 95% Results		P.value
						Mean of Low level	Mean of Uper level	
Vit. K2	Patients	50	1.350	± .18710	.16788	1.0130	1.6878	0.05
	Control	40	2.132	± .55029	.08701	1.9565	2.3085	

4.2.3 Results of serum TNF-α concentration (pg/ml) for the PsA patients and healthy control groups

The results of a TNF-α level were revealed to a mean concentrations for the patient and control groups was apperantly and significantly increased in patients than those of matched groups of healthy control, so in the second group (control) were been normal, these results as shown in Table 4.7.

Table 4.7 Mean of TNF-α con. for PsA patients and the control groups

The Study Parameter		S.	Mean	Standards DEV.	Standards of Error	Study Confidence Interval 95% Results		P.value
						Mean of Low level	Mean of Uper level	
TNF-α	Patients	50	242.5	± 31.33414	7.25974	127.9310	257.1090	0.05
	Control	40	57.18	± 10.10773	8.55518	19.8805	74.4895	

4.2.4 Results of serum adeponectine concentration (µg/ml) for the PsA patients and healthy control groups

The results of the adeponectine with mean level were revealed to a concentrations for the patient and control groups was apperantly and significantly and sark increased in

patients than those of matched groups of healthy control, so in the second group (control) were been normal, these results as shown in Table 4.8.

Table 4.8 Mean of adeponectine con. for PsA patients and the control groups

The Study Parameter		S.	Mean	Standards DEV.	Standards of Error	Study Confidence Interval 95% Results		p. value
						Mean of Low level	Mean of Uper level	
Adepo.	Patients	50	92.71	13.33	7.58362	77.4721	107.9519	0.05
	Control	40	18.64	10.01	1.74131	15.1229	22.1671	

4.2.5 Results of plasma CRP titer concentration (mg/dl) for the PsA patients and healthy control groups

The results of the C-reactive protein with a mean levels were revealed to an increase in the concentrations for CRP at the PsA patients and group. CRP levels were apperantly and significantly decreased (6 mg/dl or less than 6) in the control healthy group, Table 4.9 showed the detailed of results.

Table 4.9 Mean of CRP levels of the PsA patients and the control groups

The Study Parameter		S.	Mean	Standards DEV.	Standards of Error	Study Confidence Interval 95% Results		P.value
						Mean of Low level	Mean of Uper level	
CRP	Patients	50	43.70	± 11.7416	2.7717921	34.110725	53.289275	0.05
	Control	40	6.000	± .01	.01	6.000000	6.000000	

4.2.6 Results of serum uric acid concentration (µmol/L) for the PsA patients and healthy control groups

The present study results of the uric acid with a mean levels were revealed to an increase in the concentrations for uric acid for the PsA patients group. Uric acid levels

were significantly decreased and been normal for many times for the control healthy group, Table 4.10 showed the detailed of results.

Table 4.10 Mean of uric acid levels of the PsA patients and the control groups

The Study Parameter		S.	Mean	Standards DEV.	Standards of Error	Study Confidence Interval 95% Results		P. value
						Mean of Low level	Mean of Uper level	
Uric Acid	Patients	50	546.9	± 151.1455	21.37521	503.9649	589.8751	0.05
	Control	40	278.9	± 100.1027	15.82764	246.9356	310.9644	

4.2.7 Results of serum gultathion enzyme (GSH) concentration (µM) for the PsA patients and healthy control groups

Results of the present study of a serum glutathion (reduced state) also called GSH were revealed to decresde in these concentrations for the PsA patients group, that clear shwo in the mean of results in the Table 4.11 with other detailes. Wheres GSH levels been significantly normally in many times for the control healthy group.

Table 4.11 Mean of GSH levels of the PsA patients and the control groups

The Study Parameter		S.	Mean	Standards DEV.	Standards of Error	Study Confidence Interval 95% Results		P. value
						Mean of Low level	Mean of Uper level	
GSH	Patients	50	.2949	± .18025	.02549	.2437	.3461	0.05
	Control	40	.8382	± .33007	.05219	.7327	.9438	

4.2.8 Results of serum gultathion enzyme (GSSG) concentration (µM) for the PsA patients and healthy control groups

Results of the present study of a serum glutathion (oxidized state) also called GSSG were revealed to increased in these concentrations for the PsA patients group, that clear

shwo in the mean of results in the Table 4.12 with other detailes. Wheres GSH levels been significantly normally or in many times its lower than normal value for the control healthy group.

Table 4.12 Mean of GSSG levels of the PsA patients and the control groups

The Study Parameter		S.	Mean	Standards DEV.	Standards of Error	Study Confidence Interval 95% Results		P. value
						Mean of Low level	Mean of Uper level	
GSSG	Patients	50	1.410	± .31992	.04570	1.3185	1.5023	0.05
	Control	40	.2133	± .19430	.03072	.1511	.2754	

4.2.9 Results of blood erithrocyte sedimentation rate (ESR) concentration (mm/h) for the PsA patients and healthy control groups

The hematological uniqe parmeter of this present study was the ESR, so the results of the present study of a blood erythrocytes sedimentation rate were revealed to increased in these concentrations for the PsA patients group, that clear shwo in the mean of results in the Table 4.13 with other detailes. Wheres ESR levels been significantly normally with the normal value for the control healthy group.

Table 4.13 Mean of ESR levels of the PsA patients and the control groups

The Study Parameter		S.	Mean	Standards DEV.	Standards of Error	Study Confidence Interval 95% Results		P. value
						Mean of Low level	Mean of Uper level	
ESR	Patients	50	69.72	± 10.92588	2.37358	60.9310	78.5090	0.05
	Control	40	5.150	± 2.15490	.34072	4.4608	5.8392	

4.3 Results of The Molecular Genetic

4.3.1 The CCHCR1 gene genotyping of SNP (rs3130453) polymorphism

The CCHCR1 polymorphism of gene was been determined by polymerase chain reaction. Results of the amplified gene by PCR technique process was conducted for determination the polymorphic gene position by using the specific selection of a primer that which end result, that representd by one band that can be detected when visualized at the agarose gel electrophoresis. Band of this mentioned gene was appear at the (1100) of a base pair (bp) representing presence of PsA polymorphic site, that mean a SNP (re3130453) of a CCHCR1 gene.

The XbaI polymorphism of CCHCR1 gene was determined by the polymerase chain reaction (PCR) technique. The result of amplification by PCR process which was conducted to define the G/T polymorphic site instead the normally state (G-C) that seen in helthy group. That done by using a specific primer revealed and resulted in one band when visualized on the prepared gel agaroseby loadin via the electrophoresis technique. This band was 1.1 kilo base pair (kbp) representing presence of (G/T) polymorphic site in the CCHCR1 gene, as in Figure 4.2.

The detection of a SNP (rs3130453) represented by a mutation or a non compatible joining in the (G-T) nitrogenous bases region of the nucleotieds sequence, so the real and normal shuld be a (G-C). This appear in Figure (4-2) that shows a polymorphismed gene region, that which may be a one of the maine causes of a PsA for patients that enrolled in our study.

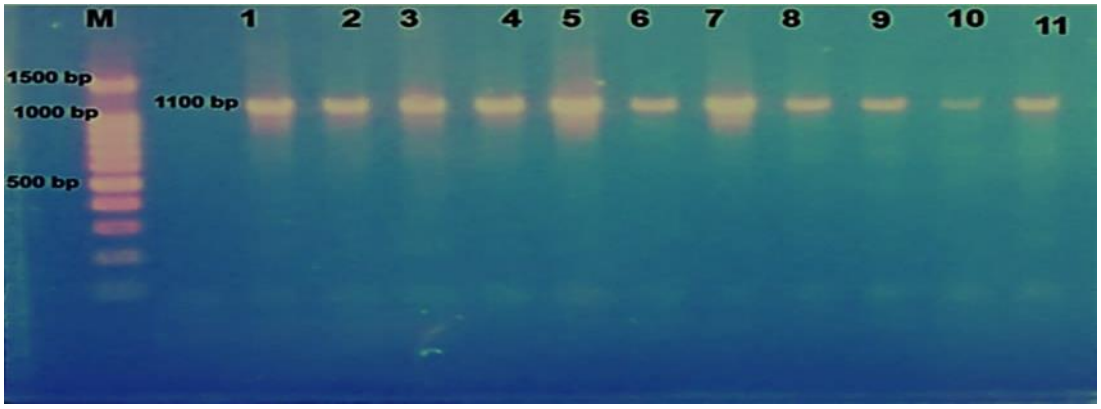

Figure 4.2 Present photo of real our results, shows the band of a CCHCR1 gene that contains an a (rs3130453) polymorphismed site of the (G-T) mutated nucleotied

After the PCR product was digested by a XbaI enzyme, the 1100-bp PCR fragment was divided into 900 bp and 200 fragments. The allele was designated either G or T depending on whether the XbaI restriction site was present or absent, respectively, as in Figure 4.3.

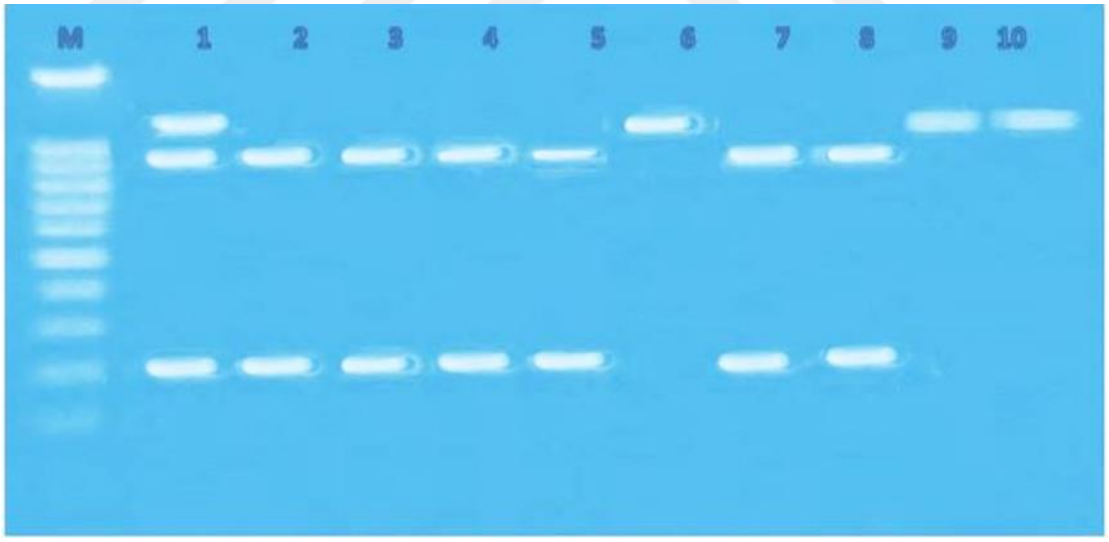

Figure 4.3 A real photo of the rflp pattern results of the (CCHCR1) Gene Polymorphism Site for The Current Study. Lane M: DNA Ladder (marker). Lane 6 XbaI (-/+) Genotype. Lane 9, 10 was a XbaI (-/-) Genotype. Lane 1, 2, 3, 4, 5, 7, and 8 XbaI Genotype (+/+)

4.3.2 The genotyping and the allele frequency of CCHCR1 gene

The detailes of an a allele frequencies and genotype of the XbaI gene variant of the present study subjects (Genetically) were shown in Table 4.14 and Table 4.15, that divided a revealed study results and gives the percentages for all alleles frequencies.

Table 4.14 Shows the genotyping percentages of CCHCR1 gene polymorphism

Groups	N	Genotype		
		XbaI (-/-)	XbaI (+/-)	XbaI (+/+)
Patients	50	10 (20%)	15 (30%)	25 (50.0%)
Healthy	40	28 (70 %)	8 (20 %)	4 (10 %)

Table 4.15 Shows the alleles frequency percentages of CCHCR1 gene with a polymorphism

Groups	N	Allele Frequency	
		XbaI (-)	XbaI (+)
Patients	50	39 %	61 %
Healthy	40	80 %	20 %

In addition to these showes below orders evaluations and these significance, these revealed results of genotyping distribution in both the healthy control group and PsA groups. The Chi square test, was used and done to investigate the odds ratio (O.R), that abbriviated in Table 4.16.

Table 4.16 The odd ration and CI (95%) for CCHCR1 gene polymorphism characterization in patient and control groups

Genotype	Patients Group	Control Group	Odds Ratio	CI (95%)	P.Value
XbaI (-/-)	2	28	Reference		
XbaI (+/-)	10	8	17.5	3.1668 to 96.70	0.001
XbaI (+/+)	38	4	133.0	22.7 to 777.8	0.001

4.4 The Correlations That Revealed of current Study Showed Results for PsA Patients Parameters

There were more than one types of a correlation between these PsA patients' results parameters. The correlations of PsA group will be shows and the discuses will be below.

4.4.1 The correlations of PASI score for PsA group with clinical parameters

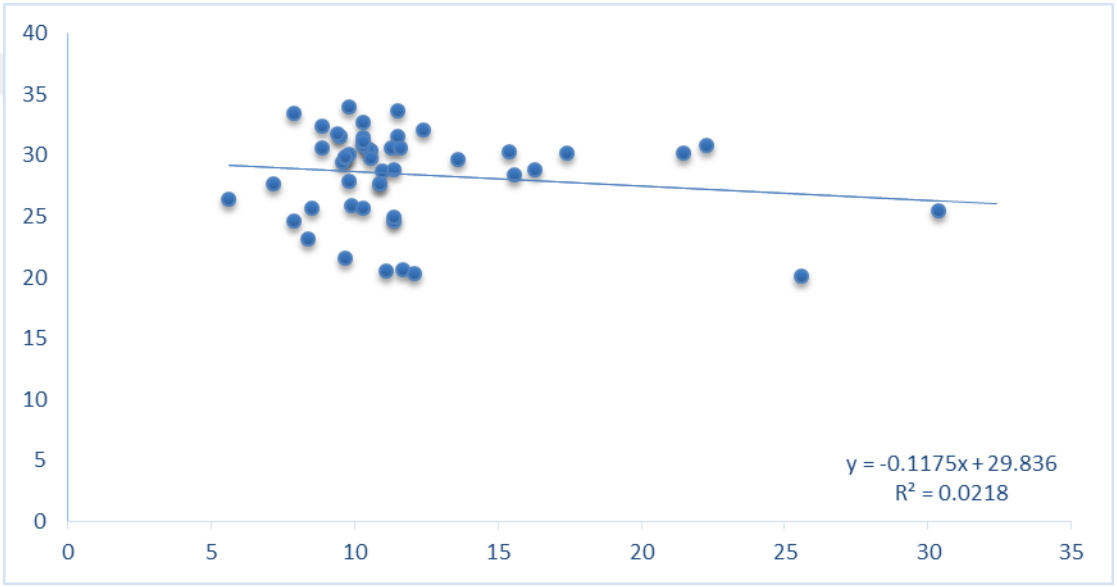

Figure 4.4 Shows a significance negative correlation between the PASI score and Vitamin D_3 for PsA Group by P. Value ≤ 0.05.

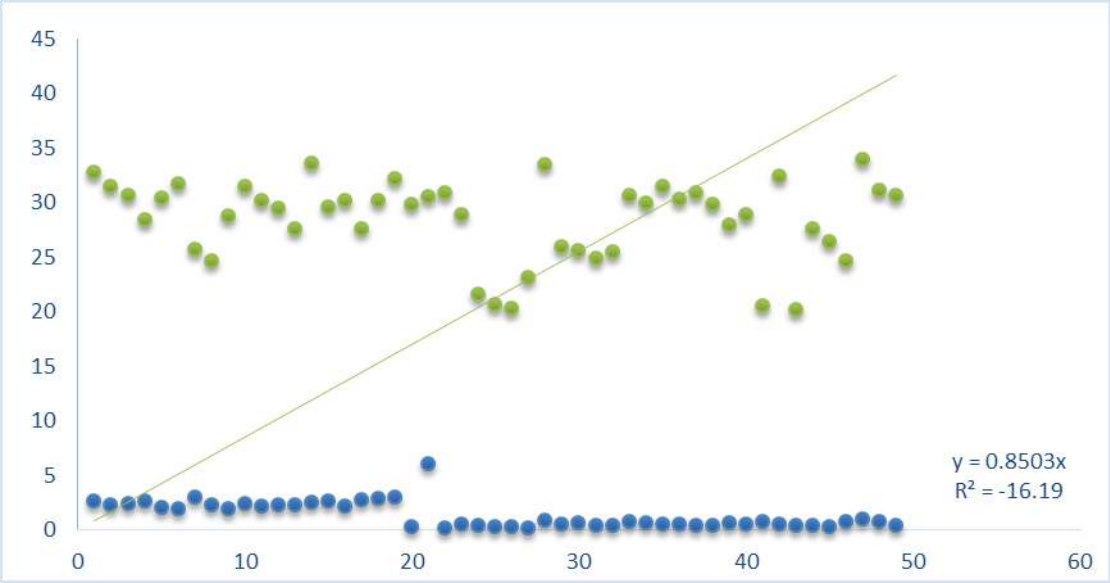

Figure 4.5 Shows a non-significance positive correlation statically between the PASI score and Vitamin K2 for PsA Group by P. Value ≤ 0.05.

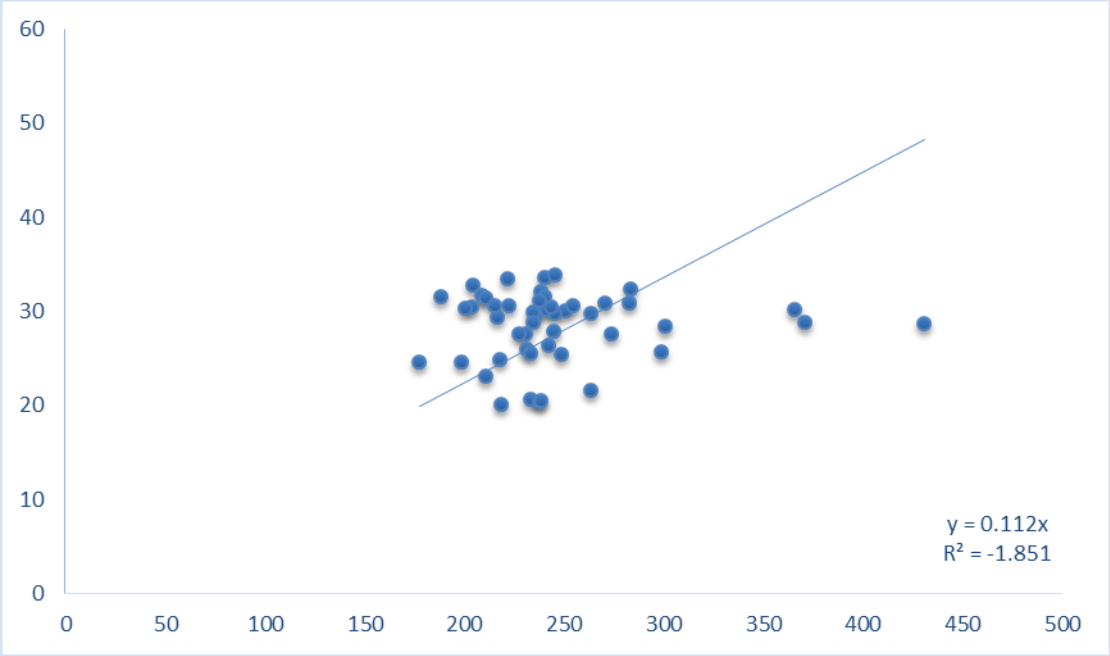

Figure 4.6 Shows an equivocal correlation between the PASI score and TNF-α for PsA Group by P. Value ≤ 0.05.

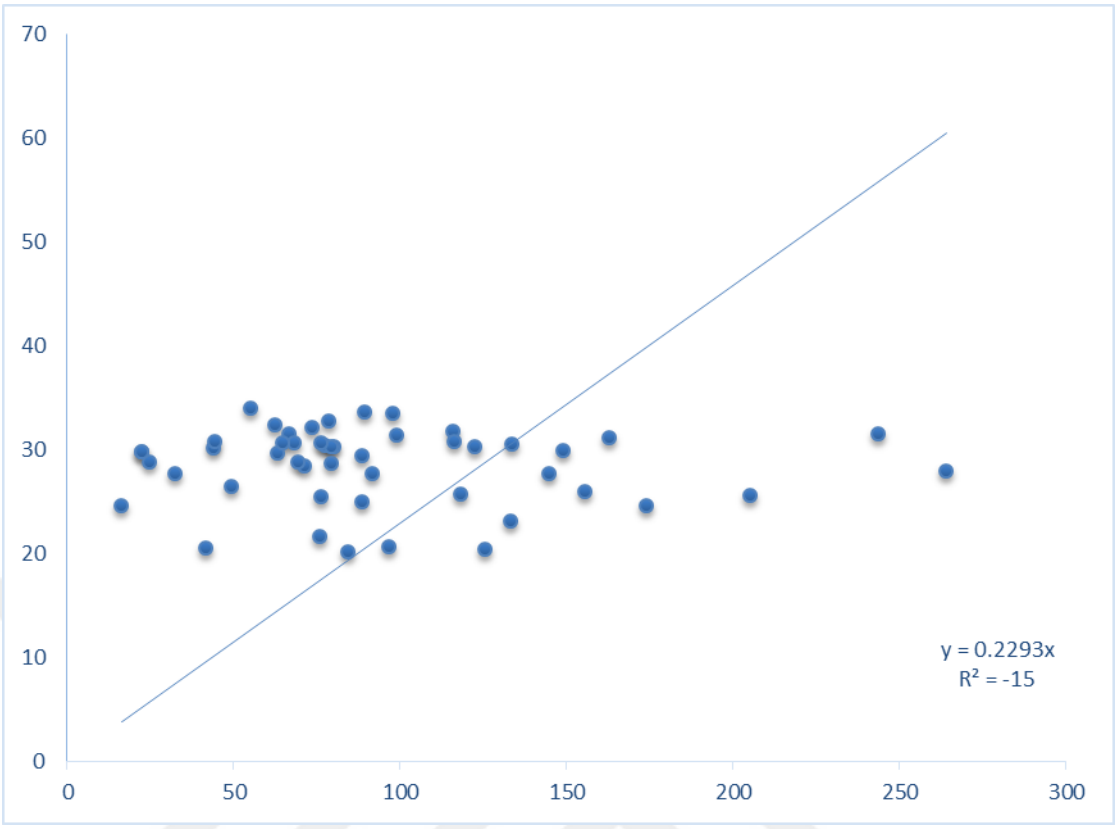

Figure 4.7 Shows a positive correlation between the PASI score and Adiponectin for PsA Group by P. Value ≤ 0.05.

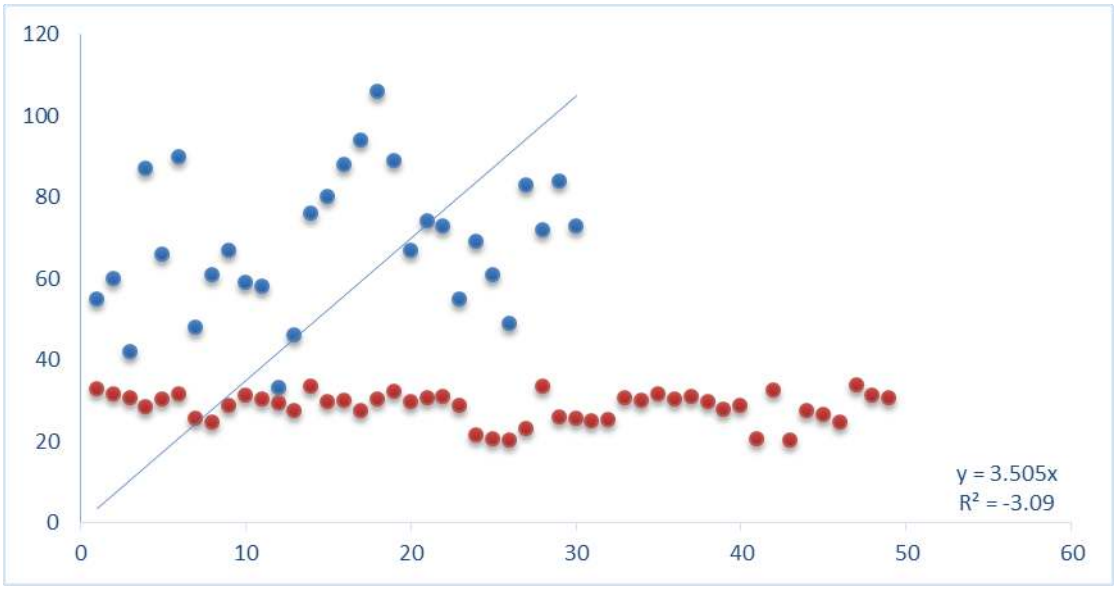

Figure 4.8 Shows a significance positive correlation between the PASI score and Plasma CRP for PsA Group by P. Value ≤ 0.05.

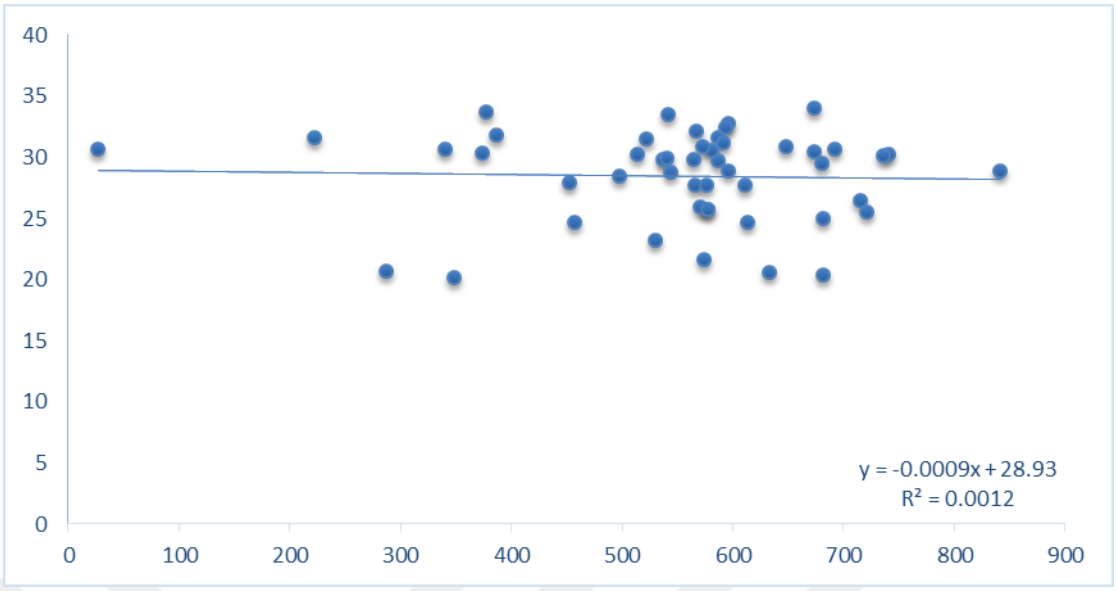

Figure 4.9 Shows a significance equivocal correlation between the PASI score and Uric Acid for PsA Group by P. Value ≤ 0.05.

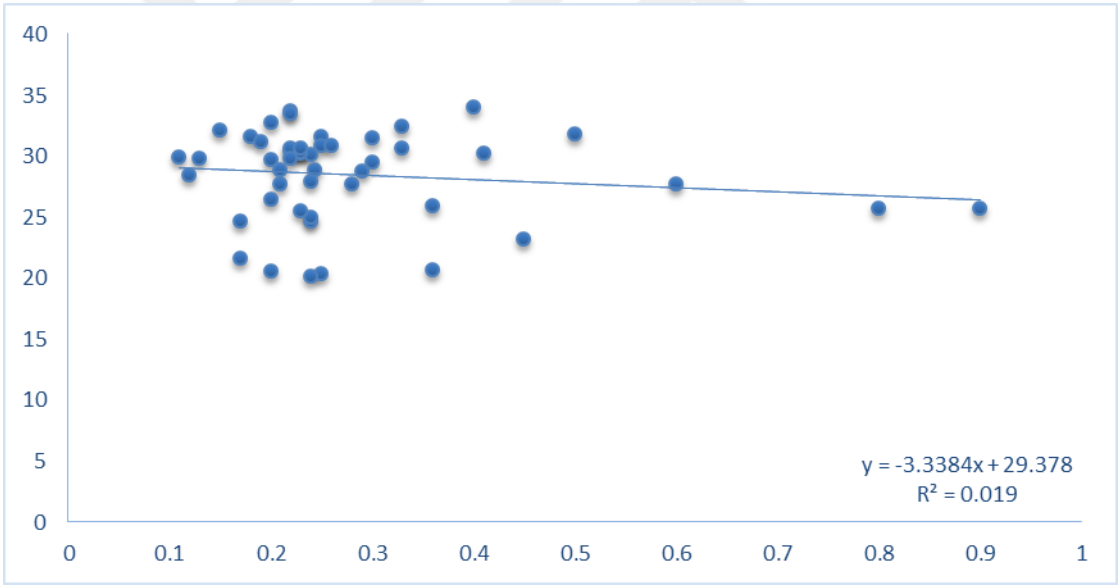

Figure 4.10 Shows a significance negative correlation between the PASI score and GSH for PsA Group by P. Value ≤ 0.05.

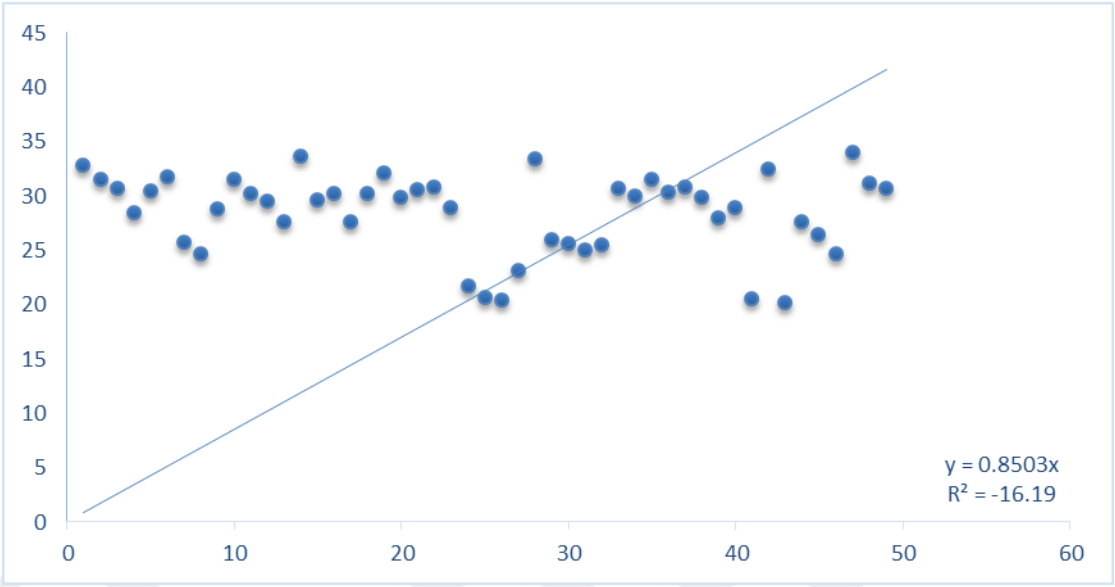

Figure 4.11 Shows a significance positive correlation between the PASI score and GSSG for PsA Group by P. Value ≤ 0.05.

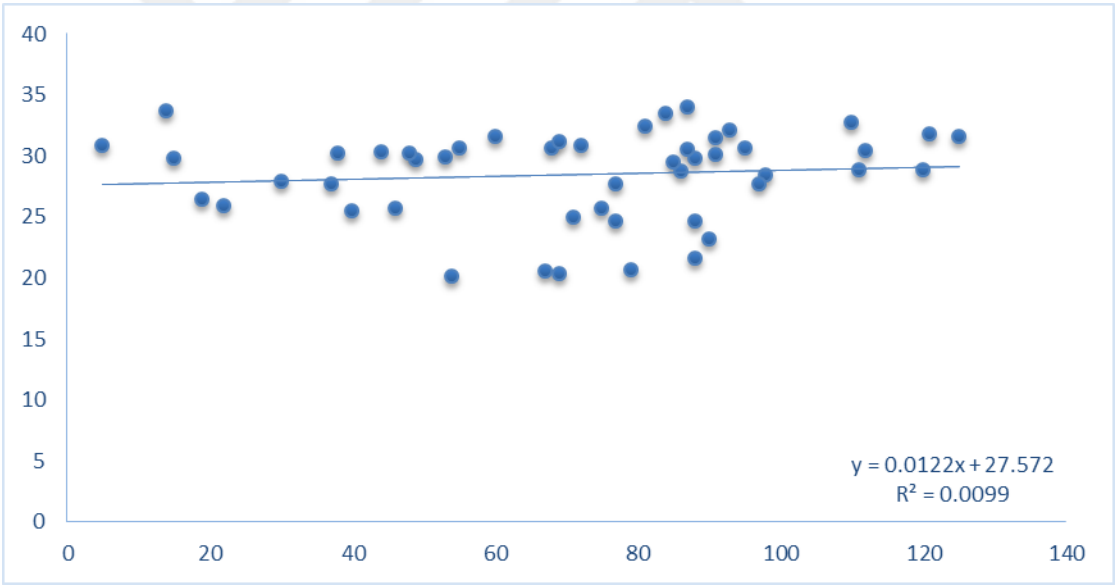

Figure 4.12 Shows a significance equivocal to positive correlation between the PASI score and ESR for PsA Group by P. Value ≤ 0.05.

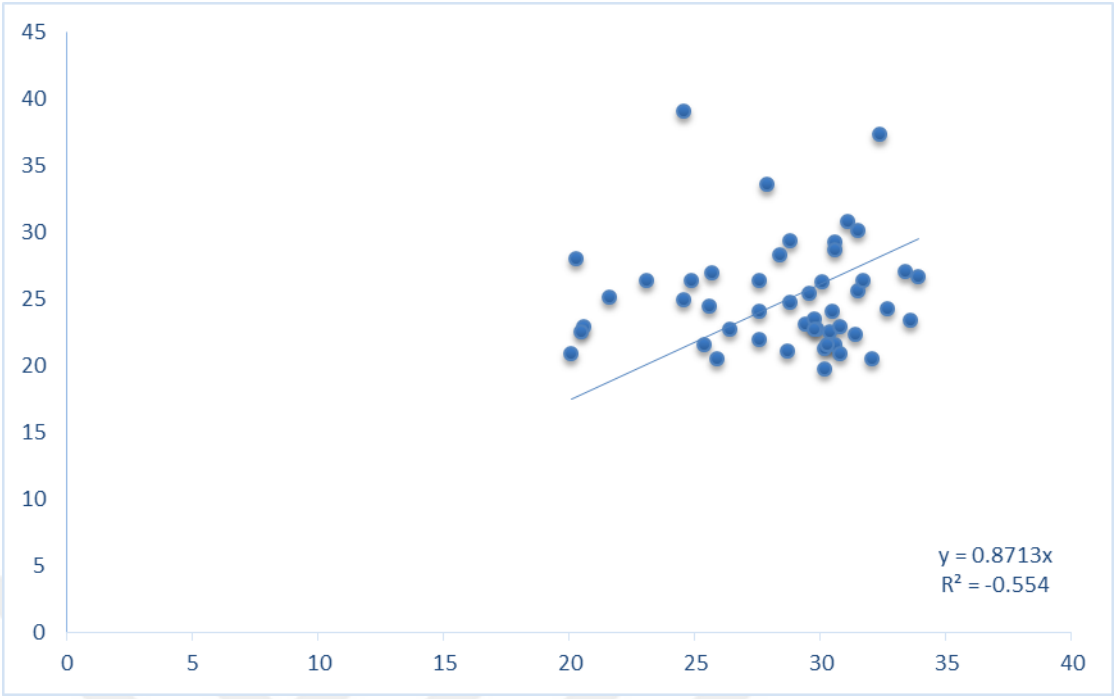

Figure 4.13 Shows a significance equivocal to positive correlation between the PASI score and Plasma CRP for PsA Group by P. Value ≤ 0.05.

4.4.2 The correlations between the clinical parameters for PsA group

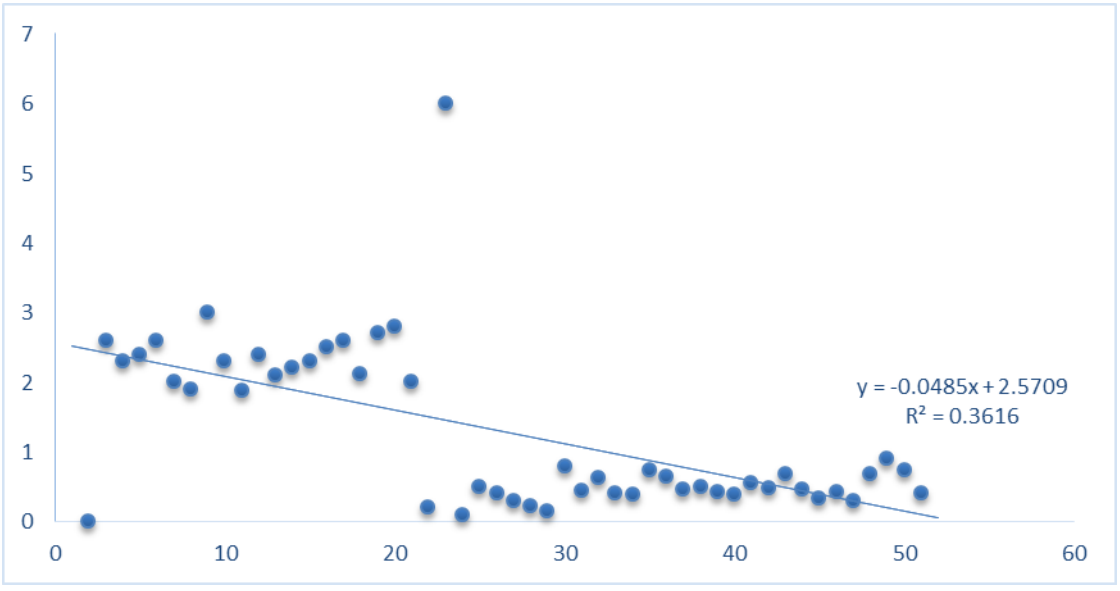

Figure 4.14 Shows a significance negative correlation between the Vit. D_3 and The Vit. K_2 for PsA Group by P. Value ≤ 0.05.

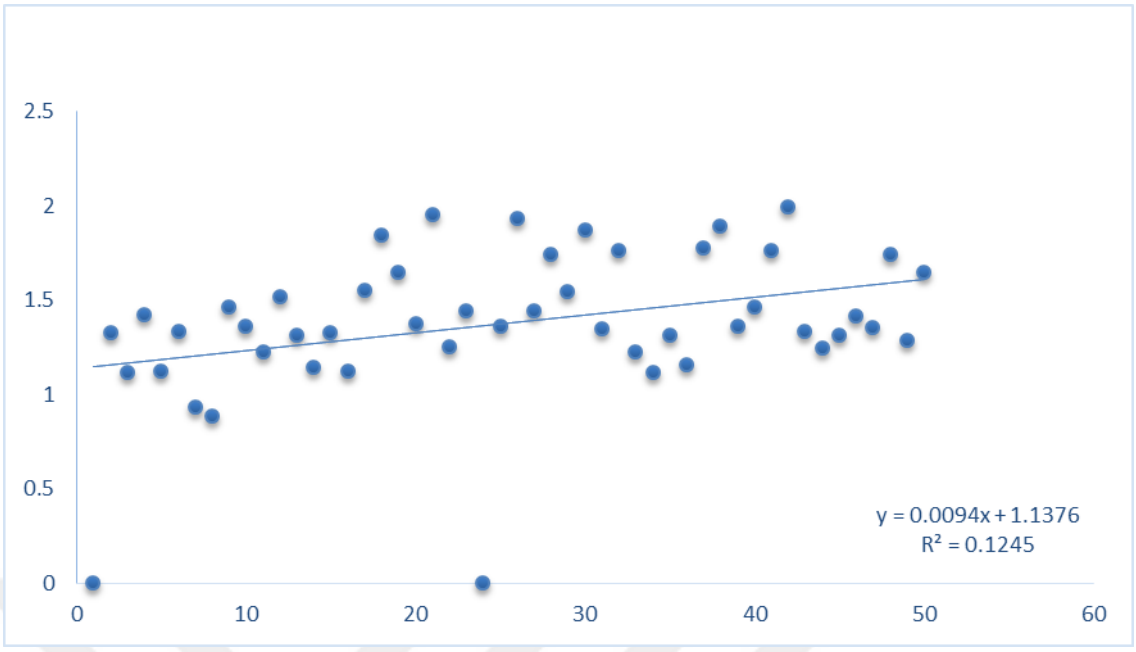

Figure 4.15 Shows a significance positive correlation between the GSH and The GSSG for PsA Group by P. Value ≤ 0.05.

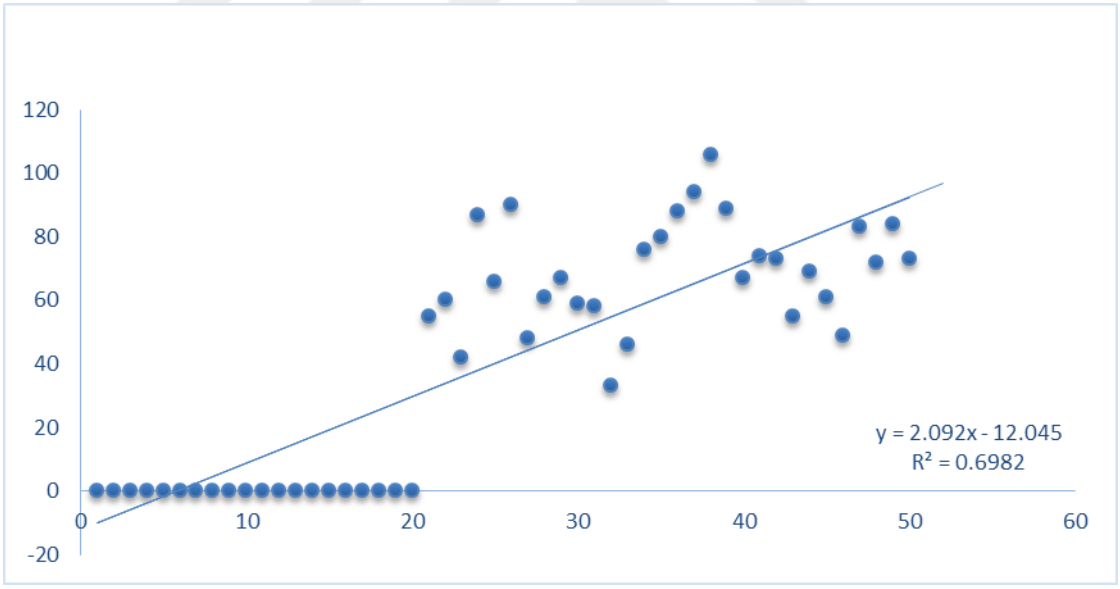

Figure 4.16 Shows a significance positive correlation between the Vit. K_2 and The plasma CRP for PsA group by P. Value ≤ 0.05. where the first 20 PsA Patients with Vit.K_2 Treatment Shows CRP Negative (≤ 6). So the significances start after pass number 20.

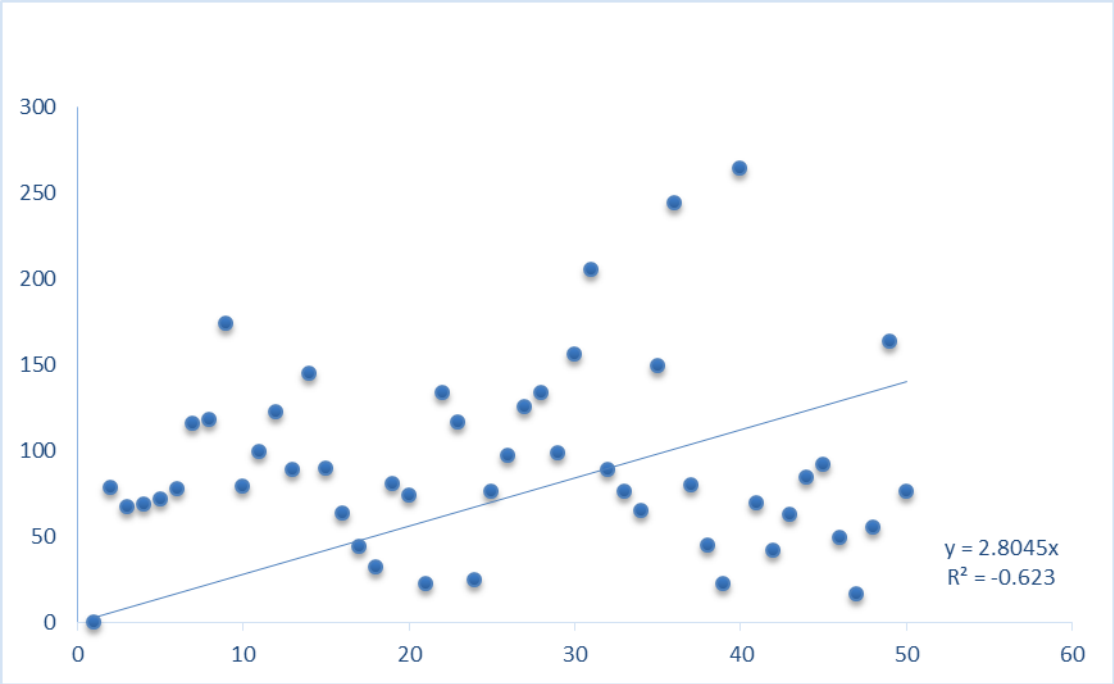

Figure 4.17 Shows a significance positive correlation between the TNF-a and The Adiponectin for PsA Group by P. Value ≤ 0.05.

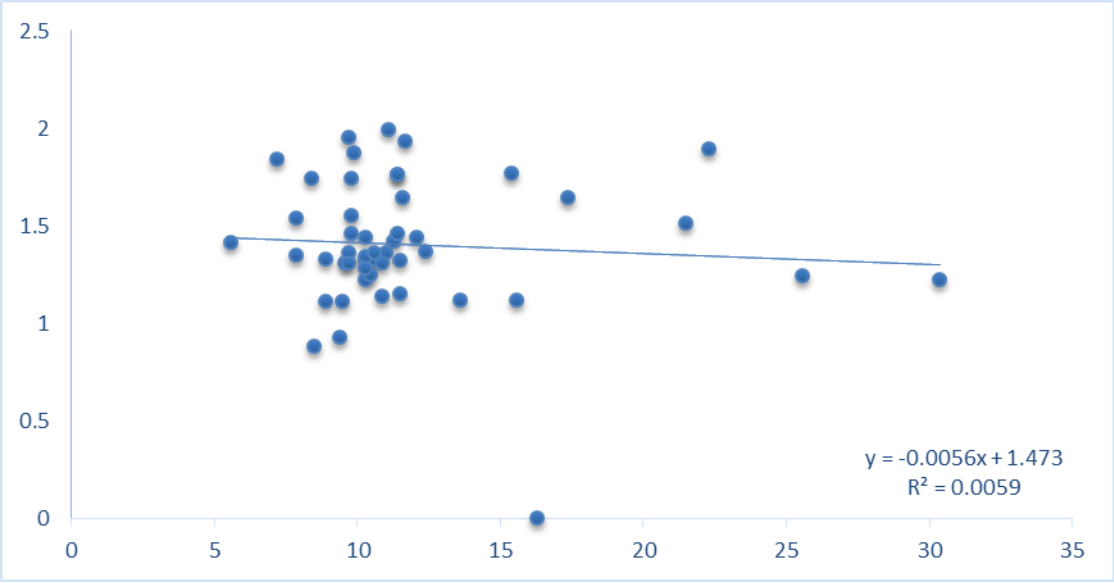

Figure 4.18 Shows a significance negative and opposite correlation between the Vit. D_3 and The GSSG for PsA Group by P. Value ≤ 0.05.

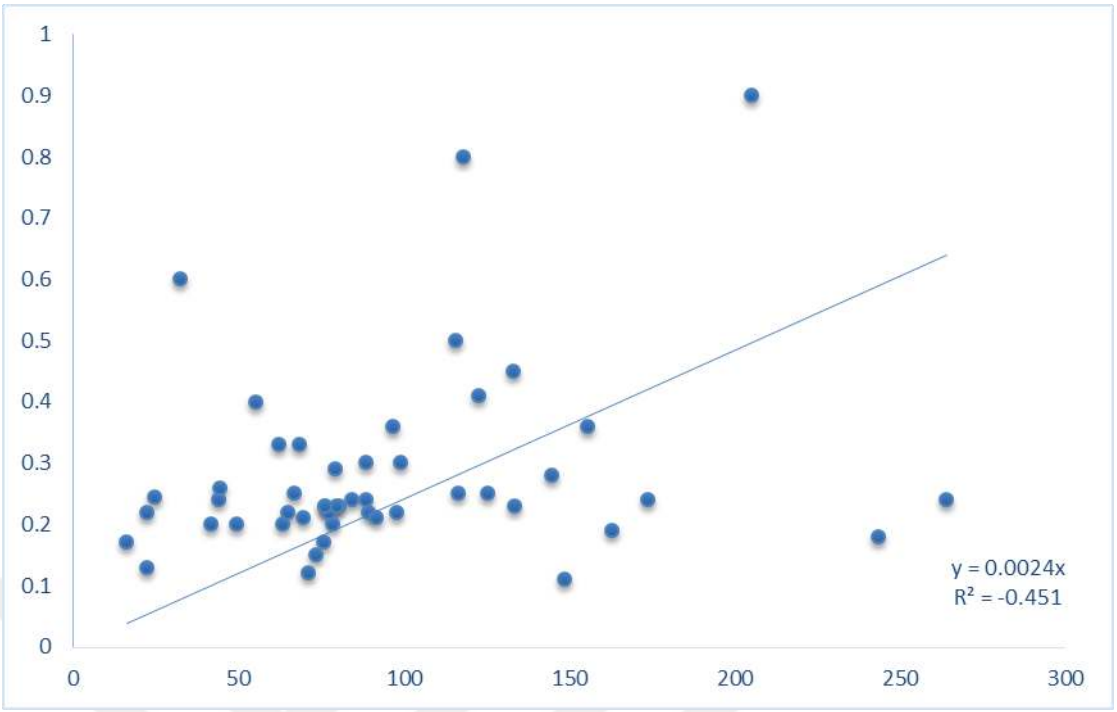

Figure 4.19 Shows a significance positive correlation between the GSH and the adiponectin for PsA Group by P. Value ≤ 0.05.

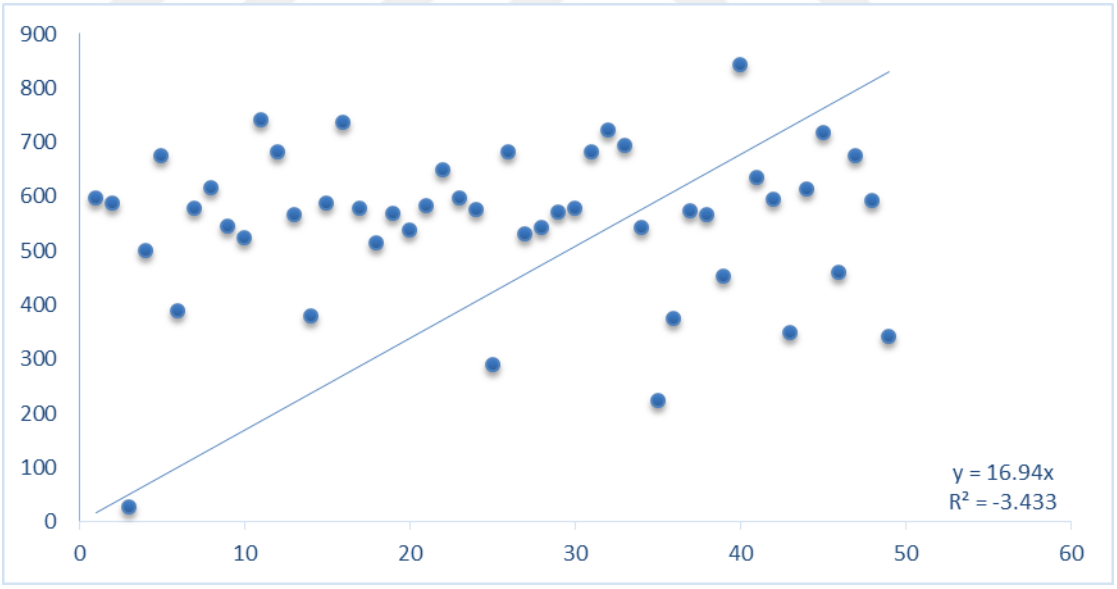

Figure 4.20 Shows a significance positive correlation between the uric acid and the GSSG for PsA Group by P. Value ≤ 0.05.

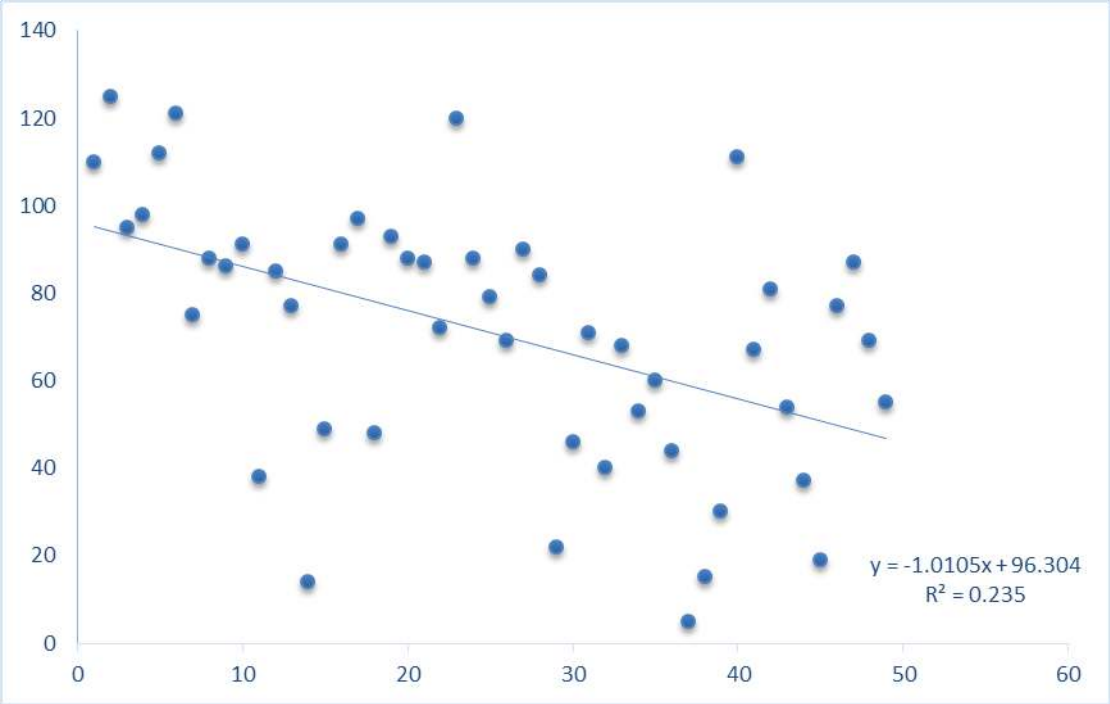

Figure 4.21 Shows a significance negative correlation between the ESR and The Plasma CRP for PsA Group by P. Value ≤0.05.

5. DISCUSSION AND CONCLUSIONS

Psoriasis arithritis is one of the commonest chronic autoimmune-mediated disorder. From the anicient decades a different theories were hypothesized to explain the PsA pathology process and exacerbations as well as the psoriasis arithritis causes. A precise causes of PsA are unknown mostly, so the general believe and the most prevalent concept it happened because the hyper immunity triggring, it may be promotioned by many factors involve the immune system. A memtioned combination of the branched like a genetic and enviromental factors were very important,for prompts an abnormal immune response, which causes inflammation and rapid production of immature keratinocytes. Recent advances in understanding the immunopathogenesis and genetics of psoriasis have shifted the focus from a single organ disease confined to dermal structures to a systemic inflammatory condition (Jeffrey et al. 2010) (Ahmed and Abdulsami 2017).

A great heterogeneity and complexity interested of PsA disease. One of the important and a challenge both in clinical research studies and in medical practice. This PhD thesis is joined between the clinical diagnosis, genetic level and the clinical biochemical parameters on well-characterized patients with PsA in a relatively large by a case control study. Present study was been different aspects of PsA which have been investigated and interesting results generated with new generations, but as often happens in most researches, new questions arise as others are answered in current search.

5.1 History, Demographic, Physical and Clinical Diagnosis

5.1.1 Age and gender (Demographics) of PsA subjects

The PsA patients selected and that enrolled in present study with mean of age was (40.5 ±5) years for males and females togather, the control group also respectively male and female mean of age was been (42.6 ±5) these present results was showen in Table 4.1.

Sixty percent of these study subjects were PsA patients been the first group with than 35 years (35-45 years), as well as forty percent were healthy control and been the second group older than 25 years (35-45 years) that showen in Figure 4.1, The Significnc P.Value was revealed 1.0 (not significant) because the matching numbers of all subjects. Finding of this work study was agreed with more than one previous studies done inside and outside Iraq for psoriasis arithritis like a Taiwan study (Liu JT, Yeh HM, 2014) and with Denmark study (Jiménez et al., 2021).

Genders of the present study were mixed (male and female) because the signs and syptoms is been compatible for all subjects and didnt diffrent between the male and female, so that profed by the physicians decisions and the diagnosis as well as the treatment that intake. As well as the parameters that predectd and done in our study werent affects by sex and the menstural cycle changess for female, so these results in agremments with American study (Yu 1999), and with Italy study that investigate a diffences between them by a cohot study and revealed that the absence of diffrences or were been very little (Lubrano et al. 2023), also in a disagreement with Spain study (Martín1 *et al.*, 2020).

5.1.2 Physical parameters of PsA patients for this study

- The BMI of PsA patients and healthy control

Our current study was found a BMI results hasnt with a big different gape in the psoriatic arithritis patients group in a mean and SD (25.18 ± 4.0), than when make a comparism with the second group of a normal healthy control in a mean and SD (25.06 ± 3.0). Also this compatibility was statistically significant found between these groups by P.Value (1.0) because the very change in mean between the two groups.

Result of this study were revealed no effect of PsA on BMI in Iraqi cases of PsA. These results were in agreements with American study of Perelman School of Medicine at the University of Pennsylvania that shown it could also help people with psoriasis shed

unhealthy body fat and therefore improve cardiovascular health (Joel *et al.* 2022), and with Swedean study that show the short-term weight loss treatment with VLED was associated with significant positive effects on disease activity in joints, entheses and skin in patients with PsA and obesity (Eva Klingberg 2019). Also these results in a disagreemnts with (McInnes *et al.* 2019).

- The PASI score of PsA patients

Most of PsA cases that selcted and enrolled at this study wrer moderate to severe diagnosed cases, PASI score level that indicated disease severity of a current study was found that there significant worsen in skin lesion of psoriasis by increase in PASI score levels in all patients by a mean (27.87 ± 4.0) when compared with the baseline values of the PASI score types. PASI score was calculated by known formula. Results of current study were shown in Table(4-3) was in agreement with a libyan study (Zaid 2021) that concluded to a high PASI scoring to have mod/high CDAI and higher psoriasis skin severity were more than two times to have Psoriasis arthritis, and wit an Egyption study (Christine *et al.* 2017). As well as in a disagreement with a Netherlands research (Fazira R Kasiem, 2022) that revealed that the PASI score was elevated in PsA patients is mostly by a mildly levels when measured using a dermatology.

- The PSAJAI score for PsA patients

All cases of PsA that selcted and enrolled at this study wrer calculated the scoring unit of disease activity by a (PSAJAI score) level, to take a more clear idea for the disease indication and severity. A results of current study was found that there significant elevation in plasma CRP, Tender Joints Count and Swollen Joints Count, the damaged bons, this lead to increase in PASJAI score levels in all most patients by a mean and SD (152 ± 25), these results were im agreements with (GLADMAN 2010).

5.2 The Clinical Study Parameters for PsA and Helthy Groups

5.2.1 Serum vitamin D_3 for PsA patients and healthy groups

Current study results were showed a significant decrease or a deficincy state in the levels of serum Vitamin D3 for the psoriatic arithritis patients group when compared to second group of a healthy controls for both gender. Table (4-5) shows the revealed differences levels between the two groups with an aceptabe P. Value less than 0.05, so the mean and a SD for PsA patients was (12.30 ± 5.47 ng/ml) and for healthy group been (53.07 ±9.94). Reveald Study resuls were in agreemnts with Croatia study (Radić 2023) that concluded PsA patients have lower vitamin D levels than the general population, also in agreements with Italy study (Rotondo *et al.* 2023) that concluded to confirms the association between vitamin D3 deficiency and more severe PsA course in terms of the presence of sacroiliitis and MTX poor response in peripheric involvement. There were no past study concluded that the Vitamin D3 was normal wirh bone disorders like PsA, but some some of them say that after patients taken a supplemental vitamins like 25-hydroxy vitamin D3 that can we make an a disgreements comparism with them like an Indain study (Bhat *et al.* 2022).

5.2.2 Serum vitamin K_2 for PsA patients and healthy groups

The Decreased levels of vitamin K2 were been detected at the current study in patients, so the vit. K2 concentration for PsA group in mean and SD (1.350 ±0.18 ng/ml) and for the secon group been a (2.132 ±0.55 ng/ml) that showed by a Table (4-6), some of PsA patients that enrolled at the present study have a normal vit. K2 because supplement intake there were have a negative or been normal plasma CRP and excluded from this parameter statistical analysis. These results were in agreements with (Elizabeth Usedom 2017) that mentioned Further research is needed on vitamin K to determine the potential benefit of supplementation in psoriasis patients, and with (Ebina 2013). As well as there were no past study in a disagreements with our results. Vitamin K_2 was very important for the diseases suppresents that showed by chines study (Meiyu *et al.* 2021).

5.2.3 Serum tumer necrosis factor-α for PsA patients and healthy groups

Tumer Necrosis Factor-α increases these values of PsA patients serum, or in the psoriatic patients group with mean and SD (242.5 ± 31.3) than the healthy control group (57.18 ± 10.1) and these differences were shown in Table 4.7. Results of this study were in agreements with USA study (Mantravadi. *et al.*2017) TNF including underlying disease type or severity, body weight, immunogenicity, and the concomitant use of other medications such as MTX, (Cagnotto *et al.* 2020, Ovcina-Kurtovic 2022). Study was in disagreements with a study (Kane 2004).

5.2.4 Serum adeponectine for PsA patients and healthy groups

Adipokines like adiponectine the parameter that done at this study, results of adiponectine reveald to elevated levels in PsA patients group by mean and SD (92.71± 13.33 ng/ml), when compared with second group of the healthy subjects (18.64± 10.10 ng/ml), these results were showed in Table (4-8), also its in agreements with (Kiełbowski. *et al.* 2023) and with (Oguz. *et al.* 2016), as wwell as the china study that revealed to the increas amount of evidence has high lighted the core role of adipokines (adeponectine) in adipose tissue and the immune system (Ruiyang1. *et al.* 2021). Also these results in a disagreements with the Barazilizan study (Bavoso. *et al.* 2019).

5.2.5 Plasma CRP for PsA patients and healthy groups

Our CRP results been elevated in patients with psoriatic arthritis (PsA) first group with mean and SD (43.70 ± 11.74 mg/dl), however for the second group of a healthy in a mean and SD (6.0 ± .01 mg/dl) that showen in a Table 4.8. CRP testing of the present study was in agreements with USA study (Ogdie *et al.* 2022b), and with (Houttekiet. *et al.* 2022). Also in a disagreement with (Sokolova *et al.* 2020).

5.2.6 Serum uric acid for PsA patients and healthy groups

Table 4.10 was showed a uric acid results of the present study with the means and SD (546.9 ± 151.14 mmol/L) for the PsA patients group, and (278.9 ±100.10 mmol/L for the healthy control group, these results with an agreements with Italy study (Cesare. *et al.* 2021) (Tripolino. *et al.* 2021), and with (Widawski *et al.* 2022). Results in disagreements with (Lambert 1977).

5.2.7 Serum GSH for PsA patients and healthy groups

Glutathione of PsA serums patients group levels and or its activity in patients with psoriasis arithritis were significantly lower than in general population (healthy control group). Table (4-11) was showen the mean and SD results for PsA group (.2949 ± .18025µg/mL) and for the healthy group been (.8382 ± .33007 µg/mL). Very clear gap between the two groups with an acceptale P.Value less than 0.05 due to sever oxidative stress than found in PsA group, so these results in agreements with Italy study (Campione E. *et al.* 2022), and with (Ia Khmaladze. *et al.* 2015).

5.2.8 Serum GSSG for PsA patients and healthy groups

The GSSG (oxidized form of the Glutathion enzyme) results level of the present study for the PsA were elevated than the normal healthy group by a mean and SD (1.410 ± .31992 µg/mL), and for the second group of control been (.2133 ± .19430 µg/mL). There were no previous study estimated this parameter for the psoriasis arithritis patients, as well as its elevatedd in PsA patients due to the large size of oxidative stress state and free radical hyper activity, present resuls were showed in Table (4-12).

5.2.9 The ESR for PsA patients and healthy groups

Current study results of the ESR parameter for the PsA patients were revealed that its elevated levels than the normal reference values with a mean and SD (69.72 ± 10.9

mm/hr), so control group with (5.15 ± 2.1 mm/hr). These test results at an agreements with (Haroon. *et al.*2018) and with (WebMD 2023) that they said ESR was gives a rough idea of how much inflammation is in your body, which could be caused by psoriatic arthritis, and in disagreements with (Punzi *et al.* 2007) that mentioned a low ESR seems protective, while an ESR >15 mm/h is one of the factors associated with an increased mortality in PsA. Our present resuls were showed in Table 4.13.

5.3 The Molecular Genetic Examination

Polymerase chain reaction (PCR) was used to analyze the CCHCR1 gene for the (rs3130453) polymorphism detection. The A/C polymorphism site was defined by performing a PCR amplification using site-specific primers, and the result was seen as a single band on an agarose gel electrophoresis. This done for a single gene (CCHCR1) and for a single SNP (rs3130453) by REFLIP design. Figure 4.2 shows that the control outer band was 314 bp, the A allele was 203 bp, and the C allele was 157 bp in the gene. Table 4-3 displays the frequency of alleles for the CCHCR1 gene polymorphism (Garibyan 2013, Yang *et al.*2021) .

At the present study the PsA genetic examination was done in a CCHCR1 gene at the chromosome region 6p21.3 and as specificly the (rs3130453) Polymorphismed a normal (G-C) SNP to a (G-T) mutated nucleotied mostly for a patients group. To ensure that this gene was encodes a polymorphism which lead for the psoriasis aritritis apperly signs and symptoms as well as a main cause rof PsA pathogenesis, we done a molecular and gentic analysis results, and made a correltion between the clinical parameters with the molecular results (Gandhi *et al.* 2011).

Our present study was revealed that the CCHCR1 gene is contain a mutation by a SNP polymophism at the (rs3130453), this found in PsA patients group of this study. The concept concluded that CCHCR1 gene was responsible for the PsA pathognesis, and make the disease more clear clinical syptoms and signs (Loft *et al.* 2018).

5.3.1 Molecular genetic of CCHCR1 polymorphism SNP (rs3130453)

Firstly revealed of the results of our study that showed in Table 4.14, Figure 4.3 revealed and exhibit about 60% of all subjects were (50 persons) of PsA patients from the all (90 persons) that there enrolled in our present study. The all subjects were divided into three sub groups due to the genetic results analysis that revealed. So the first sub group represented a 20% (10) patients from the PsA big group they have a XbaI (-/-) polymorphism. As well as a 30% (15) patients of PsA represents the second sub group, they found with XbaI (-/+). The thierd group is represented the big bulk of a PsA patients that detected with a clear polymorpism (+/+), that they composed a 50% (25) of all patients number that enrolled at our present study. Subjects of healthy control group was in an opposite results that shows in mentioned table (Tervaniemi *et al.* 2012).

The second group of a healthy control enrolled at our present study were also divided into three sub groups, but with an opposite reveled results that also showed in a Table 4.14. The big sub group or a bulk with a negative mutation polymorphism XbaI (-/-), when make a correlation between the two big group we will find a significance relationship, due to the significance diffrenet between them.

5.3.2 Alleles frequencies of CCHCR1 gene polymorphism SNP (rs3130453)

Table of 4.15 was showen the results of the allels frequency at our study, for the PsA patient and control groups, these results were revealed that the XbaI (+) was been for (61%) of PsA patients and (20%) for the control groups. As well as the XbaI (-) was been (39%) for a patients and (80%) for a control groups.

5.3.3 Odd ration of CCHCR1 gene polymorphism

Our study results were revealed at the Table 4.16 that the odd ration for (28 subjects) from control group and (2 subjects) from patients' group where been a reference for the

all participant because the clear negative results with genotyping (-/-). Also the our results were shows a (+/-) genotyping type with an odd ration (17.5) for (10 persons) from the patients group, (8 persons) with the control group.

As well as the most prevalent or a big bulk of all subjects that enrolled were been a (+/+) genotyping for the patients group with (38 persons), and very rare positive for the control group with only (4 persons) from 40 original subjects, that abbriviated with an odd ration (133.0). Present results were in agreements with china study (Kwan *et al.* 2018, Suleman *et al.*2022).

REFERENCES

Abdel-Rahman, M. S., Alkady, E. A. and Ahmed, S. 2015. Menaquinone-7 as a novel pharmacological therapy in the treatment of rheumatoid arthritis: A clinical study. European Journal of Pharmacology, 761, 273-278.

Abramson, N. 2006. Rouleaux formation. Blood, 107(11): 4205.

Aceto, A., Martini, F., Dragani, B., Bucciarelli, T., Sacchetta, P. and Di Ilio, C. (1992). Purification and characterization of glutathione transferase from psoriatic skin. Biochemical medicine and metabolic biology, 48(3): 212-218.

Achari, A. E. and Jain, S. K. 2017. Adiponectin, a therapeutic target for obesity, diabetes, and endothelial dysfunction. International journal of molecular sciences, 18(6): 1321.

Al-Awadhi, A. 2007. 'Angiotensin-Converting enzyme gene polymorphism in patients with psoriatic arthritis.', Rheumatol. Int., 27: 1119–1123.

Alhajj, M., Zubair, M. and Farhana, A. 2023. Enzyme linked immunosorbent assay. StatPearls, 6: 89.

AlMease, F. 2013. Psoriatic arthritis affects about 30% of people with psoriasis. National Psoriasis Foundation, 3: 65.

Al-Mokhtar, A. M., Alta'ee, A. H. and Al-Hattab, M. K. 2017. Leptin and Resistin Induce Oxidative Stress in Patients with Chronic Plaque Psoriatic. Research journal of pharmaceutical biological and chemical sciences, 8(1): 135-142.

Almukhtar, A. 2016. Correlation of Leptin and Resistin with Oxidative Stress in Chronic Plaque Psoriasis. 1(2): 16-20.

Alshami, M. A. 2010. Clinical profile of psoriasis in Yemen, a 4 years retrospective study of 241 patients. In Journal of the European Academy of Dermatology and Venereology, 24: 14-14.

Altman1991 2023. Web site. https://www.medcalc.org/calc/odds_ratio.php. Date of access: 05.11.2023.

Ansari, S. L. N. H., Wang, C., Wang, L. and Srivastava, S. K. 1996. A rapid HPLC method for the quantification of GSH and GSSG in ocular lens. Current eye research, 15(7): 726-732.

App, M. 2021. Web site. https://www.mdaco/disease-activity-in-psoriatic-arthritis-dapsa-calculator-612. Date of access: 01.09.2023.

Arithritis, T. 2023. Psoriasis and Psoriatic Arthritis May Increase Gout Risk. Arthritis Foundation, 6: 44.

Augustin, M. 2021. Patient-reported well-being in value-based care using tildrakizumab in a real-world setting: protocol of a multinational, phase IV, 1-cohort prospective observational study (the POSITIVE study). BMJ Open, 13(2): 75.

Augustin, M., Radtke, M. A., Glaeske, G., Reich, K., Christophers, E., Schaefer, I. and Jacobi, A. 2015. Epidemiology and comorbidity in children with psoriasis and atopic eczema. Dermatology, 231(1): 35-40.

Baran, A., Flisiak, I., Jaroszewicz, J. and Świderska, M. 2015. Effect of psoriasis activity on serum adiponectin and leptin levels. Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii, 32(2): 101-106.

Baran, A., Flisiak, I., Jaroszewicz, J. and Świderska, M. 2015. Effect of psoriasis activity on serum adiponectin and leptin levels. Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii, 32(2): 101-106.

Bavoso, N. C., Pinto, J. M., Soares, M. M. S., Diniz, M. D. S. and Teixeira, A. L. 2019. Psoriasis in obesity: comparison of serum levels of leptin and adiponectin in obese subjects-cases and controls. Anais brasileiros de dermatologia, 94, 192-197.

Bedi, T. R. 1995. Clinical profile of psoriasis in North India. Indian Journal of Dermatology, Venereology and Leprology, 61, 202.

Berner, H. S., Lyngstadaas, S. P., Spahr, A., Monjo, M., Thommesen, L., Drevon, C. A. and Reseland, J. E. 2004. Adiponectin and its receptors are expressed in bone-forming cells. Bone, 35(4): 842-849.

Bhat, G. H., Guldin, S., Khan, M. S., Yasir, M. and Prasad, G. 2022. Vitamin D status in Psoriasis: impact and clinical correlations. BMC nutrition, 8(1): 115.

Biolabs, U. 2016. New England, XbaI | NEB. www.neb.com. Retrieved, 4: 5-8.

Boehncke, G. 2015. 'Psoriasis. Lancet, 386, 983–994.

Booth, S. L. 2009. Roles for vitamin K beyond coagulation. Annu Rev Nutr, 29: 89–110.

Bradley, J.R. 2008. TNF-Mediated inflammatory disease J. Pathol, 214: 149–160.

Braidy, N., Zarka, M., Jugder, B. E., Welch, J., Jayasena, T., Chan, D. K. and Bridge, W. 2019. The precursor to glutathione (GSH): γ-Glutamylcysteine (GGC): can ameliorate oxidative damage and neuroinflammation induced by Aβ40 oligomers in human astrocytes. Frontiers in aging neuroscience, 11, 177.

Brooks, D. E., Devine, D. V., Harris, P. C., Harris, J. E., Miller, M. E., Olal, A. D. and Xie, Z. C. 1999. RAMPTM: a rapid, quantitative whole blood immunochromatographic platform for point-of-care testing. Clinical Chemistry, 45(9): 1676-1678.

Burtis, C. A., Ashwood, E. R. and Tietz, N. W. 1999. Tietz textbook of clinical chemistry. Sciences, 2: 54.

Byjus, 2022. Web site. https://byjus.com/biology/pcr. Date of access: 07.09.2023.

Cagnotto, G., Compagno, M., Scire, C. A. and Bruschettini, M. 2020. Tumor necrosis factor (TNF) inhibitors for the treatment of psoriatic arthritis. The Cochrane Database of Systematic Reviews, 2: 205.

Callen, J. P. 1995. Dermatological signs of internal disease. Sciences, 7: 66.

Campione, E., Mazzilli, S., Di Prete, M., Dattola, A., Cosio, T., Lettieri Barbato, D. and Bianchi, L. 2022. The role of Glutathione-S transferase in psoriasis and associated comorbidities and the effect of dimethyl fumarate in this pathway. Frontiers in Medicine, 9: 760852.

Campione, E., Mazzilli, S., Di Prete, M., Dattola, A., Cosio, T., Lettieri Barbato, D. and Bianchi, L. 2022. The role of Glutathione-S transferase in psoriasis and associated comorbidities and the effect of dimethyl fumarate in this pathway. Frontiers in Medicine, 9, 760852.

Carl, A. 2012. Tietz textbook of clinical chemistry and molecular diagnostics. Sciences, 2: 5.

Carroll, D., Howard, D., Zhu, H., Paumi, C. M., Vore, M., Bondada, S. and Clair, D. K. S. 2016. Simultaneous quantitation of oxidized and reduced glutathione via LC-MS/MS: An insight into the redox state of hematopoietic stem cells. Free Radical Biology and Medicine, 97: 85-94.

Clinic, C. 2022. Web site. https://my.clevelandclinic.org/health/articles/22439-adiponectin#:~:text=Adiponectin%20is%20a%20hormone%20and,body%20produce%20it%20as%20well. Date of access: 22.08.2023.

Crook, M. 2013. Clinical biochemistry and metabolic medicine. CRC press, 4: 99.

Danielsen, K., Olsen, A. O., Wilsgaard, T. and Furberg, A. S. 2013. Is the prevalence of psoriasis increasing? A 30-year follow-up of a population-based cohort. British Journal of Dermatology, 168(6): 1303-1310.

de Vlam, K. 2018. Overview of psoriatic arthritis pathogenesis. Oxford Textbook of Psoriatic Arthritis, Oxford Textbooks In Rheumatology, 5: 64.

Delaigle, A. M., Jonas, J. C., Bauche, I. B., Cornu, O. and Brichard, S. M. 2004. Induction of adiponectin in skeletal muscle by inflammatory cytokines: in vivo and in vitro studies. Endocrinology, 145(12): 5589-5597.

Deneke, S. M. 1989. Regulation of cellular glutathione. The American Journal of PhysiologY, 257: 163–73.

Diez, J. J. and Iglesias, P. 2003. The role of the novel adipocyte-derived hormone adiponectin in human disease. European Journal of endocrinology, 148(3): 293-300.

Diez, J. and Iglesias, P. 2010. The role of the novel adipocyte-derived protein adiponectin in human disease: an update. Mini reviews in medicinal chemistry, 10(9): 856-869.

Dikbas, O., Tosun, M., Bes, C., Tonuk, S. B., Aksehirli, O. Y. and Soy, M. 2016. Serum levels of visfatin, resistin and adiponectin in patients with psoriatic arthritis and associations with disease severity. International journal of rheumatic diseases, 19(7): 672-677.

Ebina, K., Shi, K., Hirao, M., Kaneshiro, S., Morimoto, T., Koizumi, K. and Hashimoto, J. 2013. Vitamin K2 administration is associated with decreased disease activity in patients with rheumatoid arthritis. Modern rheumatology, 23(5): 1001-1007.

Ebina, K., Shi, K., Hirao, M., Kaneshiro, S., Morimoto, T., Koizumi, K. and Hashimoto, J. 2013. Vitamin K2 administration is associated with decreased disease activity in patients with rheumatoid arthritis. Modern rheumatology, 23(5): 1001-1007.

Ebina, K., Shi, K., Hirao, M., Kaneshiro, S., Morimoto, T., Koizumi, K. and Hashimoto, J. 2013. Vitamin K2 administration is associated with decreased disease activity in patients with rheumatoid arthritis. Modern rheumatology, 23(5): 1001-1007.

Eder, L., Jayakar, J., Pollock, R., Pellett, F., Thavaneswaran, A., Chandran, V., Rosen, C.F. and Gladman, D.D. 2013 ‘Serum adipokines in patients with psoriatic

arthritis and psoriasis alone and their correlation with disease activity', Annals of the rheumatic diseases, 72(12): 1956–1961.

Ediz, D. 2012. Tumor necrosis factor-alpha antagonist therapy-induced psoriasis in Turkey: analysis of 514 patients. Mod Rheumatol, 22: 738–742.

Evaluation, I. for H.M. and 2012 'Global Burden of Disease Results by Cause'.

Fantuzzi, F., Del Giglio, M., Gisondi, P. and Girolomoni, G. 2008. Targeting tumor necrosis factor α in psoriasis and psoriatic arthritis. Expert opinion on therapeutic targets, 12(9): 1085-1096.

Farrag, D. A., Asaad, M. K. and Ghobrial, C. K. 2017. Evaluation of IL-34 in psoriasis and psoriatic arthritis patients: correlation with disease activity and severity. The Egyptian Rheumatologist, 39(1): 25-31.

Fredriksson, T. 2023. Web site. https://www.mdcalc.com/calc/10182/psoriasis-area-severity-index-pasi#creator-insights. Date of access: 03.07.2023.

Gamil, A. H., Abdel-Mawla, M. Y., Khalifa, N. A. and Nasr, M. M. 2021. Serum adiponectin level in patients with psoriasis and its correlation with the clinical severity. The Egyptian Journal of Hospital Medicine, 84(1): 2014-2019.

Gandhi, G., Buttar, B. S., Albert, L., Hasan, Q. and Aggarwal, R. K. 2011. Psoriasis-associated genetic polymorphism in North Indian population in the CCHCR1 gene and in a genomic segment flanking the HLA-C region. Disease markers, 31(6): 361-370.

García-Alegría, A. M. anduro-Corona, I., Pérez-Martínez, C. J., Guadalupe Corella-Madueño, M. A., Rascón-Durán, M. L. and Astiazaran-Garcia, H. 2020. Quantification of DNA through the NanoDrop spectrophotometer: methodological validation using standard reference material and Sprague Dawley rat and human DNA. International journal of analytical chemistry, 2020.

Garibyan, L. and Avashia, N. 2013. Research techniques made simple: polymerase chain reaction (PCR). The Journal of investigative dermatology, 133(3): e6.

George, C. M., Perin, J., Parvin, T., Bhuyian, M. S. I., Thomas, E. D., Monira, S. and Tofail, F. 2022. Diarrhea prevalence and child growth faltering are associated with subsequent adverse child developmental outcomes in Bangladesh (CHoBI7 Program). The American Journal of Tropical Medicine and Hygiene, 106(1): 233.

Gerdes, S., Rostami-Yazdi, M. and Mrowietz, U. 2011. Adipokines and psoriasis. Experimental dermatology, 20(2): 81-87.

Gibbs, S. A. M. (1996). Skin disease and socioeconomic conditions in rural Africa: Tanzania. International journal of dermatology, 35(9): 633-639.

Girolomoni, G., Altomare, G., Ayala, F., Berardesca, E., Calzavara-Pinton, P., Chimenti, S. and Vena, G. A. 2012. Safety of anti-TNFα agents in the treatment of psoriasis and psoriatic arthritis. Immunopharmacology and immunotoxicology, 34(4): 548-560.

Gisondi, P., Targher, G., Cagalli, A. and Girolomoni, G. 2014. Hyperuricemia in patients with chronic plaque psoriasis. Journal of the American Academy of Dermatology, 70(1): 127-130.

Gisondi, P., Tessari, G., Conti, A., Piaserico, S., Schianchi, S., Peserico, A. and Girolomoni, G. 2007. Prevalence of metabolic syndrome in patients with psoriasis: a hospital-based case–control study. British Journal of Dermatology, 157(1): 68-73.

Gladman, D. D., Antoni, C., Mease, P., Clegg, D. O. and Nash, P. 2005. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. Annals of the rheumatic diseases, 64(2): 14-17.

Gladman, D. D., Sampalis, J. S., Illouz, O. and Guérette, B. 2010. Responses to adalimumab in patients with active psoriatic arthritis who have not adequately responded to prior therapy: effectiveness and safety results from an open-label study. The Journal of rheumatology, 37(9): 1898-1906.

Griffith, O. W. (1980). Determination of glutathione and glutathione disulfide using glutathione reductase and 2-vinylpyridine. Analytical biochemistry, 106(1): 207-212.

Griffiths, C. E. and Barker, J. N. 2007. Pathogenesis and clinical features of psoriasis. The Lancet, 370(9583): 263-271.

Gui, X. Y., Jin, H. Z., Wang, Z. J. and Xu, T. D. 2018. Serum uric acid levels and hyperuricemia in patients with psoriasis: a hospital-based cross-sectional study. Anais brasileiros de dermatologia, 93, 761-763.

Guntherberg, H. and Rost, J. 1966. Glutathion. Analytical Biochemistry, 7: 205–210.

Harden, J. L., Krueger, J. G. and Bowcock, A. M. 2015. The immunogenetics of psoriasis: a comprehensive review. Journal of autoimmunity, 64, 66-73.

Haroon, M., Ahmad, M., Mason, O. and FitzGerald, O. 2018. THU0321 Acute phase markers in psoriatic arthritis identify patients with a more severe phenotype. Sciences, 7: 88 .

Hashim, H. O. and Al-Shuhaib, M. B. S. 2019. Exploring the potential and limitations of PCR-RFLP and PCR-SSCP for SNP detection: A review. Journal of applied biotechnology reports, 6(4): 137-144.

Hicks, J. M. 1984. Fluorescence immunoassay. Human pathology, 15(2): 112-116.

Holmgren, A., Johansson, C., Berndt, C., Lönn, M. E., Hudemann, C. and Lillig, C. H. 2005. Thiol redox control via thioredoxin and glutaredoxin systems. Biochemical Society Transactions, 33(6): 1375-1377.

Hopkins, J. 2022. Web site. https://www.hopkinsmedicine.org/health/conditions-and-diseases/arthritis/psoriatic-arthritis. Date of access: 09.08.2023.

Horiuchi, T., Mitoma, H., Harashima, S. I., Tsukamoto, H. and Shimoda, T. 2010. Transmembrane TNF-α: structure, function and interaction with anti-TNF agents. Rheumatology, 49(7): 1215-1228.

Houttekiet, C., de Vlam, K., Neerinckx, B. and Lories, R. 2022. Systematic review of the use of CRP in clinical trials for psoriatic arthritis: a concern for clinical practice?. RMD open, 8(1): 54.

Hu, E., Liang, P. and Spiegelman, B. M. 1996. AdipoQ is a novel adipose-specific gene dysregulated in obesity. Journal of biological chemistry, 271(18): 10697-10703.

Husni, E. and Michael, M. 2018. Epidemiology of psoriatic arthritis. Sciences, 5: 53.

Ilie, M. A., Caruntu, C., Lixandru, D., Tampa, M., Georgescu, S. R., Constantin, M. M. and Boda, D. 2019. In vivo confocal laser scanning microscopy imaging of skin inflammation: Clinical applications and research directions. Experimental and therapeutic medicine, 17(2): 1004-1011.

Iskusnykh, I. Y., Zakharova, A. A. and Pathak, D. 2022. Glutathione in brain disorders and aging. Molecules, 27(1): 324.

Jang, D. I., Lee, A. H., Shin, H. Y., Song, H. R., Park, J. H., Kang, T. B. and Yang, S. H. 2021. The role of tumor necrosis factor alpha (TNF-α) in autoimmune disease

and current TNF-α inhibitors in therapeutics. International journal of molecular sciences, 22(5): 2719.

Joel, M. and Gelfand, M. D. 2022. Penn Research Finds Psoriasis Medication Apremilast Leads to Fat Loss in People with Psoriasis. JAMA Dermatology, 4: 42.

Johnson-Huang, L. M., Lowes, M. A. and Krueger, J. G. 2012. Putting together the psoriasis puzzle: an update on developing targeted therapies. Disease models and mechanisms, 5(4): 423-433.

Jones, J. 2023. Web site. https://www.healthline.com/nutrition/foods-high-in-vitamin-k. Date of access: 22.09.2023.

Kampfrath, T. 2022. C Reactive Protein (CRP Blood Test). Sciences, 2: 8.

Kane, D. 2004. Tumor Necrosis Factor-_ in Psoriasis and Psoriatic Arthritis: A Clinical, Genetic, and Histopathologic Perspective. Kane and FitzGerald, 1(11): 54.

Kasiem, F. R., Kok, M. R., Luime, J. J., Tchetverikov, I., Wervers, K., Korswagen, L. A. and CICERO. 2022. The burden of psoriasis in patients with early psoriatic arthritis. Rheumatology, 61(4): 1570-1578.

Kaur, S., Zilmer, K., Kairane, C., Kals, M. and Zilmer, M. 2008. Clear differences in adiponectin level and glutathione redox status revealed in obese and normal-weight patients with psoriasis. British Journal of Dermatology, 159(6): 1364-1367.

Khmaladze, I., Nandakumar, K. S. and Holmdahl, R. 2015. Reactive oxygen species in psoriasis and psoriasis arthritis: relevance to human disease. International archives of allergy and immunology, 166(2): 135-149.

Kiełbowski, K., Bakinowska, E., Ostrowski, P., Pala, B., Gromowska, E., Gurazda, K. and Pawlik, A. 2023. The role of adipokines in the pathogenesis of psoriasis. International Journal of Molecular Sciences, 24(7): 6390.

Kirkham, B. 2018. Immunology and cytokine pathways. Oxford Textbooks In Rheumatology, 2: 54.

Klingberg, E., Bilberg, A., Björkman, S., Hedberg, M., Jacobsson, L., Forsblad-d'Elia, H. and Larsson, I. 2019. Weight loss improves disease activity in patients with psoriatic arthritis and obesity: an interventional study. Arthritis research and therapy, 21(1): 1-10.

Kökçam, İ. and Nazıroğlu, M. (1999). Antioxidants and lipid peroxidation status in the blood of patients with psoriasis. Clinica Chimica Acta, 289(1-2): 23-31.

Krüger, D. H. and Bickle, T. A. (1983). Bacteriophage survival: multiple mechanisms for avoiding the deoxyribonucleic acid restriction systems of their hosts. Microbiological reviews, 47(3): 345-360.

Laborde, C. M., Larzabal, L., González-Cantero, Á., Castro-Santos, P. and Díaz-Peña, R. 2022. Advances of Genomic Medicine in Psoriatic Arthritis. Journal of Personalized Medicine, 12(1): 35.

Lambert, J. R. and Wright, V. (1977). Serum uric acid levels in psoriatic arthritis. Annals of the Rheumatic Diseases, 36(3): 264.

Langley, R. G., Strober, B. E., Gu, Y., Rozzo, S. J. and Okun, M. M. 2010. Benefit-risk assessment of tumour necrosis factor antagonists in the treatment of psoriasis. British Journal of Dermatology, 162(6): 1349-1358.

Lasemi, R. 2019. The role and mechanisms of vitamin K2 in multiple sclerosis. Sciences, 5: 97.

Lee, K. Y., Leung, K. S., Tang, N. L. and Wong, M. H. 2018. Discovering genetic factors for psoriasis through exhaustively searching for significant second order SNP-SNP interactions. Scientific reports, 8(1): 15186.

Li, J., Wang, H. and Rosenberg, P. A. 2009. Vitamin K prevents oxidative cell death by inhibiting activation of 12-lipoxygenase in developing oligodendrocytes. Journal of neuroscience research, 87(9): 1997-2005.

Liu, J. T., Yeh, H. M., Liu, S. Y. and Chen, K. T. 2014. Psoriatic arthritis: epidemiology, diagnosis, and treatment. World journal of orthopedics, 5(4): 537.

Liu, J. Z. and Anderson, C. A. 2014. Genetic studies of Crohn's disease: past, present and future. Best Practice and Research Clinical Gastroenterology, 28(3): 373-386.

Loft, N. D., Skov, L., Rasmussen, M. K., Gniadecki, R., Dam, T. N., Brandslund, I. and Andersen, V. 2018. Genetic polymorphisms associated with psoriasis and development of psoriatic arthritis in patients with psoriasis. PloS one, 13(2): e0192010.

Lories, R. 2018. Mechanisms of bone destruction and proliferation in psoriatic arthritis. Oxford Textbooks In Rheumatology, 5: 76.

Lowes, M. A., Russell, C. B., Martin, D. A., Towne, J. E. and Krueger, J. G. 2013. The IL-23/T17 pathogenic axis in psoriasis is amplified by keratinocyte responses. Trends in immunology, 34(4): 174-181.

Lu, S. C. 2013. Glutathione synthesis. Biochimica et Biophysica Acta (BBA)-General Subjects, 1830(5): 3143-3153.

Lubrano, E., Scriffignano, S., Fatica, M., Triggianese, P., Conigliaro, P., Perrotta, F. M. and Chimenti, M. S. 2023. Psoriatic Arthritis in Males and Females: Differences and Similarities. Rheumatology and Therapy, 10(3): 589-599.

Luo, Y. and Liu, M. 2016. Adiponectin: a versatile player of innate immunity. Journal of molecular cell biology, 8(2): 120-128.

Maeda, K., Okubo, K., Shimomura, I., Funahashi, T., Matsuzawa, Y. and Matsubara, K. (1996). cDNA cloning and expression of a novel adipose specific collagen-like factor, apM1 (AdiPoseMost abundant Gene transcript 1). Biochemical and biophysical research communications, 221(2): 286-289.

Mantravadi, S., Ogdie, A. and Kraft, W. K. 2017. Tumor necrosis factor inhibitors in psoriatic arthritis. Expert review of clinical pharmacology, 10(8): 899-910.

Martín, J. L., Campo, E. P., Benavente, L. C., Martínez, M. P., Castro, S. A., Fernández, S. and Silva, R. Q. 2020. Sat0436 patients with psoriatic arthritis who achieve the mda response show less subclinical atherosclerosis than those in dapsa remission Sciences, 6: 99.

McInnes, I. B., Ferraccioli, G., D'Agostino, M. A., Le Bars, M., Banerjee, S., Ahmad, H. A. and Mease, P. J. 2019. Body mass index and treatment response to subcutaneous abatacept in patients with psoriatic arthritis: a post hoc analysis of a phase III trial. RMD open, 5(1): 934.

Mease, P. J. 2011. Measures of psoriatic arthritis: Tender and Swollen Joint Assessment, Psoriasis Area and Severity Index (PASI): Nail Psoriasis Severity Index (NAPSI): Modified Nail Psoriasis Severity Index (mNAPSI): Mander/Newcastle Enthesitis Index (MEI): Leeds Enthesitis Index (LEI): Spondyloarthritis Research Consortium of Canada (SPARCC): Maastricht Ankylosing Spondylitis Enthesis Score (MASES): Leeds Dactylitis Index (LDI): Patient Global for Psoriatic Arthritis, Dermatology Life Quality Index (DLQI): Psoriatic .... Arthritis care and research, 63(11): 64-85.

Medical, U. of R. 2022. Health Encyclopedia. Sciences, 2: 98.

Medicine, N. L. Web site. 2022. ‘https://medlineplus.gov/lab-tests/c-reactive-protein-crptest/#:~:text=CRP%20is%20a%20protein%20that,health%20condition%20that%20causes%20inflammation. Date of access: 09.08.2023.

Meister, A. (1988). Glutathione metabolism and its selective modification. Journal of biological chemistry, 263(33): 17205-17208.

Meister, A. and Anderson, M. E. 1983. Glutathione. Annual review of biochemistry, 52(1): 711-760.

Meister, A. and Larsson, A. 1989. Glutathione synthetase deficiency and other disorders of the gamma-glutamyl cycle. The Metabolic and Molecular Bases of Inherited Disease, 1, 1461-1495.

Membrive Jiménez, C., Pérez Ramírez, C., Sánchez Martín, A., Vieira Maroun, S., Arias Santiago, S. A., Ramirez Tortosa, M. D. C. and Jiménez Morales, A. 2021. Influence of genetic polymorphisms on response to biologics in moderate-to-severe psoriasis. Journal of Personalized Medicine, 11(4): 293.

Merola, J. F., Espinoza, L. R. and Fleischmann, R. 2018. Distinguishing rheumatoid arthritis from psoriatic arthritis. RMD open, 4(2): 33.

Mladěnka, P., Macáková, K., Kujovská Krčmová, L., Javorská, L., Mrštná, K., Carazo, A. and OEMONOM Researchers and Collaborators. 2021. Vitamin K–sources, physiological role, kinetics, deficiency, detection, therapeutic use, and toxicity. Nutrition reviews, 80(4): 677-698.

Motohashi, K. 2019. Development of highly sensitive and low-cost DNA agarose gel electrophoresis detection systems, and evaluation of non-mutagenic and loading dye-type DNA-staining reagents. PLoS One, 14(9): 209.

Mulder, M. L., van Hal, T. W., Wenink, M. H., Koenen, H. J., van den Hoogen, F. H., de Jong, E. M. and Vriezekolk, J. E. 2021. Clinical, laboratory, and genetic markers for the development or presence of psoriatic arthritis in psoriasis patients: a systematic review. Arthritis Research and Therapy, 23(1): 1-22.

Myo Clinic, 2022a. Web site. Https://www.mayoclinic.org/diseases-conditions/arthritis/symptoms-causes/syc-20350772, Arthritis. Date of access: 25.08.2023.

Myo Clinic, 2022b. Web site. https://www.mayoclinic.org/diseases-conditions/psoriasis/symptoms-causes/syc-20355840, Psoriasis. Date of access: 25.08.2023.

Myoclinic, 2022. Web site. https://www.nhs.uk/conditions/psoriatic-arthritis/#:~:text=Psoriatic%20arthritis%20is%20a%20type,that%20can%20get%20progressively%20worse., Psoriatic arthritis. Date of access: 21.09.2023.

Nacca, F., Cozzolino, C., Carillo, P., Woodrow, P., Fuggi, A. and Ciarmiello, L. F. 2021. An HPLC-automated Derivatization for Glutathione and Related Thiols Analysis in Brassica rapa L. Agronomy, 11(6): 1157.

NCBI (1993). ICSH recommendations for measurement of erythrocyte sedimentation rate. International Council for Standardization in Haematology (Expert Panel on Blood Rheology). J Clin Pathol., 46(3): 198–203.

NCBI, 2023. Web site. https://www.ncbi.nlm.nih.gov/gene/54535#reference-sequences. Date of access: 19.09.2023.

Nehring, S. M., Goyal, A. and Patel, B. C. 2022. C Reactive Protein. 2021 Dec 28. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing, 3: 75.

Nick Dand1, 2, Satveer K. Mahil3, Francesca Capon1, Catherine H. Smith3, M.A.S. and J.N.B. 2019 'Psoriasis and Genetics', Acta Derm Venereol, 2(1): 100.

Nograles, K. E., Brasington, R. D. and Bowcock, A. M. 2009. New insights into the pathogenesis and genetics of psoriatic arthritis. Nature clinical practice Rheumatology, 5(2): 83-91.

O'Rielly, D. D. and Rahman, P. 2015. Genetic, epigenetic and pharmacogenetic aspects of psoriasis and psoriatic arthritis. Rheumatic Disease Clinics, 41(4): 623-642.

O'Rielly, D. D., Jani, M., Rahman, P. and Elder, J. T. 2019. The genetics of psoriasis and psoriatic arthritis. The Journal of Rheumatology Supplement, 95: 46-50.

Ogawa, E., Sato, Y., Minagawa, A. and Okuyama, R. 2018. Pathogenesis of psoriasis and development of treatment. The Journal of dermatology, 45(3): 264-272.

Ogdie, A., Tillett, W., Booth, N., Howell, O., Schubert, A., Peterson, S. and Coates, L. C. 2022. Usage of C-reactive protein testing in the diagnosis and monitoring of psoriatic arthritis (PsA): results from a Real-World Survey in the USA and Europe. Rheumatology and therapy, 9(1): 285-293.

Ogdie, A., Tillett, W., Booth, N., Howell, O., Schubert, A., Peterson, S. and Coates, L. C. 2022. Usage of C-reactive protein testing in the diagnosis and monitoring of psoriatic arthritis (PsA): results from a Real-World Survey in the USA and Europe. Rheumatology and therapy, 9(1): 285-293.

Oikonomopoulou, Katerina, and V.C. 2018. Biomarkers of psoriatic arthritis outcomes. Oxford Textbooks In Rheumatology, 4: 22.

Ojaimi, S., Skinner, N. A., Strauss, B. J., Sundararajan, V., Woolley, I. and Visvanathan, K. 2013. Vitamin D deficiency impacts on expression of toll-like receptor-2 and cytokine profile: a pilot study. Journal of translational medicine, 11, 1-7.

Opinion, S. 2017. Dietary reference values for vitamin K. EFSA Journal, 15(5): e04780.

Organization., W.H. 2016. 'Global report on PSORIASIS. WHO, 2: 51.

ORIGENE, L. 2023. Cchcr1 Mouse qPCR Primer Pair (NM_146248). OriGene Technologies, 1: 6.

Ovcina-Kurtovic, N. and Kasumagic-Halilovic, E. 2022. Serum Levels of Tumor Necrosis Factor-alpha in Patients With Psoriasis. Materia Socio-medica, 34(1): 40.

Pariser, D., Schenkel, B., Carter, C., Farahi, K., Brown, T. M., Ellis, C. N. and Psoriasis Patient Interview Study Group. 2016. A multicenter, non-interventional study to evaluate patient-reported experiences of living with psoriasis. Journal of Dermatological Treatment, 27(1): 19-26.

Pastore, A., Piemonte, F., Locatelli, M., Lo Russo, A., Gaeta, L. M., Tozzi, G. and Federici, G. 2001. Determination of blood total, reduced, and oxidized glutathione in pediatric subjects. Clinical chemistry, 47(8): 1467-1469.

Patel, J. V., Abraheem, A., Dotsenko, O., Creamer, J., Gunning, M., Hughes, E. A. and Lip, G. Y. H. 2008. Circulating serum adiponectin levels in patients with coronary artery disease: relationship to atherosclerotic burden and cardiac function. Journal of Internal Medicine, 264(6): 593-598.

Pepys, M. B. and Hirschfield, G. M. 2003. C-reactive protein: a critical update. The Journal of clinical investigation, 111(12): 1805-1812.

Prussick, R., Prussick, L. and Gutman, J. 2013. Psoriasis improvement in patients using glutathione-enhancing, nondenatured whey protein isolate: a pilot study. The Journal of Clinical and Aesthetic Dermatology, 6(10): 23.

Punzi, L., Poswiadek, M., Oliviero, F., Lonigro, A., Modesti, V., Ramonda, R. and Todesco, S. 2007. Laboratory findings in psoriatic arthritis. Reumatismo, 59(s1): 52-55.

Radić, M., Đogaš, H., Kolak, E., Gelemanović, A., Nenadić, D. B., Vučković, M. and Radić, J. (2023, April). Vitamin D in psoriatic arthritis–a systematic review and meta-analysis. In Seminars in Arthritis and Rheumatism, pp. 152200, WB Saunders.

Ran, D., Cai, M. and Zhang, X. 2019. Genetics of psoriasis: a basis for precision medicine. Precision clinical medicine, 2(2): 120-130.

Ratini, M. 2022. Web site. https://www.webmd.com/arthritis/psoriatic-arthritis/vitamin-d-psoriatic-arthritis#:~:text=the%20research%20shows.-,Why%20Is%20Vitamin%20D%20Important%20for%20Psoriatic%20Arthritis%3F,the%20development%20of%20psoriatic%20arthritis. Date of access: 16.08.2023.

Reddi, K., Henderson, B., Meghji, S., Wilson, M., Poole, S., Hopper, C. and Hodges, S. J. 1995. Interleukin 6 production by lipopolysaccharide-stimulated human fibroblasts is potently inhibited by naphthoquinone (vitamin K) compounds. Cytokine, 7(3): 287-290.

Rendon, A. and Schäkel, K. 2019. Psoriasis pathogenesis and treatment. International journal of molecular sciences, 20(6): 1475.

Ritchlin, C. T., Colbert, R. A. and Gladman, D. D. 2017. Psoriatic arthritis. New England Journal of Medicine, 376(10): 957-970.

Rocha-Pereira, P., Santos-Silva, A., Rebelo, I., Figueiredo, A., Quintanilha, A. and Teixeira, F. 2004. Erythrocyte damage in mild and severe psoriasis. British Journal of Dermatology, 150(2): 232-244.

Rostami-Yazdi, M., Clement, B., Schmidt, T. J., Schinor, D. and Mrowietz, U. 2009. Detection of metabolites of fumaric acid esters in human urine: implications for their mode of action. The Journal of investigative dermatology, 129(1): 231-234.

Rotondo, C., Cantatore, F. P., Cici, D., Erroi, F., Sciacca, S., Rella, V. and Corrado, A. 2023. Vitamin D Status and Psoriatic Arthritis: Association with the Risk for Sacroiliitis and Influence on the Retention Rate of Methotrexate Monotherapy and First Biological Drug Survival—A Retrospective Study. International Journal of Molecular Sciences, 24(6): 5368.

Ruiyang, B., Panayi, A., Ruifang, W., Peng, Z. and Siqi, F. 2021. Adiponectin in psoriasis and its comorbidities: a review. Lipids in Health and Disease, 20(1): 1-11.

Sadeghi, K., Wessner, B., Laggner, U., Ploder, M., Tamandl, D., Friedl, J. and Spittler, A. 2006. Vitamin D3 down-regulates monocyte TLR expression and triggers hyporesponsiveness to pathogen-associated molecular patterns. European journal of immunology, 36(2): 361-370.

Saha, A. K., Schmidt, B. R., Wilhelmy, J., Nguyen, V., Do, J., Suja, V. C. and Davis, R. W. 2018. Erythrocyte deformability as a potential biomarker for chronic fatigue syndrome. Blood, 132: 4874.

Salgado-Boquete, L., Carrascosa, J. M., Llamas-Velasco, M., Ruiz-Villaverde, R., de la Cueva, P. and Belinchón, I. 2021. A new classification of the severity of psoriasis: what's moderate psoriasis?. Life, 11(7): 627.

Scherer, P. E., Williams, S., Fogliano, M., Baldini, G. and Lodish, H. F. 1995. A novel serum protein similar to C1q, produced exclusively in adipocytes. Journal of Biological chemistry, 270(45): 26746-26749.

Seifert, O., Holmberg, J. and Linnarsson, B. M. 2007. Decreased activity of neutrophil glutathione peroxidase in chronic plaque-type psoriasis. Journal of the American Academy of Dermatology, 57(3): 528-529.

Sharifi-Zarchi, A., Gerovska, D., Adachi, K., Totonchi, M., Pezeshk, H., Taft, R. J. and Araúzo-Bravo, M. J. 2017. DNA methylation regulates discrimination of enhancers from promoters through a H3K4me1-H3K4me3 seesaw mechanism. BMC genomics, 18: 1-21.

Shibata, S., Tada, Y., Hau, C. S., Mitsui, A., Kamata, M., Asano, Y. and Sato, S. 2015. Adiponectin regulates psoriasiform skin inflammation by suppressing IL-17 production from γδ-T cells. Nature communications, 6(1): 7687.

Simes, D. C., Viegas, C. S., Araújo, N. and Marreiros, C. 2020. Vitamin K as a diet supplement with impact in human health: current evidence in age-related diseases. Nutrients, 12(1): 138.

Sokolova, M. V., Simon, D., Nas, K., Zaiss, M. M., Luo, Y., Zhao, Y. and Schett, G. 2020. A set of serum markers detecting systemic inflammation in psoriatic skin, entheseal, and joint disease in the absence of C-reactive protein and its link to clinical disease manifestations. Arthritis research and therapy, 22: 1-8.

Sonagra, AD, D.S. 2022. Electrophoresis. Treasure Island (FL), 2: 54.

Stella Bard, M. 2021. Psoriatic arthritis and genetics. Sciences, 3: 77.

Stuart, P. E., Nair, R. P., Tsoi, L. C., Tejasvi, T., Das, S., Kang, H. M. and Elder, J. T. 2015. Genome-wide association analysis of psoriatic arthritis and cutaneous psoriasis reveals differences in their genetic architecture. The American Journal of Human Genetics, 97(6): 816-836.

Suh, J. H., Lee, Y., Ohn, J., Kim, E. J., Kim, T. G., Jo, S. J. and Chung, J. H. 2022. Adiponectin-derived pentapeptide ameliorates psoriasiform skin inflammation by suppressing IL-17 production in γδT cells. Journal of Dermatological Science, 106(1): 45-52.

Suleman, S., Chhabra, G., Raza, R., Hamid, A., Qureshi, J. A. and Ahmad, N. 2022. Association of CARD14 Single-Nucleotide Polymorphisms with Psoriasis. International Journal of Molecular Sciences, 23(16): 9336.

Szczerkowska-Dobosz, A., Krasowska, D., Bartosińska, J., Stawczyk-Macieja, M., Walczak, A., Owczarczyk-Saczonek, A. and Nedoszytko, B. 2020. Pathogenesis of psoriasis in the “omic” era. Part IV. Epidemiology, genetics, immunopathogenesis, clinical manifestation and treatment of psoriatic arthritis. Advances in Dermatology and Allergology/Postępy Dermatologii i Alergologii, 37(5): 625-634.

Tervaniemi, M. H., Siitonen, H. A., Söderhäll, C., Minhas, G., Vuola, J., Tiala, I. and Elomaa, O. 2012. Centrosomal localization of the psoriasis candidate gene product, CCHCR1, supports a role in cytoskeletal organization. PloS one, 7(11): e49920.

Tishkowski K, G. V. 2023. Erythrocyte Sedimentation Rate. Treasure Island (FL): StatPearls Publishing, 4: 5.

Tiwari, B.L. 2023. Web site. https://www.ncbi.nlm.nih.gov/books/NBK547710. Date of access: 15.09.2023.

Tripolino, C., Ciaffi, J., Ruscitti, P., Giacomelli, R., Meliconi, R. and Ursini, F. 2021. Hyperuricemia in psoriatic arthritis: epidemiology, pathophysiology, and clinical implications. Frontiers in Medicine, 8: 737573.

Usedom, E. 2022. Fat soluble vitamins to improve psoriasis. Psoriasis, 3: 66.

Usedom, E., Neidig, L. and Allen, H. B. 2017. Psoriasis and Fat-soluble Vitamins: A Review. J Clin Exp Dermatol Res, 8(05): 1-6.

Vadakayil, A. R., Dandekeri, S., Kambil, S. M. and Ali, N. M. 2015. Role of C-reactive protein as a marker of disease severity and cardiovascular risk in patients with psoriasis. Indian dermatology online journal, 6(5): 322.

Watson, S. 2022. Tests to Diagnose and Track Psoriatic Arthritis.

WICK, R. 2015. ST AIA-PACK 25-OH Vitamin D, ST AIA-PACK 25-OH Vitamin D Calibrator Set. Public Health Service, 6: 88.

Widawski, L., Fabacher, T., Spielmann, L., Gottenberg, J. E., Sibilia, J., Duret, P. M. and Felten, R. 2022. Psoriatic arthritis with hyperuricemia: more peripheral, destructive, and challenging to treat. Clinical Rheumatology, 41(5): 1421-1429.

Wielders, J. P. 2013. What are the needs for measuring vitamin D? Does the new TOSOH method fulfill the requirements?. Clinical Biochemistry, 12(46): 1147.

Williams, L. A. 2019. The History, Symptoms, Causes, Risk Factors, Types, Diagnosis, Treatments, and Prevention of Gout, Part 2. International Journal of Pharmaceutical Compounding, 23(1): 14-21.

Winchester, Robert, Darren D. and O'Rielly, P.R. 2018. Genetics of psoriatic arthritis. Oxford Textbooks In Rheumatology, 7: 80.

Woolf, L. 2013. Peace Psychology. The Encyclopedia of Cross-Cultural Psychology, 3, 983-985.

Wozniak A, Drewa G, K.-M.E. 2007. Oxidant-antioxidant balance in patients with psoriasis', Med Sci Monit, 13(1): 30–33.

Yakupova, S. P. 2018. Gout. New opportunities of diagnosis and treatment. Terapevticheskii arkhiv, 90(5): 88-92.

Yan, H., Yu, B., Tian, J., Xia, D., Xu, Y. and Li, C. 2022. Serum leptin and adiponectin: Indicators of cardiovascular disease secondary to psoriasis. Indian Journal of Dermatology, 67(2): 109.

Yang, X. M., Liang, J. P., Huang, X. J., Wang, X. R., Sun, Y., Dong, C. and Hui, W. L. 2021. A Novel PCR Method for Detecting ACE Gene Insertion/Deletion Polymorphisms and its Clinical Application. Biological Procedures Online, 23(1): 1-10.

Yap, L. P., Sancheti, H., Ybanez, M. D., Garcia, J., Cadenas, E. and Han, D. 2010. Determination of GSH, GSSG, and GSNO using HPLC with electrochemical detection. Methods in enzymology, 473, 137-147.

Yildirim, M., Inaloz, H. S., Baysal, V. and Delibas, N. 2003. The role of oxidants and antioxidants in psoriasis. Journal of the European Academy of Dermatology and Venereology, 17(1): 34-36.

Ying, Z., Wang, K., Wu, J., Wang, M., Yang, J., Wang, X. and Sha, O. 2022. CCHCR1-astrin interaction promotes centriole duplication through recruitment of CEP72. BMC biology, 20(1): 1-21.

Yoda-Murakami, M., Taniguchi, M., Takahashi, K., Kawamata, S., Saito, K., Choi-Miura, N. H. and Tomita, M. 2001. Change in expression of GBP28/adiponectin in carbon tetrachloride-administrated mouse liver. Biochemical and biophysical research communications, 285(2): 372-377.

Yu, H. and Berkel, H. 1999. Prostate-specific antigen (PSA) in women. The Journal of the Louisiana State Medical Society: official organ of the Louisiana State Medical Society, 151(4): 209-213.

Zaid, F. E. 2021. Clinical Patterns of Psoriatic Arthritis and the Relationship between Pso-riasis Skin Severity and Joint Activity in Libya. J Rheum Dis Treat, 7, 089.

Zhang, G., Fenyö, D. and Neubert, T. A. 2008. Use of DNA Ladders for Reproducible Protein Fractionation by Sodium Dodecyl Sulfate− Polyacrylamide Gel Electrophoresis (SDS− PAGE) for Quantitative Proteomics. Journal of Proteome Research, 7(2): 678-686.

Zhang, M., Miura, T., Suzuki, S., Chiyotanda, M., Tanaka, S., Sugiyama, K. and Hirano, T. 2021. Vitamin K2 suppresses proliferation and inflammatory cytokine production in mitogen-activated lymphocytes of atopic dermatitis patients through

the inhibition of mitogen-activated protein kinases. Biological and Pharmaceutical Bulletin, 44(1): 7-17.

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