"CROSS-SECTIONAL STUDY OF LIVER FIBROSIS IN PSORIATIC PATIENTS USING ULTRASOUND SHEAR WAVE ELASTOGRAPHY"

By

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DISSERTATION SUBMITTED TO

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DERMATOLOGY, VENEREOLOGY AND LEPROSY

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ABSTRACT

INTRODUCTION:

Chronic inflammatory papulosquamous psoriasis is characterised by remissions and relapses on several occasions. Psoriasis has been linked to several metabolic comorbidities, including a higher risk of diabetes and cardiovascular problems, obesity, abnormalities in "liver function tests," and liver disease. Newer recommendations place a strong emphasis on non-invasive techniques like "Shear wave Ultrasound elastography" as the initial method of assessing "liver fibrosis". This study is being conducted because further research is needed to demonstrate the use of "Shear wave Ultrasound hepatic elastography" for the diagnosis of "liver fibrosis" in patients with psoriasis due to the dearth of literature in this area.

MATERIALS AND METHODS:

SAMPLING TECHNIQUE:

OPD estimates 7 cases per month amounting for 126 cases for one and half years and required sample size being 60, considering sample interval of 2, these 60 cases will be recruited by systematic random sampling technique.

After acquiring all patients' willing written informed consent for participation in the trial, data will be gathered. Every case will have a thorough history taken, along with any linked diseases' histories. Shear wave ultrasound elastography will be used to identify "liver fibrosis."

hepatic fibrosis measurement by shear wave elastography. The Philips EPIQ5 system, which has a shear wave point quantification feature employing a curvilinear broadband transducer, will be used for all "Ultrasound" examinations (C5 - 1).

Using radiation force from a concentrated ultrasound beam, this method creates shear waves inside the tissue. The speed of shear-wave propagation is measured by the ultrasound machine using a "Doppler-like

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LIST OF ABBREVIATIONS

SL NO	ABBREVATIONS	FULL FORMS
1.	OPD	Out Patient Department
2.	YM	Young's Modulus
3.	kPa	Kilo Pascal
4.	2D-SWE	2 dimensional Shear wave elastography
5.	ICD 10	International Classification of Disease 10th Revision
6.	WHO	World Health Organisation
7.	UK	United Kingdom
8.	USA	United States of America
9.	HLA-Cw	Human Leucocyte Antigen C Working Group
10.	Tc	Cytotoxic T cell
11.	GWAS	Genome Wide Association
12.	SNP	Single nucleotide polymorphism
13.	EDC	Epidermal Differentiation Complex
14.	NF-kB	Nuclear Factor Kappa-Light-Chain-Enhancer of activated B cells
15.	TNF-α	Tumour Necrosis Factor Alpha
16.	INF	Interferon
17.	IL	Interleukin
18.	HIV	Human Immuno Deficiency Virus

Sl.No	ABBREVATIONS	FULL FORMS
19.	ACE	Angiotensin Converting Enzyme
20.	pDC	Plasmacytoid Dendritic Cell
21.	DNA	Diribo Nucleic Acid
22.	ADAMTS	A Disintegrin and Metalloproteinase with Thrombospondin Motifs
23.	mDC	Myeloid Dendritic Cell
24.	NK	Natural Killer cells
25.	JAK-STAT	Janus Kinases - Signal Transducer and Activator of Transcription Protein
26.	PDE	Phosphodiesterase
27.	cAMP	Cyclic Adenosine Mono Phosphate
28.	AMP	Adenosine Mono Phosphate
29.	APC	Antigen Presenting Cell
30.	DC	Dendritic Cell
31.	LC	Langerhans Cell
32.	Breg	Regulatory B cells
33.	Mϕ	Macrophage
34.	NGF	Nerve Growth Factor
35.	TRM	Resident Memory T cells
36.	RNA	Ribs Nucleic Acid
37.	UV	Ultra Violet

Sl.No	ABBREVATIONS	FULL FORMS
38.	BCG	Bacillus of Calmette and Guerin
39.	BMI	Body Mass Index
40.	DM	Diabetes Mellitus
41.	HDL	High Density Lipoprotein
42.	DLQI	Dermatology Life Quality Index
43.	PsA	Psoriatic Arthritis
44.	PEST	Psoriasis Epidemiology Screening Tool
45.	PPP	Psoriasis Pustulosa Palmoplantaris
46.	CVD	Cardio Vascular Disease
47.	HF	Heart Failure
48.	AF	Atrial Fibrillation
49.	MI	Myocardial Infarction
50.	VHD	Valvular Heart Disease
51.	CNS	Central Nervous System
52.	CRP	C-Reactive Protein
53.	AS	Ankylosing Spondylitis
54.	RA	Rheumatoid Arthritis
55.	SLE	Systemic Lupus Erythematosus
56.	SSc	Systemic Sclerosis

Sl.No	ABBREVATIONS	FULL FORMS
57.	DM/PM	Dermatomyositis/Polymyositis
58.	BP	Bullous Pemphigoid
59.	MetS	Metabolic Syndrome
60.	NCEP	National Cholesterol Education Program
61.	ATP III	Adult Treatment Panel III
62.	VEGF	Vascular Endothelial Growth Factor
63.	CD	Cluster of Differentiation
64.	K	Keratin
65.	H&E	Haematoxylin and Eosin
66.	S100	Saturated Amino Sulphate 100
67.	ELISA	Enzyme Linked Immunosorbent Assay
68.	MTX	Methotrexate
69.	LFT	Liver Function Test
70.	PIIINP	Amino Terminal Propeptide Type 3 Collagen
71.	MRI	Magnetic Resonance Imaging
72.	HMRS	Proton Magnetic Resonance Spectroscopy
73.	FDA	Food and Drug Administration
74.	PUVA	Psoralen plus Ultraviolet-A
75.	PASI	Psoriasis Area and Severity Index

SL NO	ABBREVATIONS	FULL FORMS
76.	TKY	Tyrosine Kinase
77.	USE	Ultrasound Shear Wave Elastography
78.	SWI	Shear Wave Imaging
79.	TE	Transient Elastography
80.	ASQ	Acoustic Structure Quantification ™
81.	VTIQ	Virtual Touch ™ Quantification
82.	SSI	Super Sonic Imaging
83.	CLD	Chronic Liver Disease
84.	PH	Portal Hypertension
85.	WFUMB	World Federation for Ultrasound in Medicine and Biology
86.	SD	Standard Deviation

ABSTRACT

INTRODUCTION:

Psoriasis is a chronic inflammatory papulosquamous disease characterized by multiple remissions and relapses. Psoriasis has been associated with a number of metabolic comorbidities, in particular an increased incidence of diabetes and cardiovascular events, obesity, liver function test abnormalities and liver disease. Newer guidelines emphasize on non-invasive modalities such as Shear wave Ultrasound elastography as the first line of assessment for liver fibrosis. Due to paucity of literature in this aspect more studies are required to prove the use of Shear wave Ultrasound liver elastography for the detection of liver fibrosis in patients with psoriasis, hence this study is undertaken.

MATERIALS AND METHODS:

SAMPLING TECHNIQUE:

OPD estimates 7 cases per month accounting for 126 cases for one and half years and required sample size being 60, considering sample interval of 2, these 60 cases will be recruited by systematic random sampling technique.

Data will be collected after obtaining written informed consent from all patients who are willing to participate in the study. In every case detailed history and history of associated diseases will be noted down. Detection of liver fibrosis will be made by shear wave ultrasound elastography.

Quantification of liver fibrosis by shear wave elastography. All Ultrasound examinations will be performed using Philips EPIQ5 system equipped with shear wave point quantification using curvilinear broadband transducer (C5 - 1)

This technique generates shear waves inside the tissue using radiation force from a focused ultrasound

beam. The ultrasound machine, monitoring the shear-wave propagation using a Doppler-like ultrasound technique, measures the speed of propagation, which is then used to compute tissue stiffness, also known as the Young modulus (YM) of elasticity, in kilopascals (kPa).

Liver stiffness: F1: 6.48–6.60 kPa, F2: 6.60–8.07 kPa, F3: 8.07–9.31 kPa, and F4: >9.31 kPa.

SWE will be performed by one sonographer. Each SWE acquisition comprises 10 sequential measurements of the liver which are obtained at a depth of 8cm from the skin surface. Patients will not sedate. Informed consent will be taken from the patients and this study will be conducted after Institution Ethical Committee clearance. Relevant laboratory investigations will be done. ICD 10 diagnostic criteria will be used to exclude alcohol dependent patients .The data thus collected will be entered in to a specially designed Case Record Form and subjected to statistical analysis like proportion and Chi-square test.

RESULTS:

In our study Out of 60 study participants, 24(40%) were female and remaining (60%) were males. The mean age of the study participants was 40.63 with standard deviation of 13.802 years. The minimum age being 12 and maximum being 75 years. It is observed that 14(23.3%) belongs to age 1 to 29 years,18(30%) belongs to age 30 to 39 years, 12(20%) belongs to age group 40 to 49 years, 9(15%) belongs to age group 50 to 59 years and remaining belongs to age more than 60 years. Most (71.1%) had Chronic Plaque Psoriasis followed by Palmo-Plantar Psoriasis (13.3%), Pustular Psoriasis (6.7%) Scalp Psoriasis and Psoriatic Arthritis (5%) each. 1.7% each had Guttate Psoriasis and Nail Psoriasis. Out of total, 11.7% had hypertension, 6.7% each had Diabetes Mellitus and Obesity. It is observed that none were underweight. Most (65%) were overweight followed by normal (28.3) and obese (6%). At baseline, 46.7% had ultrasound shear wave elastography ranging between 1 to 5kp and remaining above 6kp (53.3%). At 6 months, 45% had ultrasound shear wave elastography ranging between 1 to 5kp and remaining above 6kp

(55%). The study revealed that there is a moderate positive correlation between ultrasound shear wave elastography scores at baseline and Non-alcoholic fatty liver disease score (r=0.551, p value =0.0001). Further, The study revealed that there is a slight positive correlation between BMI and Non-alcoholic fatty liver disease score (r=0.269, p value =0.049).

CONCLUSION:

The study suggests that Ultrasound Shear Wave Elastography and Non-alcoholic fatty liver disease score (NAFLDs) are both reliable methods to asses liver fibrosis.

Hence Ultrasound Shear Wave Elastography can be used as an ideal non-invasive technique as that compared to invasive liver biopsy in assessment and monitoring of liver fibrosis in psoriatic patients as a routine investigation.

Thus early can aid in the early detection of liver damage in patients and help in the formulation of treatment and care in these patients.

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INTRODUCTION

INTRODUCTION

Psoriasis is a chronic, immune-mediated, recurrent, inflammatory skin disease that is characterized by the clinical appearance of sharply demarcated, erythematous papules or plaques covered with silvery-white scales. Psoriasis is, one of the most common inflammatory skin disease, whose incidence has been slightly increasing in the past thirty years. Psoriasis affects about 2–4% of the world's population. It affects both sexes equally, while Psoriasis is seen mainly in adults and most often occurs in two age groups, between 2^{nd} decade and 3^{rd} decade and 5^{th} decade and 6^{th} decade.

In the past**,** it was considered to affect only the skin, now, it is commonly believed as a systemic disease of inflammation. Systemic inflammation is caused by the "psoriatic march", which is due to the increase in proinflammatory cytokines not only in psoriatic skin but in patients' circulation as well. It aids in the evolution of concomitant diseases, where 73% of patients, especially those with severe psoriasis, have one comorbidity at least.

The most common of these are psoriatic arthritis and Crohn's disease, which share the same pathological and genetic component with psoriasis. There is also an increased risk of metabolic syndrome, nonalcoholic-fatty liver disease, cardiovascular illness, respiratory disorders, and autoimmune conditions, such as Hashimoto's thyroiditis, autoimmune hepatitis, multiple sclerosis, malignancies like T-cell skin lymphoma, and psychological disorders, primarily anxiety and depression. Grave disease prognosis has shown to increase overall mortality and reduce life expectancy more so in women than in men by 4.4 years and 3.5 years respectively, compared with population who do not suffer from psoriasis. The causes of death in patients suffering from psoriasis is accounted to cardiovascular incidents brought about by infections, malignancies, diseases of the hepato-biliary, renal, respiratory, and digestive system. In recent times it is understood that psoriasis is a disease caused by multiple factors with interaction of the genetic and the environmental components. [1]

Elastography is a tissue elasticity imaging technique, which enables non-invasive evaluation of hepatic fibrosis. Two-dimensional shear wave elastography (2D-SWE) is an imaging technique that has proven to be an efficient and reproducible non-invasive technique for the detection and staging of hepatic fibrosis. Obesity and elevated waist circumference were associated with unreliable results owing to the poor transmission of the ultrasonic beams. However, one of the advantages of this technique is that it can be performed during a routine ultrasound examination; therefore, 2D-SWE is the only non-invasive imaging modality that is practically available in daily clinical practice. [2]

AIMS & OBJECTIVES

OBJECTIVES

AIMS AND OBJECTIVES OF THE STUDY:

1. To assess the utility of shear wave ultrasound elastography in detecting liver fibrosis in patients with psoriasis.

2. To correlate shear wave ultrasound elastography findings with Non-alcoholic fatty liver disease score in patients with psoriasis.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

EPIDEMIOLOGY

WHO (World Health Organization), estimates that about 0.09–11.43% of the global population suffer from psoriasis and the case load varies from 1.50% to 5.00% in developed countries. [3]

Psoriasis affects both the genders equally, with females being first to show symptoms and in individuals with family history. Its seen that the peak age of onset in patients is divided into two age groups namely in men 30–39 years and 60–69 years, and 10 years sooner in women.[4] Almost 75% of cases begin before the age of 40.[5]

An estimated 60 million people have psoriasis worldwide, with country-specific prevalence varying between 0.05% of general population in Taiwan and 1.88% in Australia. It is more common in high income areas and those with older populations. In the UK, it affects 1.52% of the general population.[4] The overall incidence in india ranges from 0.44% to 2,2% with an overall prevalence of 1.02% [6]

Psoriasis is seen more among the developed countries about 4.6% in Canada and the USA than that of 0.4% – 0.7% low income nations of African and Asian region .[5]

PATHOGENESIS

GENETIC FACTORS IN THE DEVELOPMENT OF PSORIASIS

Psoriasis, has a polygenic model of inheritance. Research into the families affected by psoriasis has revealed areas on the chromosome related to the onset of the condition, called PSORS (from the psoriasis susceptibility locus). 12 areas are identified till date, the most important being PSORS1 region, accountable for 35–50% of inherited psoriatic cases. It also contains the first gene accountable for psoriasis, HLA-Cw6 (from human leukocyte antigen C), has been seen in 10.5–77.2% of cases and which plays an important part in regulation of cytotoxic T-cells' (Tc) function and antigen presentation. Based on HLA type, psoriasis is classified into two.[1]

Type I: Seen in 65% of patients, as having HLA-Cw6, are at a higher risk of having early onset and severe course of the disease of about 9–23-fold, while history of psoriasis is positive among other family members.

Type II: Seen in patients past 4th decade of life, in whom HLA-Cw6 allele is not present, and has a much lenient course clinically.

Many PSORS-region genes are yet to be found, research into genome-wide association (GWAS) have been done in recent years. New researches into the single nucleotide polymorphisms (SNPs), have found excess of 50 additional areas with potential of developing the disease. With changes in one base increase the risk of psoriasis, the combined action of multiple factors allows the formation of the disease. Notably, only a few of the identified genes code for the skin proteins, like epidermal differentiation complex (EDC), while most genes code for proteins with functions in the innate & adaptive immune system, as well as tumor necrosis factor-alpha (TNF-α), nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), interferon type I (IFN-I), interleukin (IL)-12 and 23, and those involved in the development and polarization of helper T17 lymphocytes (Th17) and cytotoxic T17 lymphocytes (Tc17).[7]

ENVIRONMENTAL FACTORS IN THE DEVELOPMENT OF PSORIASIS

Environmental stimuli such as infections, can initiate the onset or worsen the course of psoriasis. Streptococcal infection can cause guttate and chronic stationary psoriasis, while type I HIV contributes to the increase in severity of psoriasis. The disease course is influenced by presence of Metabolic and hormonal irregularities, for example, hypocalcemia can lead to the formation pustular psoriasis and herpetiform impetigo, while hormonal changes during pregnancy improves psoriasis in 40–50% of individuals and worsens in about half of the women after child birth. Drugs such as lithium, beta-blockers, angiotensin-converting enzyme (ACE) inhibitors, interferons, nonsteroidal antirheumatic drugs, and antimalarials may cause the outset or cause the aggravation of pre-existing disease, just as abrupt stoppage of systemic corticosteroids may exacerbate plaque or pustular psoriasis. To make matters worse smoking and obesity lead to the development of psoriasis, while the preexisting disease is aggravated by consumption of alcohol.[5]

In about $1/4^{th}$ of patients, physical injury aids in the development of new psoriatic lesions on previously unaffected skin, known as the Köebner phenomenon. It is seen commonly in the active phase of psoriasis and with increase in severity of the condition and seen in injuries brought on by surgeries, tattooing, injections, arthropod bites, burns, X-rays, and use of irritants. But its seen ultraviolet radiation ususally contributes to the improvement of psoriasis clinically, however in few patients, strong sunlight can aid in the onset of photosensitive psoriasis. Psychosocial stress is documented to be a trigger, which has the ability to bring about or worsen an existing illness.[1]

IMMUNOPATHOGENESIS OF PSORIASIS

It is divided into the initiation phase and the maintenance phase. The proinflammatory cytokine cascade is activated by plasmacytoid dendritic cells (pDC) excitation by complexes of DNA and the antimicrobial peptide cathelicidin (LL-37), which is emitted by injured keratinocytes. In addition, damaged melanocytes can produce ADAMTS-like protein 5, the other viable autoantigen in psoriasis. In response to the stimulus, pDCs secrete IFN-α, a key cytokine of the initiation phase. It sets off local myeloid dendritic cells (mDCs) and activates their movement to lymph nodes. Other innate immune cells, i.e., keratinocytes, macrophages, and NKT cells, also contribute to mDCs activation by producing INF-γ, TNF-α, IL-1-β, and IL-6. Excited mDCs then secrete TNF-α, IL-12, and IL-23, which brings about differentiation and proliferation of naïve T lymphocytes into mature T1 (Th1 and Tc1), T17 (Th17 and Tc17), and T22 (Th22 and Tc22) lymphocytes, which acquire the ability to populate the skin via bloodstream. Activated T1 lymphocytes produce IFN-γ and TNF-α, while T17 lymphocytes produce the central executive proinflammatory cytokine IL-17A, which is also secreted by γδ T lymphocytes, NK cells, mastocytes, and innate lymphoid cells (ILCs). The IL-23/Th17 axis produces cytokines IL-22 and IL-17A/F, which cause proliferation and damaged differentiation of keratinocytes, producing a characteristic psoriatic phenotype. Keratinocytes are not just bystanders they secrete antimicrobial peptides, cytokines, and chemokines, in response to stimuli, which in turn leads to activation of T lymphocytes and movement of other inflammatory cells, fundamentally macrophages, dendritic cells, and neutrophils, hence leading the formation of chronic inflammation, i.e., phase of disease maintenance. Angiogenesis brought out by the inflammatory cascade contributes to the additional movement of immune cells into the psoriatic lesion. Eventually, the cytokines' effect is reached by switching on the intracellular pathways, thus stimulating the transcription of important messenger genes. Thus INF-γ, IL-12, IL-22, and IL-23 activate the JAK-STAT (Janus Kinases—Signal Transducer and Activator of Transcription proteins) pathway, whereas phosphodiesterase-4 (PDE-4) suppresses the anti-inflammatory action of cAMP.[8]

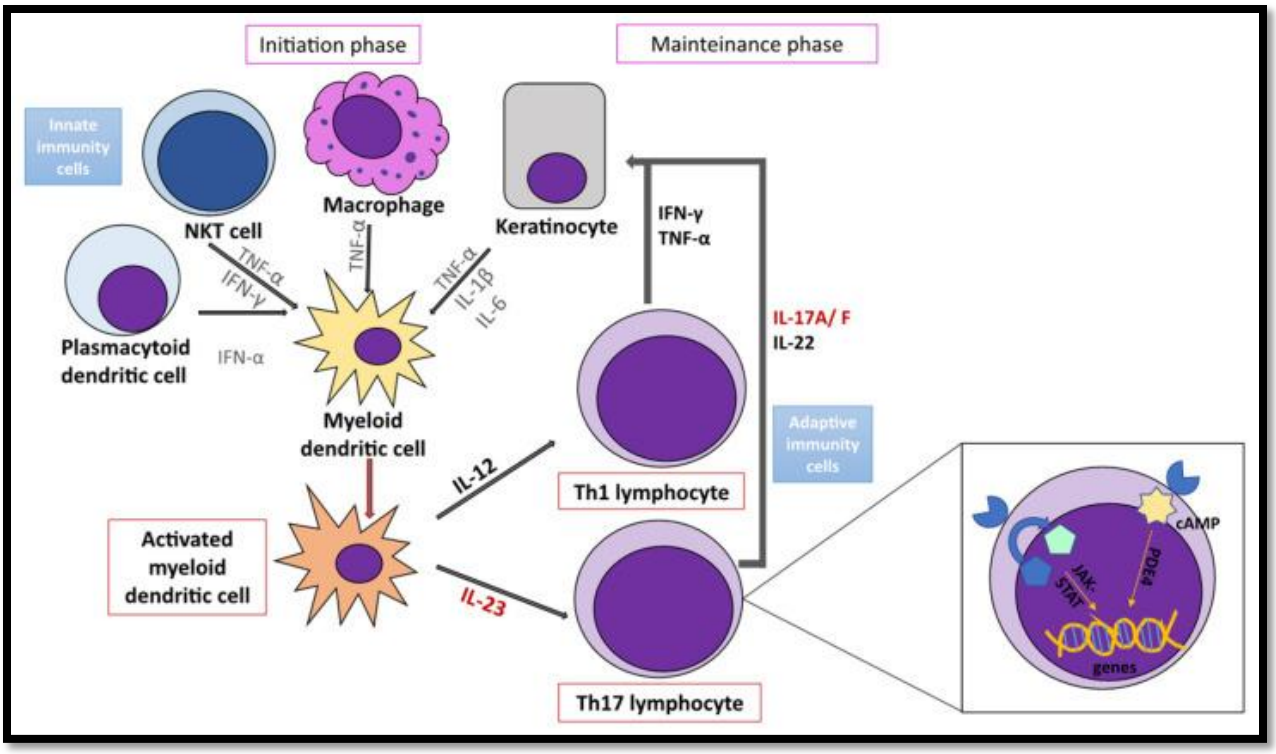


Figure 1. THE PATHOGENESIS OF PSORIASIS

Important cells and signaling pathways in the immunopathogenesis of psoriasis. Which involves a complex inflammatory cascade, initially triggered by innate immune cells (keratinocytes, dendritic cells, NKT cells, macrophages) simultaneously, progression and maintenance of the disease is through interaction with adaptive immune cells (T lymphocytes). The main mechanism of the disease is the IL-23/Th17 axis, whose executive cytokines IL-22 and IL-17A/F lead to proliferation of keratinocyte, synthesis of proinflammatory cytokines, chemokines and AMP, and the initiation of a positive feedback loop, which maintains the inflammatory process. Cytokines in cells activate signaling and transcription pathways (cAMP, JAK-STAT), which achieve increased transcription of messenger genes and cytokines involved in the pathogenesis.

Adapted from[1]

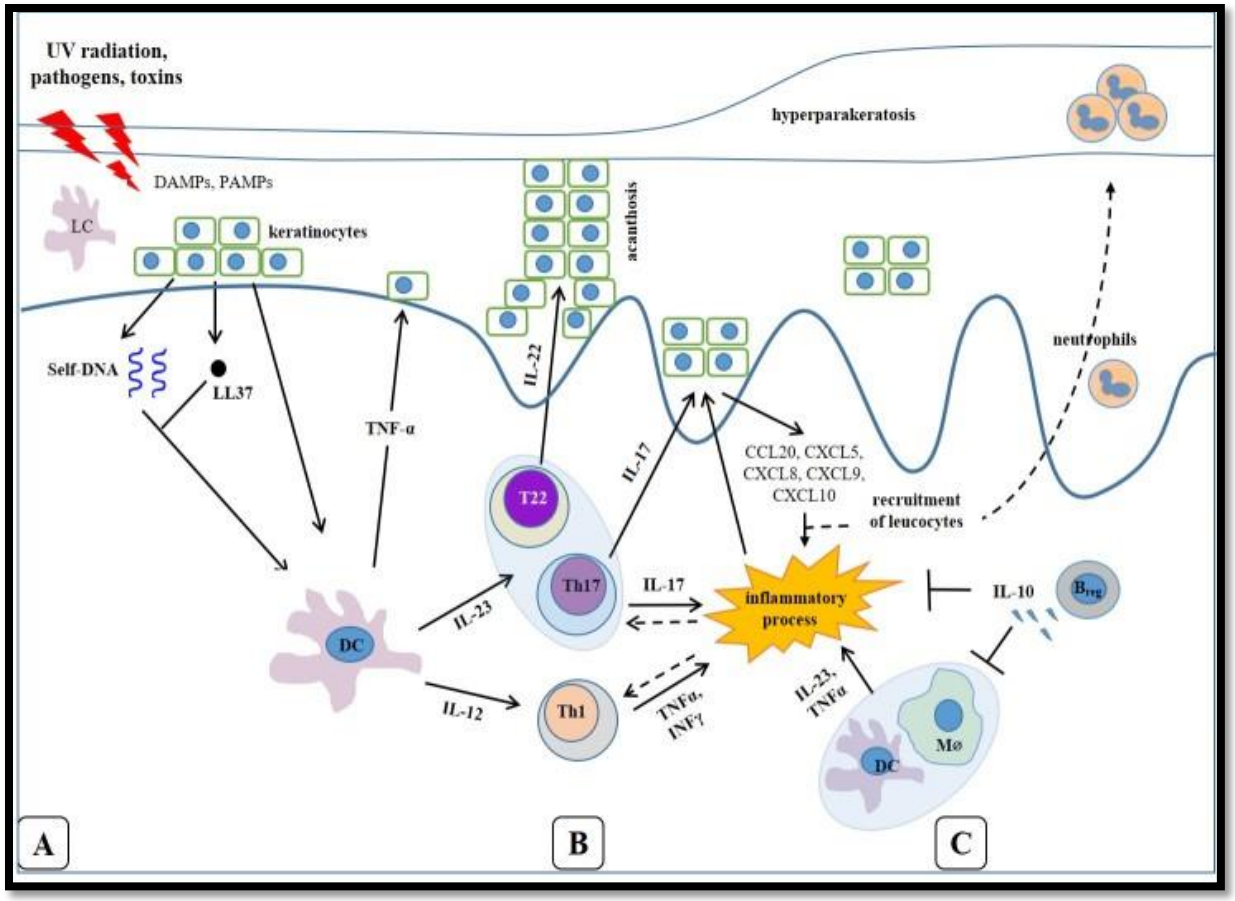


Figure 2 THE PATHOGENESIS OF PSORIASIS.

A) Damaged keratinocytes during exposure to microbial or mechanical injury foster activation of antigen-presenting cells (APC) such as macrophages and dermal dendritic cells (DC).

B) APCs including Langerhans cells (LC), DCs and potentially B cells interact with T cells leading to their activation and pro-inflammatory cytokine production.

C) Regulatory B cells (B_{reg}) may modulate inflammation. B_{reg} secrete IL-10 that interferes with activation of other leukocytes including macrophages (MØ) and T cells to counteract inflammation

Adapted from[9]

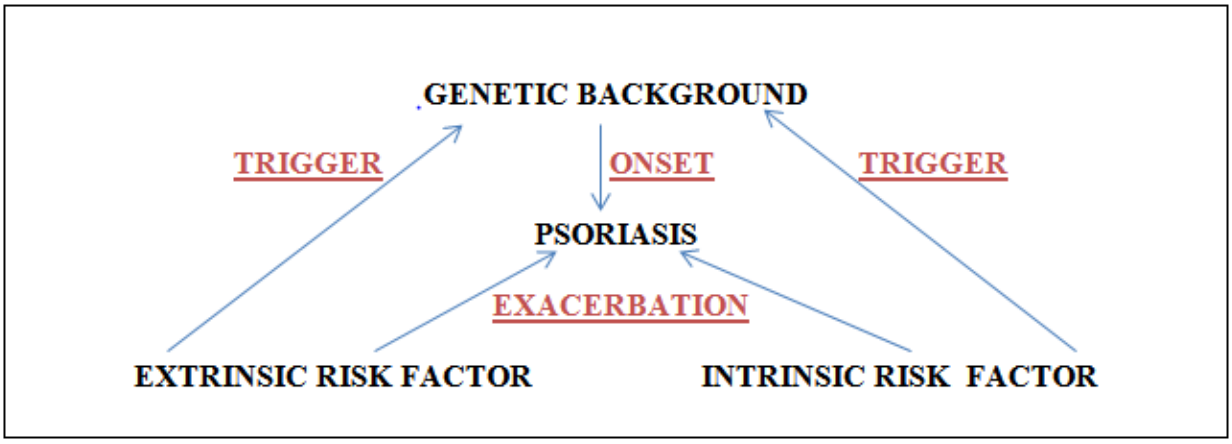
RISK FACTORS FOR THE DEVELOPMENT OF PSORIASIS

RISK FACTORS FOR THE DEVELOPMENT OF PSORIASIS

The risk factors for the onset and exacerbation of psoriasis is divided into two the Extrinsic and the intrinsic factors which are also associated with the onset and exacerbation of the condition[10]

Table. No: 1: EXTRINSIC RISK FACTOR AND INTRINSIC RISK FACTOR

EXTRINSIC RISK FACTOR	INTRINSIC RISK FACTOR
MECHANICAL STRESS	METABOLIC SYNDROME
AIR POLLUTION	OBESITY
DRUGS	DIABETES MELLITUS
VACCINATION	DYSLIPIDEMIA
INFECTION	HYPERTENSION
SMOKING, ALCOHOL	MENTAL STRESS



Adapted from[10]

EXTRINSIC RISK FACTORS

1. MECHANICAL STRESS

In Psoriatic patients, lesions appear on uninvolved skin after different forms of injuries; this is defined as Koebner phenomenon. Surgeries, tattooing, burns, intramuscular injections and even a mild skin irritation are known to bring about new lesions. Although this is true, psoriatic lesions do not always develop over unaffected skin after injury. Appropriate circumstances are required for the development of Koebner phenomenon such as dermal trauma with epidermal involvement. A clear mechanisms for the development of Koebner phenomenon is unknown. Nerve growth factor (NGF) a neurotrophic factor which seen in both the nervous system and peripheral organs is found to be associated with the Koebner phenomenon. Following a cutaneous injury, keratinocyte proliferation and up-regulation of NGF in basal keratinocytes is the earliest event which occurs before epidermotropism of T lymphocytes. In addition, NGF is found to be produced by the psoriatic keratinocytes which is in excess and functionally active. Resident memory T cells (TRM) are non-circulating memory T cell subset that persists in the peripheral tissues after resolution of psoriatic lesions; since TRM-mediated autoimmunity is seen in psoriasis it might play a role in formation of new psoriatic lesions following trauma. It is seen that psoriatic lesions can be brought about and sustained by skin-resident pathogenic T cells in the unaffected skin of psoriasis patients. Type 1 interferons (IFNs), such as IFN-α from dermal plasmacytoid dendritic cells and IFN-β from keratinocytes, play an important role in the onset of psoriasis following injury. Host antimicrobial peptide LL37 potentiates double-stranded RNA immune pathways and single-stranded RNA or DNA pathways in plasmacytoid dendritic cells.[10]

2. AIR POLLUTANTS AND SUN EXPOSURE

Air pollutants include polycyclic aromatic hydrocarbons, volatile organic compounds, oxides, particulate matter, ozone, heavy metals, and UV damage the skin by causing oxidative stress over time, which has had significant consequences on human skin. One of the air contaminants that has an impact on the pathogenesis of psoriasis is cadmium. Blood cadmium levels were greater in patients with severe psoriasis than in the general population. According to this study, cadmium exposure in the environment may impair immunity, and little environmental changes may increase the risk of psoriasis flare-ups. In the past several decades, phototherapy has been widely used to treat psoriasis. Currently, psoriasis is treated with narrowband UVB (311 nm) and excimer laser (308 nm), with psoralen UVA (PUVA) being utilised as a second-line therapy with preference for recalcitrant psoriatic plaques. One subgroup of patients with extremely photosensitive psoriasis has a disease that is primarily photodistributed and gets worse in the summer. Patients with photosensitive psoriasis in this study displayed a notable female preponderance, a very low mean age of onset, familial history of the condition, a strong correlation with HLA-Cw*0602, and a rapid aberrant clinical reaction to broadband UVA, consisting of erythema and/or scaling plaques. Histopathological research was used to identify a subpopulation of psoriasis that is phenotypically unique. After UV exposure, psoriasis might appear in a certain population.[10]

3. DRUGS

The emergence and worsening of psoriasis linked to specific medicines is known as drug-related psoriasis. In clinical settings, it might be challenging to pinpoint drug-related causes of psoriasis. This is due to the fact that there might be significant drug-to-drug variations in the latency period between the start of the therapy and the appearance of psoriatic skin lesions. Even after the suspected medicine has been stopped using, the psoriasis flare may occasionally linger. Additionally, the clinical and histological results of psoriasis and drug-related psoriasis may not differ much. Plaque psoriasis, palmoplantar psoriasis, nail

psoriasis, scalp psoriasis, pustular psoriasis, and erythrodermic psoriasis are all seen in drug-related psoriasis. Ingesting a drug may cause pre-existing psoriasis to worsen, induce psoriatic lesions on clinically unaffected skin in psoriasis patients, or precipitate the illness in patients without a family history of psoriasis as well as in those who are prone to it. -blockers, lithium, anti-malarial medications, interferons, imiquimod, angiotensin-converting enzyme inhibitors, terbinafine, tetracycline, nonsteroidal anti-inflammatory drugs, and fibrate medications are the drugs that are most commonly accepted. The molecular underpinnings underlying drug-related psoriasis are complex, and the mechanisms are still not completely understood. However, keratinocyte hyperproliferation and the IL-23/IL-17 axis have been linked to various medications. A-blockers cause a decrease in intraepidermal cAMP, which results in keratinocyte hyperproliferation. Cyclic adenosine monophosphate (cAMP) is an intracellular messenger that is responsible for the stimulation of proteins for cellular differentiation and control of proliferation. The most extensively used psoriasis animal model is skin inflammation brought on by imiquimod. Imiquimod, a toll-like receptor-7/8 activator, can cause and aggravate psoriasis, and it is highly dependent on the IL-23/IL-17 axis. Immune check point inhibitors and molecular inhibitors, which are now used to treat cancer and autoimmune disorders, may have an adverse effect on the immune system and cause the onset of psoriasis. Although biologicals are used in the treatment of psoriasis they can also cause psoriasis, and this is known as a paradoxical reaction. While tumour necrosis factor (TNF) inhibitors have been linked to the majority of paradoxical events, additional biologics that target interleukin (IL)-23 and IL-17 are becoming more and more popular. Immune signalling pathways are blocked by biologics that target TNF-, IL-23, and IL-17, which might result in an imbalance of cytokines. According to current theories, paradoxical reactions result from an imbalance in cytokine production, which includes an excess of IFN- and altered cell recruitment and migration. Patients with suspected drug-related psoriasis should stop taking their suspected medications and switch to an alternative.[11]

4. VACCINATION

Psoriasis patients are more likely to contract an infection, primarily as a result of their immunosuppressive or immunomodulatory medication regimen. Therefore, immunisation is advised to stop particular illnesses. However, immunisation frequently causes and worsens psoriasis. The correlation between influenza vaccination and psoriasis flare-up is supported by a number of studies. The influenza vaccine may potentially cause psoriasis to develop. The live attenuated strain of Mycobacterium bovis known as the Bacillus Calmette-Guerin (BCG) vaccination is largely used to prevent tuberculosis. After receiving the BCG vaccine, psoriasis may develop. A instance of erythrodermic pustular psoriasis caused by BCG immunotherapy has been documented, and BCG has also been used as local immunotherapy for bladder cancer. Psoriasis was discovered in a retrospective analysis to arise more commonly following adenovirus vaccination. Other vaccinations like the tetanus-diphtheria vaccine and the pneumococcal polysaccharide vaccine may also cause psoriasis. Though the exact pathomechanisms of vaccination-induced psoriasis are still unknown, it is believed that these vaccinations cause T helper 1 (Th1) and Th17 immune responses, which cause the start and worsening of psoriasis. Vaccination is therapeutically beneficial in psoriasis patients; the frequency of psoriasis caused by vaccination is extremely low.[10]

5. INFECTION

It is commonly known that streptococcal infection and psoriasis are related. The most typical kind of psoriasis, guttate psoriasis, develops following streptococcal infection. Even if the symptoms are self-limiting, they may return if the streptococcal infection returns. Psoriasis development is also linked to Staphylococcus (S.) aureus. Psoriasis has been demonstrated to be linked to dysregulated skin microbiomes. About 60% of psoriasis patients have been shown to have S. aureus colonisation in the lesions, compared to 5% to 30% of normal healthy skin. Furthermore, the production of enterotoxins by the isolated S. aureus strains substantially corresponds with the severity of psoriasis. Candida species,

which are a typical component of the human microbiota, were frequently found in the mucous membranes or the skin of psoriasis patients. For mucosal membranes, a statistically greater rate of Candida species identification was also noted. In comparison to healthy controls, psoriasis patients had significantly higher rates of Candida species identification, particularly in the oral mucosa milieux. The rate of Candida species isolated from the skin, however, does not significantly differ between psoriasis patients and healthy controls. Antifungal immunity is promoted by Candida species and its colonisation, which may be related to the aetiology of psoriasis. Malassezia is a lipophilic yeast that can be found on the skin and other bodily surfaces; it may play a role in the psoriasis flare-up. Another well-known risk factor for psoriasis is the human immunodeficiency virus (HIV). It is ironic that psoriasis should be made worse by HIV infection even while treatments that target T cells are successful in treating the disorder. Papillomaviruses, retroviruses, and endogenous retroviruses have all been linked to the development and worsening of psoriasis, in addition to HIV infection.[10]

6. LIFESTYLE

Psoriasis has been linked to both smoking and drinking. According to a comprehensive review and meta-analysis, smokers are more likely to get psoriasis than nonsmokers. A higher risk of getting psoriasis is linked to smoking. Additionally, psoriasis pustular lesions are substantially correlated with smoking. With increasing pack-years or duration of smoking, a tendency toward an elevated incidence of psoriasis was discovered. Another investigation revealed a connection between smoking frequency and/or duration with the development of psoriasis. It's seen that drinking alcohol increases the likelihood of developing psoriasis. A previous systematic study, however, came to the conclusion that there was insufficient data to determine whether alcohol use was in fact a risk factor. However, it was shown that psoriasis sufferers consumed more alcohol than the general population did. Alcohol misuse positively correlates with the severity of psoriasis and lower treatment effectiveness, despite the fact that the association between psoriasis and alcohol consumption is complex and multifaceted. A considerable increase in mortality rates

is also linked to alcohol addiction. The intestinal microbiome may be significantly maintained by dietary quality changes, and diet-induced dysbiosis may result in the cytokine imbalances linked to the aetiology of psoriasis. Dietary changes including antioxidants, folic acid, vitamin D, and polyunsaturated fatty acid supplements can also be thought of as adjuncts in the treatment of psoriasis. To yet, randomised controlled trials have generated inconsistent results. Diet is a complex collection of foods from many groups; nutrients and the great diversity of such foods may contribute to its protective benefits against psoriasis.[10]

INTRINSIC RISK FACTORS

1. OBESITY

Patients with psoriasis frequently have metabolic syndrome, and obesity is closely linked to the development and worsening of psoriasis. Psoriasis patients are much more likely to be obese and are also at a higher risk of becoming obese. According to research, psoriasis and body mass index (BMI) are positively correlated. However, because it misses identifying 50% of those with extra body fat, BMI has low sensitivity but good specificity to diagnose adiposity. Contrarily, the waist circumference is a more accurate indicator of body fat, and numerous research have found a substantial correlation between the two conditions. Obesity is a low-grade inflammatory state, contributing to the pathogenesis of psoriasis. Adipose tissue produces pro-inflammatory adipokines like TNF-, IL-6, leptin, and adiponectin. In patients with type 2 DM, blocking the TNF- signalling pathway relieves the inflammatory cycle of psoriasis but does not enhance insulin sensitivity. Adipose tissue hormone leptin serves as an afferent signal in a negative feedback loop that keeps the mass of adipose tissue under control. Leptin is a crucial metabolic status regulator that also affects immunological and inflammatory responses. The generation of inflammatory cytokines by macrophages, granulocyte chemotaxis, and increased Th17 proliferation are all enhanced by leptin. Elevated leptin levels in adipose tissue hinder regulatory T cells, which uphold tolerance and prevent psoriasis, from differentiating. In actuality, psoriasis sufferers' serum or plasma

levels of leptin are higher than those of healthy controls. Additionally, psoriasis patients' skin has higher tissue levels of leptin. Reduced response to oral systemic treatments and biologics is likely to be improved by weight loss, which also seems to improve psoriasis symptoms. Additionally, losing weight may lessen the chance of systemic therapy causing drug toxicity.[10]

2. DIABETES MELLITUS

A meta-analysis identified a link between psoriasis and DM. The link between psoriasis and the risk of DM has also been shown in other studies. DM is separated into two categories: type 2 DM and type 1 DM. Psoriasis patients are far more likely to develop type 2 diabetes. However, patient age or the severity of their psoriasis have no effect on the occurrence of type 2 DM. Regardless of how severe it is, psoriasis is a sign of a higher risk of developing type 2 diabetes. It's unknown if type 2 DM or psoriasis develops first. Obesity is a risk factor for psoriasis, as was already mentioned. Obesity directly influences the development and progression of type 2 DM. Thus, type 2 DM may not directly contribute to the pathophysiology of psoriasis, but both obesity and type 2 DM are linked to psoriasis. Unlike type 2 diabetes, type 1 diabetes is a chronic condition marked by insulin shortage brought on by the autoimmune death of insulin-producing pancreatic beta-cells, which results in hyperglycemia. TNF- and other proinflammatory cytokines contribute to the pathophysiology of type 1 diabetes. It's interesting to note that the beginning of type 1 DM may be influenced by both Th1 and Th17 cells. The TNF-/IL-23/IL-17 axis is critical in the pathogenesis of both type 1 DM and psoriasis, even though type 1 DM may not directly contribute to the pathogenesis of psoriasis.[10]

3. DYSLIPIDEMIA

Dyslipidemia is more common in psoriasis patients, and it is likely to get worse as the condition gets worse. In a previous study with 70 psoriasis patients, dyslipidemia was found in 62.85% of the patients. Hypertriglyceridemia (39%) and hypertriglyceridemia with a decreased value of high-density lipoprotein were the most prevalent conditions (HDL). Additionally, dyslipidemia can develop while receiving oral systemic psoriasis treatments. The most potent contributors to dyslipidemia are retinoids, which cause simultaneous drops in HDL cholesterol and increases in triglycerides, total cholesterol, low-density lipoprotein cholesterol, and very-low-density lipoprotein cholesterol. Dyslipidemia may also result with cyclosporine. This study came to the conclusion that fasting triglyceride levels should be monitored during cyclosporine therapy, especially after 1 to 2 months of use and in patients with preexisting increased triglycerides and/or a history of etretinate use. It is possible that cyclosporine unmasks a latent tendency for mild to moderate hypertriglyceridemia. Although immunological problems and dyslipidemia are linked, it is yet unclear if dyslipidemia affects the development and worsening of psoriasis.[12]

4. HYPERTENSION

Patients with psoriasis demonstrated higher prevalence and incidence of hypertension in a meta-analysis. A further finding of this meta-analysis was that severe psoriasis was linked to a higher risk of hypertension. Psoriasis patients appear to have hypertension that is more severe. A multicenter non-interventional observational study involving 2210 psoriasis patients found that 26% of them had hypertension, and that this condition was associated with a higher incidence of hypertension than the general population. On the other hand, there may be a link between psoriasis prevalence and hypertension. Despite the fact that psoriasis and hypertension share risk factors including smoking and obesity, the majority of research have demonstrated an independent relationship between psoriasis and hypertension when these risk factors have been taken into account. It is yet unclear what causes this relationship.[12]

5. MENTAL STRESS

Internal perceptions that create worry or other negative emotions can cause mental stress, which is a sense of strain and pressure. When people believe the expectations are greater than their capacity to handle them, mental stress results. Psoriasis is frequently thought to be triggered by mental stress, and many psoriasis sufferers and doctors think that mental stress makes the condition worse. The relationship between mental stress and psoriasis is complicated, even if evaluations on Dermatology Life Quality Index scales show that psoriasis causes a higher degree of distress. In a previous comprehensive review that included 39 trials and 32,537 patients, 46% of the patients thought their illness was stress-reactive, and 54% could recollect stressful events that had come before. However, there was no solid evidence to back up the idea that the stress that came before it greatly influenced the incidence and worsening of psoriasis. The majority of the association was based on retrospective research, which had significant drawbacks. The relationship between mental stress and the clinical course of psoriasis is not entirely known. In contrast, a prospective study indicated that worrying and scratching, at times when patients were under a lot of daily stress, were both independently connected to an increase in sickness severity and itching four weeks later. During these times, stressors also interacted with vulnerability traits, demonstrating that patients with more chronic stress as well as excessive worrying and scratching had more severe sickness symptoms. An itch-scratch-itch cycle that results from scratching in response to an itch aggravates psoriasis. More research is necessary to completely comprehend how mental stress and psoriasis are related.[13]

CLINICAL PRESENTATIONS

There are numerous ways that psoriasis can appear, including plaque, flexural, guttate, pustular, or erythrodermic psoriasis. Plaque psoriasis is the most prevalent type and affects the scalp, trunk, and extensor surfaces (particularly the elbows and knees), presenting as well-defined salmon pink plaques with silvery-white scale. On grattage bulckeley membrain removed bleeding spots may be seen (Auspitz sign). These scales are characteristically coherent giving the appearance of a scratched wax candle (Signe de la tache de bougie). A zone of hypopigmentation (Woronoff's ring) is seen occasionally surrounding a psoriatic plaque, Flexural psoriasis presents without much scaling and may affect the axillae, sub-mammary and genital areas. Flexural psoriasis can affect the axillae, sub-mammary, and vaginal areas and manifests without much scaling. Guttate psoriasis typically, but not always, is preceded by streptococcal infection and manifests as an acute, symmetrical eruption of drop-like papules or plaques that primarily affects the trunk and limbs. Plaque psoriasis can later appear in patients with guttate psoriasis. Psoriasis can cause erythroderma, a widespread erythematous rash that can be fatal due to probable consequences like hypothermia, infection risk, acute renal injury, and high-output heart failure. These cases of severe uncontrolled psoriasis are extremely rare. Psoriasis showing up in traumatised skin areas is known as the Koebner phenomenon. Affected nails may appear as nail pitting (indentation in the nails), onycholysis (separation of the nail plate from the nail bed), oil spots (discoloration of the nailbed), dystrophy, and subungual hyperkeratosis in up to 50% of patients.[4]

MULTIMORBIDITY AND PSORIASIS

Multimorbidity, which is the existence of two or more chronic illnesses, is prevalent in psoriasis sufferers. Up to 30% of people with psoriasis develop psoriatic arthritis (PsA), which is particularly prevalent in people with nail dystrophy and scalp/intergluteal/perianal psoriasis. PsA is a diverse illness that might manifest as dactylitis, enthesitis, or seronegative asymmetric oligoarthropathy. Psoriasis typically appears up to 10 years before joint disease in patients. As a result, primary care doctors and dermatologists who treat psoriasis patients are in a good position to identify PsA early on. The Psoriasis Epidemiology Screening Tool (PEST), a validated five-item questionnaire, is suggested for PsA screening. 10 Overweight, cardiac disease, non-alcoholic fatty liver disease, diabetes, and metabolic syndrome are all more common in people with psoriasis than in the general public, with rates being especially high in people with more severe psoriasis. This may be connected to common risk factors, inflammatory pathways, and hereditary features. As a result, people with severe psoriasis have a higher death rate, which is mostly brought on by cardiovascular conditions. With severe psoriasis treatment having been demonstrated to enhance cardiovascular outcomes, this may be controllable. Additionally, psoriasis has a negative psychosocial impact since incidence of mental health issues (such as anxiety and depression) are higher than in the general population.[14]

CLINICAL CLASSIFICATION

Psoriasis vulgaris, often known as plaque-type psoriasis, is the most common form of the condition's dermatological symptoms. Although the terms "psoriasis" and "psoriasis vulgaris" are interchangeable in the scientific literature, there are significant differences between the various clinical subtypes.[15]

1. PSORIASIS VULGARIS

Chronic plaque-type psoriasis accounts for about 90% of all cases of the disease. Sharply defined, erythematous, pruritic plaques covered in silvery scales are the hallmark clinical symptoms. Large skin-covering plaques can form and cover patches of skin. The scalp, the extensor surfaces of the limbs, and the trunk are typical sites.[15]

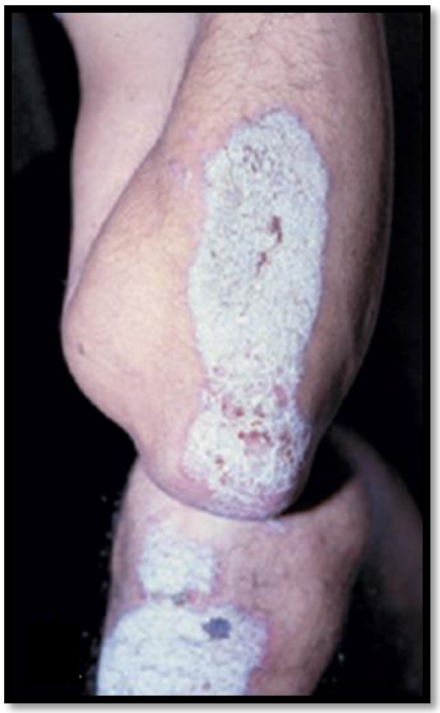


Figure 3 : Clinical photograph Psoriasis vulgaris

A) Classic psoriasis: well-demarcated plaques, covered with a silvery white scale, most commonly localized on the extensor surfaces of the knees, elbows,

Adapted from[16]

2. INVERSE PSORIASIS

Flexural (intertriginous or inverse) psoriasis is a form of psoriasis in which the most evident clinical differencefrom the classical plaque-type psoriasis is the lack of desquamation at the flexural areas. It affects between 3% and 7% of the patients with psoriasis; however, the actual incidence is still unknown. The lesions are well demarcated, erythematous and often showing, because of the moist, a shiny/glazed appearance.[15]

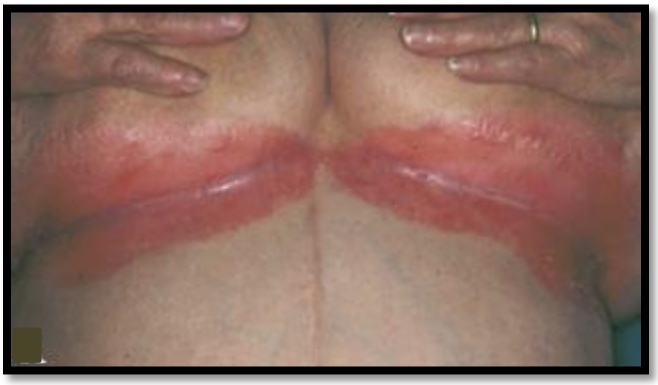


Figure 4: Clinical photograph Inverse psoriasis

Flexural psoriasis: well demarcated, erythematous plaque which is shiny/glazed. Adapted from[16]

3. GUTTATE PSORIASIS

A subtype of guttate psoriasis manifests as tiny erythematous plaques that appear suddenly. It typically affects children or adolescents and is frequently brought on by tonsillitis caused by group A streptococcal bacteria. In the course of their adult lives, about one-third of those with guttate psoriasis will also develop plaque psoriasis.[15]

4. PUSTULAR PSORIASIS

Multiple, merging sterile pustules are the defining feature of pustular psoriasis. Both localised and widespread pustular psoriasis exist. Psoriasis pustulosa palmoplantaris (PPP) and acrodermatitis continua of Hallopeau have been identified as two separate localised manifestations. PPP is limited to the palms and soles, while ACS is more distally positioned at the tips of fingers and toes and affects the nail apparatus. Both of them have an impact on the hands and feet. Acute and quickly progressing, diffuse redness and subcorneal pustules are the hallmarks of generalised pustular psoriasis, which frequently has systemic symptoms as well.[17]

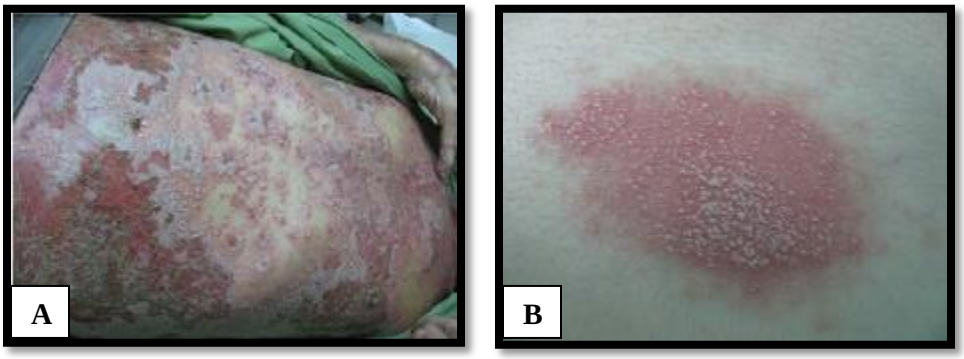


Figure 5 : Clinical photograph Pustular Psoriasis

A. Dense collection of pustules with minimal coalescence, B. widespread lesions

Adapted from[18]

5. ERYTHRODERMIC PSORIASIS

Is a severe condition when more than 90% of the entire body's surface is erythematous and swollen. The "nose sign" of exfoliative dermatitis refers to near complete absence of erythema and scaling of the nasal and to some extent, the perinasal skin. Any type of psoriasis has the potential to develop erythroderma, which calls for immediate medical attention.[19]

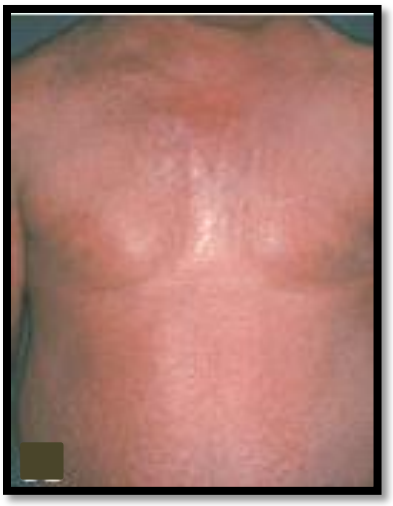


Figure 6: Clinical photograph Erythrodermic psoriasis

Erythrodermic psoriasis: Erythema and edema of the skin noted

Adapted from[16]

6. ORAL PSORIASIS

The lips, tongue, buccal mucosa, gingiva, and palate, as well as any other component of the oral mucosa. Different symptoms of lips' involvement in psoriasis can occur. Psoriatic lesions with the typical scaly, erythematous appearance may be noticed extending from the lip, crossing the vermilion boundary, and involving the mucosal area. Rarely, cutaneous psoriasis flare-ups may also be accompanied by exfoliative cheilitis. Erythema, scaling, and fissuring near the corners of the mouth have all been recorded as symptoms of angular cheilitis. Geographic tongue, which is primarily present in cases with widespread pustular psoriasis, is the oral mucosal condition that has been documented most frequently.[20]

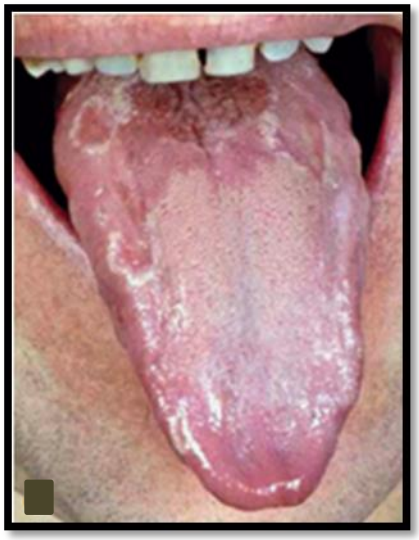


Figure 7 : Clinical photograph Oral psoriasis

Oral psoriasis: Geographic tongue seen In oral psoriasis

Adapted from[16]

7. NAIL PSORIASIS

Is a refractory condition that affects up to 80% of people with psoriatic arthritis and 50–79% of people with cutaneous psoriasis (PsA). While nail bed involvement can lead to onycholysis, oil-drop staining, nail bed hyperkeratosis, and splinter haemorrhages, nail matrix involvement can result in pitting, leukonychia, red spots in the lunula, and nail plate disintegration.[21]

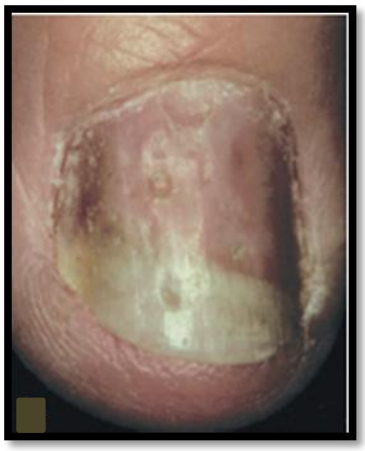


Figure 8 : Clinical photograph of Nail psoriasis

Nail Psoriasis : pitting, onycholysis, subungual hyperkeratosis, and nail discoloration noted.

Adapted from[16]

8. SEBOPSORIASIS

Sebopsoriasis is an overlap between seborrheic dermatitis and psoriasis in which findings of both diseases coexist. It has a prevalence of 5.3% of psoriatic patients.[16]

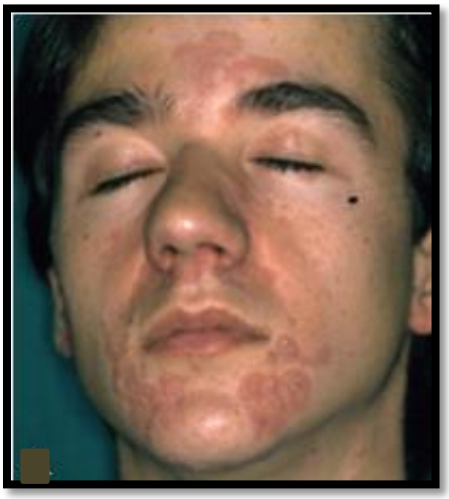


Figure 9 Clinical photograph Sebopsoriasis

Erythematous indurated plaques noted over the seborrheic areas

Adapted from[16]

9. PALMOPLANTAR PSORIASIS

Palmoplantar psoriasis represents a variant of psoriasis that develops on the palms and soles. It can be associated with many different psoriatic patterns but predominantly accompanies pustular lesions. This clinical variant accounts for 3-4% of all psoriasis cases. [16]

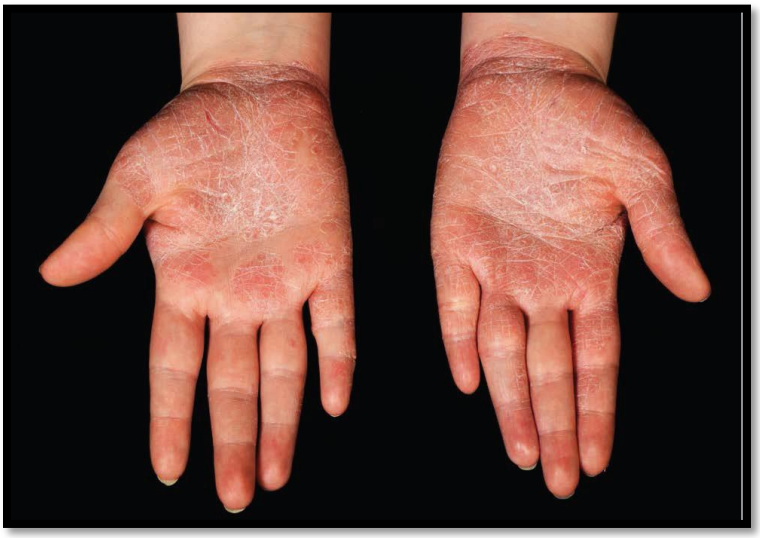


Figure 10 : Clinical photograph of palmoplantar psoriasis

Palmoplantar Psoriasis with hyperkeratosis of palms with fissuring and erythema noted

Adapted from[4]

PSORIASIS AND CO-MORBIDITY

1. PSORIASIS AND CARDIOVASCULAR DISEASE

The link between psoriasis and cardiovascular disease (CVD) has drawn increasing attention in recent years. Patients with psoriasis were more likely to have CVD than the general population, making it easier to detect. A prospective cohort research including 130,000 psoriasis patients and 500,000 control subjects found that patients with psoriasis had an overall 50% higher risk of myocardial infarction (MI) [odds ratio (OR) = 1.50]. Heart failure (HF) risk was 63% greater in psoriatic patients compared to the control group (OR = 1.63). Similar to this, a significant cohort research found that psoriasis patients had greater incidence of atrial fibrillation (AF) and ischemic stroke than the general population. The risk of valvular heart disease (VHD) among those with psoriasis was found to be similar. Some research, however, disproved the link between psoriasis and the risk of CVD. Patients with primarily mild psoriasis had no higher risk of CVD events (MI, IS, and HF) in a case-control study with an 11-year follow-up. After controlling for known CVD risk factors, a cohort research included 48,523 psoriasis patients and 208,187 healthy controls showed that psoriasis was not linked to an increased risk of CVD.

Notably, it is still unknown if psoriasis directly increases CVD risk. This is due to the fact that the classic risk factors for cardiovascular disease, such as stress, dyslipidemia, smoking, and obesity, are frequently risk factors for psoriasis as well. These research could not effectively account for these confounding variables, which would have produced erroneous associations. [22]

2. PSORIASIS AND PSORIATIC ARTHRITIS

Moll and Wright's classification of the Psoriatic arthritis (PsA) clinical subgroups and the commonly used illness description were put forth in 1973. "An inflammatory arthritis linked with psoriasis and negative for serum rheumatoid factor," according to the scientists, is what PsA is. Some scientists disagreed with this categorization since they thought the condition was actually the coexistence of two diseases, psoriasis and rheumatoid arthritis. Recent studies have offered fresh information on the pathogenesis of the disease, particularly in the fields of genetics, immunology, and epidemiology. Early treatment in PsA must begin before progressive joint damage takes place for it to be effective. Modern diagnostic imaging methods are extremely important, especially in situations with minimal symptoms.[23]

Psoriasis exists in two forms: type I, which manifests early in life (before age 40), and type II, which manifests symptoms later in life (after the age of 40). A diagnosis of type I is made in about 85% of cases, with a peak frequency between the ages of 18 and 22. The condition progresses more quickly, and arthritis frequently makes things harder. Type I coexists with PSORS1 locus and HLA-Cw * 0602 alleles (35–50%) frequently (85%). In this kind of sickness, the role of hereditary factors is very obvious. The incidence of PsA Type II peaks between the ages of 57 and 60. As opposed to type I, the association with hereditary variables is less obvious. Only 15% of people have the HLA-Cw * 0602 allele. Other authors reported experiencing similar outcomes. The disease has a milder course and is infrequently linked to arthritis.

In Psoriatic the rheumatoid factor is typically absent but the cutaneous manifestation of psoriasis coexists with arthritis. 4–42% (usually 7–10%) of psoriasis patients are predicted to have psoriatic arthritis. PsA prevalence is typically stated to be around 30% among psoriasis patients in more recent studies, translating to an overall prevalence of 0.3-1.0% in the general population. [24]

3. PSORIASIS AND MENTAL HEALTH CONDITIONS

Psychological comorbidities like depression and anxiety disorders are strongly linked to psoriasis. Using International Classification of Diseases (ICD) codes, screenings of psoriasis patients seeking treatment in dermatological clinics revealed prevalence rates for clinical depression of about 12–13%. Depressive symptoms, however, are said to be present in up to 28–55% of psoriasis patients, depending on the screening method. 7 to 48% of psoriasis sufferers have an anxiety issue. The integrative therapy of psoriasis patients in dermatological practise is crucial given the high prevalence of psychiatric comorbidities, as these diseases are a significant cause of impairment and may also obstruct effective dermatological treatment.[25]

The widespread stigmatising attitude of society as a result of the easily noticeable skin symptoms in affected people is one explanation for the close relationship between psychological burden and psoriasis. The fact that social stigmatisation appears to be a significant predictor of depressed symptoms in psoriasis patients lends credence to this notion.

Another theory that is being discussed more and more at the moment contends that immunological factors may be to blame for the link between depressive symptoms and inflammatory skin conditions like psoriasis. Since monoamine agonists alleviate symptoms in a subset of patients with depression, monoaminergic neurotransmitter reductions in the central nervous system (CNS) have been linked to depression for years. But it is now known that cytokine-mediated brain-immune system communication plays a crucial part in the aetiology of depression. In patients with depression who did not have additional inflammatory comorbidities, studies have discovered elevated serum levels of proinflammatory cytokines as tumour necrosis factor alpha (TNF-), interleukins (IL)-1, IL-1ß, IL-2, IL-6, IL-8, IL-17, IL-23, and C-

reactive protein (CRP). In contrast, people with chronic inflammatory illnesses such rheumatoid arthritis or inflammatory bowel disease have a significant prevalence of depressed symptoms. Additionally, patients receiving cytokine therapy, such as interferons, report a significant prevalence of depression as an undesirable side effect. Experimental results in healthy patients who experience depressed symptoms after peripheral immunological challenges brought on by vaccination or injection of bacterial endotoxin provide support for these clinical observations.

There are a number of hypotheses regarding how increased proinflammatory cytokines may affect the CNS's ability to process neurotransmitters. According to one idea, major depressive patients have a blood-brain barrier that is hyperpermeable, allowing serum proinflammatory cytokines to reach the central nervous system (CNS). Proinflammatory cytokines can activate neuronal and non-neuronal cells once they are present in the CNS, which is similar to how they work in the peripheral immune system. The activation of endothelial cells in the cerebral vasculature, which triggers the release of cytokines across the blood-brain barrier, is another mechanism that has been studied in the literature. A third explanation strategy argues that vagus nerve fibres, which have receptors that may bind serum proinflammatory cytokines, can act as a conduit for peripheral inflammatory signals to reach the central nervous system.

Similar to how the definition of depression has expanded, psoriasis is no longer seen as a singular skin condition. Psoriasis is currently thought to be a systemic inflammatory disease with proinflammatory effects that extend beyond the skin. [26]

4. PSORIASIS AND IMMUNE-MEDIATED DISORDERS

In psoriasis patients, immune-mediated disorders have been found to occur more frequently. Uncertainty persists regarding the precise connection between immune-mediated illnesses and psoriasis. Patients with severe psoriasis showed noticeably greater rates of rheumatoid arthritis, lupus, and Crohn's disease diagnosis compared to those with mild psoriasis. Additionally, the pathophysiology of psoriasis has been shown to involve autoreactive T cells, which raises the possibility that psoriasis is an autoimmune disease.

A population-based, cross-sectional study involving 267,230 psoriasis patients and 267,230 controls without psoriasis assessed the relationship between psoriasis and other immune-mediated rheumatic illnesses. Ankylosing spondylitis (AS), rheumatoid arthritis (RA), Behçet illness, systemic lupus erythematosus (SLE), systemic sclerosis (SSc), and dermatomyositis/polymyositis (DM/PM) were all substantially related with psoriasis. In addition, compared to female patients with psoriasis, male patients showed stronger correlations with AS, RA, SLE, SSc, and DM/PM.[27]

A case-control study comparing 287 individuals with bullous pemphigoid (BP) to 1,373 matched controls revealed that BP patients had a higher prevalence of psoriasis than controls did. Furthermore, psoriasis had been present for an average of 25.2 years prior to the diagnosis of BP. Additionally, despite controlling for confounding factors like sex, age, psoriatic arthritis, and usage of systemic anti-psoriasis medications, a cross-sectional study identified a substantial connection between psoriasis and Hashimoto's thyroiditis that persisted (odds ratio 2.49). The documented correlation between BP and psoriasis has been attributed to chronic inflammation, which leads to damage to the basement membrane. Another hypothesis is that psoriasis medication could make subclinical bullous pemphigoid worse. Additional research would clarify the precise relationship between psoriasis and BP as well as that between psoriasis and other autoimmune diseases. [28]

5. PSORIASIS AND METABOLIC SYNDROME

Even though psoriasis primarily affects the skin and joints, it is a systemic inflammatory disorder that has effects that go beyond the condition's visible lesions. It is characterised by changes to both innate and adaptive immunity. Circulating pro-inflammatory mediators in psoriasis cause a systemic inflammatory response that is commonly accompanied by concomitant conditions like cardiovascular disease (CVD) and metabolic syndrome (MetS). In individuals with psoriasis, the prevalence of MetS, a complicated disorder marked by the coexistence of multiple factors that raise the risk of cardiovascular disease, ranges from 20% to 50% and rises with increasing psoriasis severity. The National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) guidelines state that at least three of the following conditions must be present in order to diagnose MetS: waist circumference >102 cm (for men) or >88 cm (for women); triglycerides 150 mg/dL; high-density lipoprotein (HDL) 40 mg/dL (for men) or 50 mg/dL (for women); blood pressure 130/85. MetS is a serious worry for people with psoriasis and is becoming a major public health issue.[29]

Although no clear causal link has been established, metabolic problems in psoriasis patients may be caused by a confluence of genetics, widespread signalling networks, and environmental variables. These connections and the fact that both psoriasis and MetS are chronic inflammatory diseases could have an impact on how clinical and therapeutic psoriasis therapy is carried out. Investigations are being conducted to determine how the systemic anti-inflammatory action of biologics used to treat psoriasis affects the incidence, progression, and effects of MetS as well as the efficacy and safety of these medications for the treatment of psoriasis. [30]

MANAGEMENT OF PSORIASIS

MANAGEMENT OF PSORIASIS INCLUDES INVESTIGATIONS AND TREATMENT.

INVESTIGATIONS

The diagnosis of psoriasis can usually be made on clinical grounds alone and a biopsy is rarely, if ever required.

CLASSIC PLAQUE PSORIASIS

Both epidermal and dermal changes are visible from a histopathological perspective. When magnified by scanning, the epidermis displays a typical psoriasiform hyperplasia with elongated rete ridges that are the same size and length as the intercalated dermal papillae, higher basal and suprabasal keratinocyte mitotic activity, occasionally enlarged club-shaped rete ridges, and suprapapillary plate thinning. Confluent hypogranulosis and parakeratosis are signs of aberrant keratinization. Neutrophils have a propensity to migrate from the dermis into the epidermis, where they might accumulate to produce Kogoj's spongiform pustules or Munro-microabscesses Sabouraud's in the stratum spinosum. One of the more distinctive histological characteristics of early psoriasis is Munro-microabscesses. Sabouraud's Another pathognomonic feature of psoriasis is the alternating accumulation of neutrophils between layers of parakeratosis. (Figure 11).

In classic psoriasis, features of inflammation can be seen throughout the dermis; typical symptoms include large and dilated tortuous arteries and modest papillary dermal edoema. (Figure 12). There is clear evidence of VEGF and CD34 overexpression in psoriatic skin. Regarding the age of the lesion, there are differences. Early psoriasis symptoms can be non-specific and frequently include dermal alterations such skin edoema, vessel dilation and congestion, and a sparse superficial perivascular T-lymphocytic infiltration. Minimal spongiosis then develops in conjunction with infrequent neutrophil and/or T-lymphocyte exocytosis. The lumen of the arteries may be filled with neutrophils. Later, a superficial

inflammatory infiltration of mononucleated cells, neutrophils, Langerhans cells, and indeterminate cells without eosinophils is visible along with tiny mounds of parakeratosis containing neutrophils.[31]

Extravasated erythrocytes are occasionally seen, especially in cases of acute onset. (Figure 2C). Additionally, lymphatic pathways are expanded. The epidermis of well-established lesions has considerable psoriasiform epidermal hyperplasia, pallor in the outermost layers, regular rete ridge elongation with typical bulbous expansion of their tips, sparing the thin suprapapillary area. Elongated dermal papillae with tortuous, dilated capillaries and fibrillary collagen are seen. In the majority of instances, Munro's microabscesses and confluent parakeratosis coexist. Little to no spongiosis is present. The papillary dermis contains a perivascular inflammatory infiltration composed of T lymphocytes, less Langerhans cells, CD163-positive spindle-shaped macrophages, and sporadic neutrophils. In the lowest layers of the epidermis, some exocytosis of lymphocytes is seen; plasma cells and eosinophils are typically absent. Due to increased mitotic activity in the basal and suprabasal layers, keratinocyte proliferation is increased.

This is accompanied by increase in the apoptotic rate and a decrease in bcl-2 expression in basal cells. An increase in mitotic activity is confirmed by an increase in Ki-67 expression. Basal keratinocytes in psoriatic skin continue to express basal keratinocyte-specific keratins, whereas suprabasal cell-specific keratins (K1 and K10) are replaced by so-called hyperproliferation-associated keratins (K6 and K16 in addition to K17). Acanthosis and elongation of rete ridges with obvious enlargement of the tips accompanied with narrowing of the bases with some "bridging" development are the key characteristics of late resolving lesions. With the restoration of a granular layer, the stratum corneum reactivates to become orthokeratotic. [16]

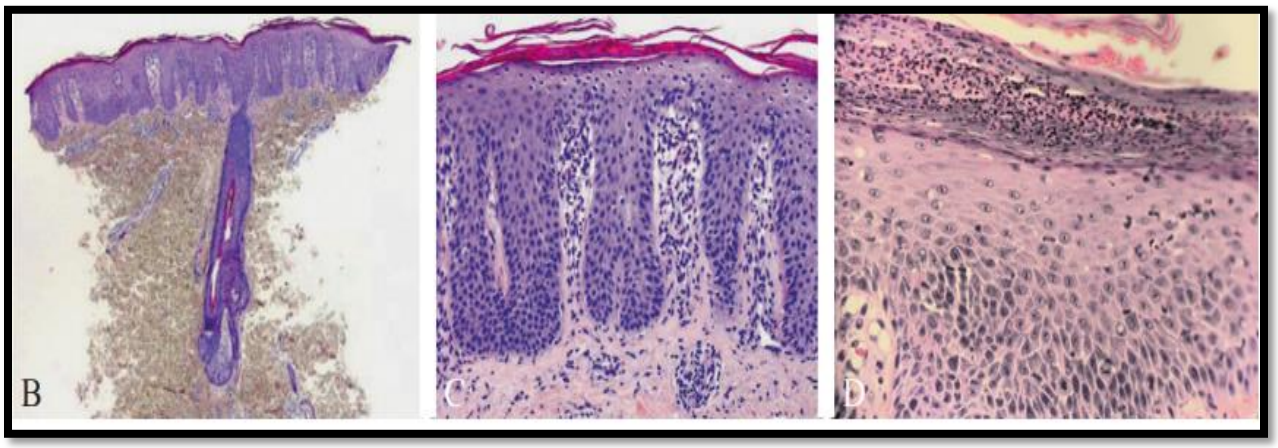


Figure 11: Histopathological photograph of classic plaque psoriasis

B) psoriasiform hyperplasia, parakeratosis with regular elongation of rete ridges and characteristic bulbous enlargement of the tips with mutual elongation of dermal papillae (H&E stain, 5×);

C) parakeratosis and thinned suprapapillary plate (H&E stain, 40×);

D) Munroe microabscesses with basal and suprabasal mitosis (H&E stain, 60×)

Adapted from[16]

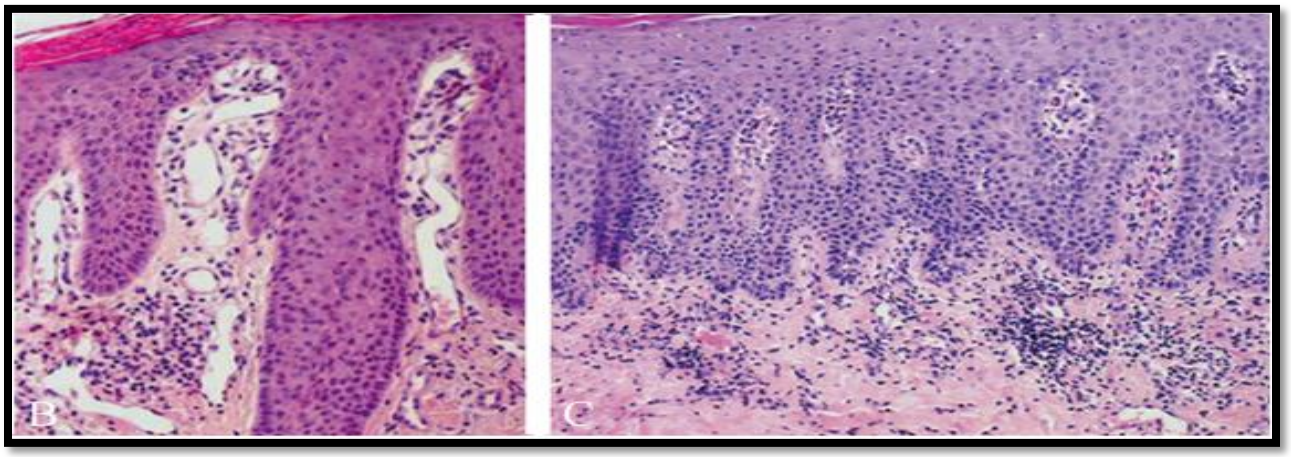


Figure 12: Histopathological photograph of classic plaque psoriasis

B) Dilated tortuous capillaries and fine fibrillary collagen, with thinning of the suprapapillary plate; plasma and neutrophils outside the ectasic capillaries configuring the "squirting papilla" (H&E stain, 40×);

C) lymphocytes and granulocytes infiltrate the ede- matous dermis, and extravasation of erythrocytes (H&E stain, 20×).

Adapted from[16]

SEBOPSORIASIS

Seborrheic dermatitis and psoriasis overlap to create sebopsoriasis, which exhibits symptoms of both conditions. Although there are no clear histological markers that distinguish between psoriasis and seborrheic dermatitis, those that favour psoriasis include mounds of parakeratosis with neutrophils, spongiform micropustules of Kogoj, clubbed and uniformly elongated rete ridges, and higher mitotic figures. Seborrheic dermatitis is indicated by irregular acanthosis, follicular hyperkeratosis, shoulder parakeratosis, spongiosis, microvesicles, and exocytosis of lymphocytes in addition to the absence of significant psoriasis criteria. (Figure 13). [16]

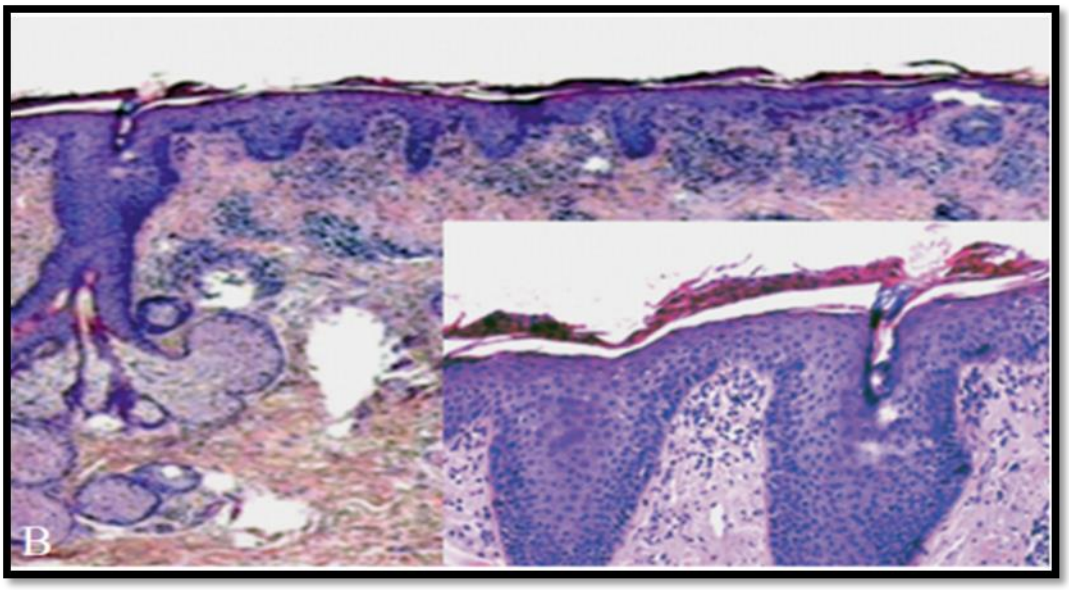


Figure 13: Histopathological photograph of sebopsoriasis

Follicular hyperkeratosis and parakeratosis on the shoulder, associated with lymphocytic exocytosis (H&E stain, 10×) and follicular dilatation and plugging (inset), marked ostial parakeratosis and hypogranulosis with a neutrophilic infiltrate (H&E stain, 40×)

Adapted from[16]

FOLLICULAR PSORIASIS

Similar to conventional psoriasis, the lesion's histological characteristics change with time. Follicular dilatation and clogging, pronounced ostial parakeratosis, and hypogranulosis with a neutrophil infiltrate are all signs of established lesions. Perivascular and perifollicular infiltrates characterise the dermal inflammatory infiltration. The primary differential diagnosis is pityriasis rubra pilaris, which is characterised by irregular acanthosis, localised or confluent hypergranulosis, and parakeratosis that alternates in the vertical and horizontal orientations. (Figure 13). [16]

ORAL PSORIASIS

The particular manifestations are distinguished by histological characteristics resembling skin psoriasis. Geographic tongue and fissured tongue are the two basic non-specific lesions. In this instance, the simultaneous occurrence of cutaneous and oral mucosal lesions, validated histopathologically, allows for the diagnosis of oral psoriasis. In geographic tongue, we see subepithelial infiltrates with neutrophil predominance, diffuse exocytosis, and the development of microabscesses and, occasionally, pustules. Clinically erythematous areas have more pronounced vascular ectasia in the chorion. In the upper epithelial layers of the tongue with fissures, there is an increased thickness of the lamina propria, which is infiltrated by a mixed inflammatory infiltration, hyperplasia of the rete ridges, and neutrophilic microabscesses. (Figure 14). [16]

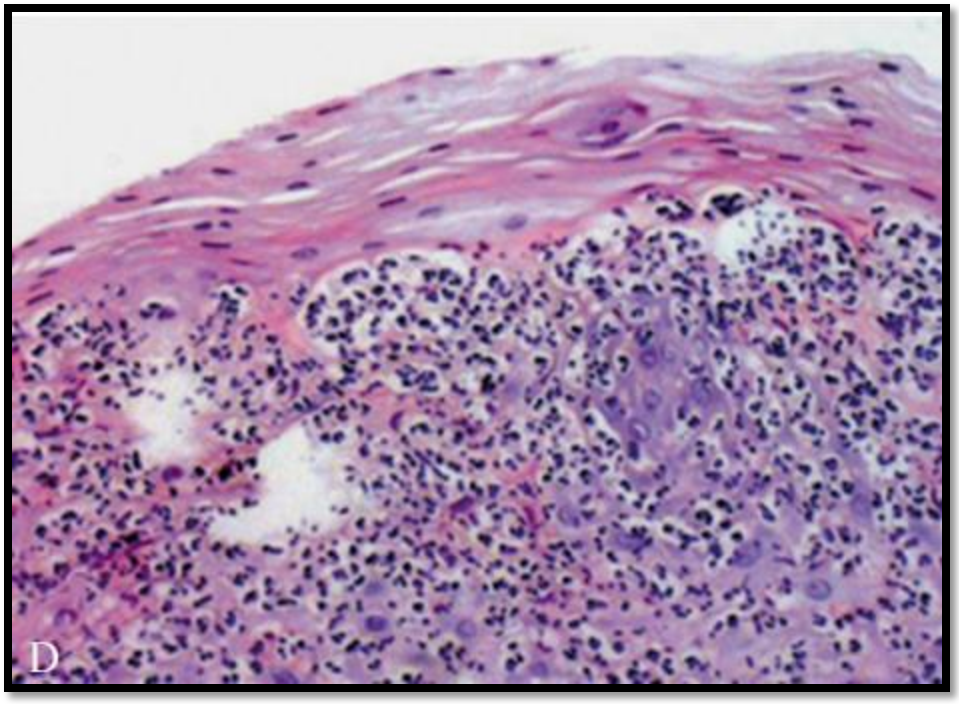


Figure 14: Histopathological photograph of oral psoriasis

Geographic tongue showing subepithelial infiltrates with predominance of neutrophils, and diffuse exocytosis, forming microabscesses and, in some cases, pustules (H&E stain, 60×)

Adapted from[16]

FLEXURAL PSORIASIS

Reduced epidermal hyperplasia and more severe spongiosis are both indicators of reduced scaling in flexural psoriasis histopathologically (Figure 15). Due to the persistent microbial challenge in this region, there are less lesional CD161+ cells in the dermis of flexural psoriatic lesions. Neutrophil collections from Kogoj and Munro-Sabouraud have also been characterised as being related to the thickening of the Malpighian layer, elongation of the papillae, hypogranulosis, and parakeratosis. [16]

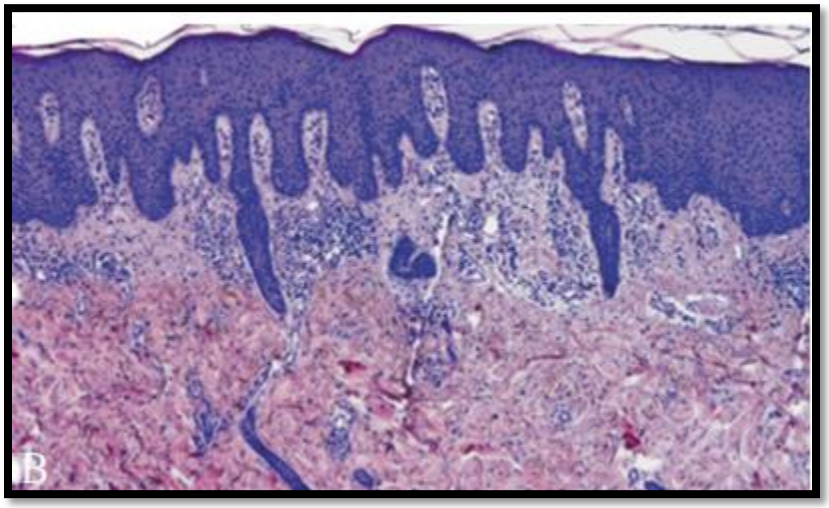


Figure 15: Histopathological photograph of flexural psoriasis

Marked reduction of the stratum corneum and dominance of the dermal alterations (H&E stain, 10×);

Adapted from[16]

GENITAL PSORIASIS

Histologically, genital and non-genital psoriasis appear to be identical. Epidermal hyperplasia, less scaling, and more obvious exocytosis are present (Figure 16). On the mucosal side of vulvar and penile psoriatic lesions, the normal psoriasis symptoms could be less noticeable. When compared to other cutaneous sites, mucosal involvement frequently results in less epidermal hyperplasia and less scaling, but spongiosis may be more obvious. [16]

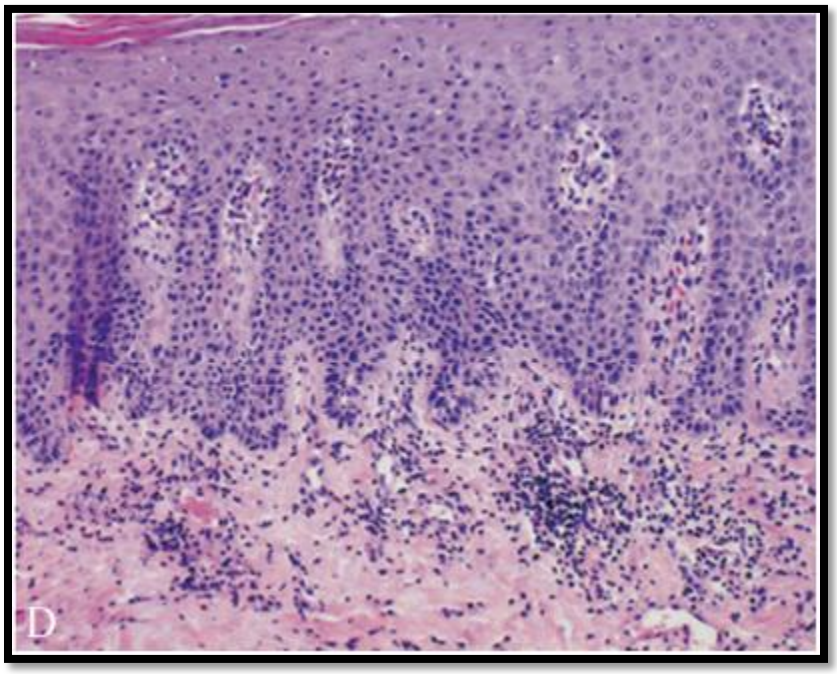


Figure 16: Histopathological photograph of genital psoriasis

Epidermal hyperplasia and less scaling, exocytosis more prominent (this epidermal hyperplasia can be absent on biopsies taken on the mucosal side) (H&E stain, 60×).

Adapted from[16]

PALMOPLANTAR PSORIASIS

Vesicles, as well as fissures and hyperkeratosis, can occasionally be detected. According to Haydin et al., several parakeratotic foci that were arranged vertically and alternated with ortho hyperkeratosis should be taken into account when diagnosing palmoplantar psoriasis. According to research on immunohistochemistry, irregular epidermal hyperplasia and a higher proportion of dendritic cells positive for the S100 protein favour the diagnosis of contact dermatitis. Regular epidermal hyperplasia and marked parakeratosis were found to be more common in psoriasis than in contact dermatitis. Eosinophils, which are frequently found in allergic contact dermatitis, are also uncommon in psoriasis lesions. In contact dermatitis, dilated and tortuous capillaries in the dermis are typically absent. Because spongiosis predominates during acute psoriasis start and, as a hint on palms and soles, is frequently confined to the lower epidermis, there is initially some diagnostic uncertainty. Initial biopsies in this case reveal a significant amount of spongiosis, some vesiculation, dilated arteries in the papillary dermis, and a modest, superficial perivascular lymphocyte infiltration (Figure 17). Psoriasis was more likely to be diagnosed when several parakeratotic foci were present, arranged vertically and alternated with orthohyperkeratosis. In palmoplantar psoriasis, neutrophils and serum are frequently found in the parakeratotic layers, although neutrophils are rarely seen at the apex of the parakeratotic mounds. Numerous areas of parakeratosis, uneven epidermal hyperplasia, and weakening of rete ridges are seen in pompholyx, the non-allergic dyshidrotic eczema. Dyskeratotic cells, papillary dermal edoema, and dilated capillaries, however, do not differ significantly from psoriasis in any way. [16]

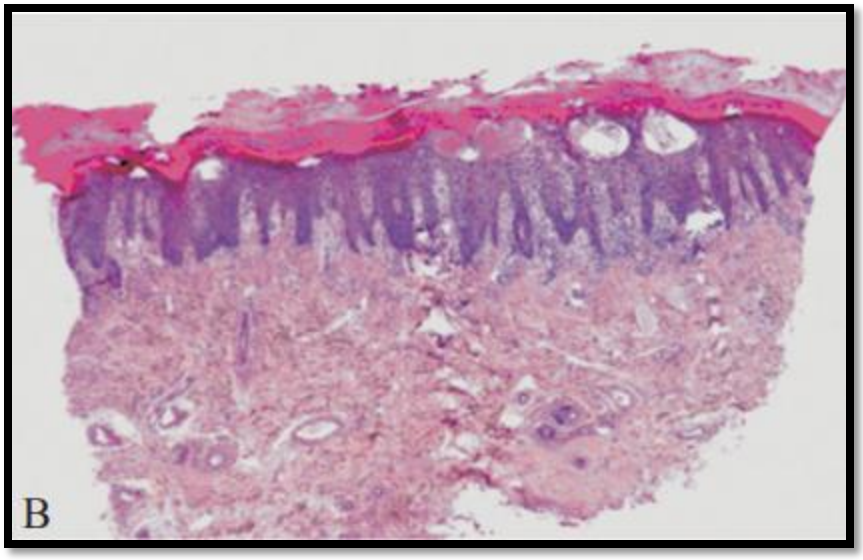


Figure 17: Histopathological photograph of palmo-plantar psoriasis

Regular epidermal hyperplasia, multiple foci of parakeratosis, placed vertically, alternating with orthohyperkeratosis and dilated capillaries favor the diagnosis of psoriasis (H&E stain, 5×)

Adapted from[16]

NAIL PSORIASIS

Histopathology of nail psoriasis contains neutrophils are present in the nail bed epithelium. Other minor criteria include the presence of hyperkeratosis, parakeratosis, serum globules, bleeding in the stratum corneum, focal hypogranulosis, and psoriasiform hyperplasia of the nail bed (Figure 18). The most prevalent histological pattern in a research examining 42 individuals was hyperkeratosis with parakeratosis in the hyponychium and distal region of the nail bed along with varied neutrophil exocytosis into the parakeratotic layers. One typical aspect of nail psoriasis is spongiosis. Onychomycosis and psoriasis may exhibit comparable histology, hence in the majority of cases periodic acid schiff stain is required before making a diagnosis of nail psoriasis. [16]

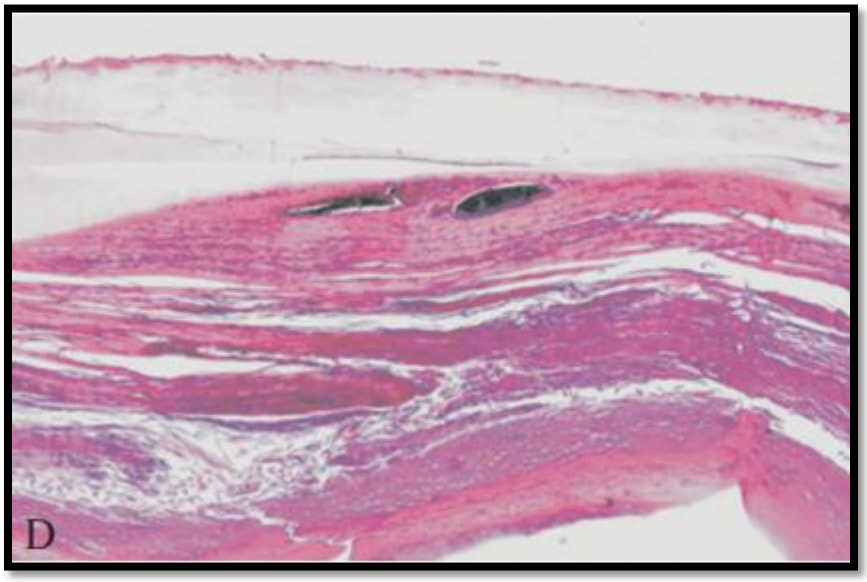


Figure 18: Histopathological photograph of nail psoriasis

Neutrophils in the nail bed epithelium associated by hyperkeratosis, parakeratosis, serum globules and hemorrhage in the stratum corneum (H&E stain, 40×)

Adapted from[16]

PUSTULAR PSORIASIS

As the pustular eruption begins before the time required to produce the normal epidermal hyperplastic alterations and is predominated by the presence of intraepidermal pustules at various stages of development, the histopathological features reflect the acute manifestation. There is a parakeratosis and extension of the rete ridges, which together with many neutrophils migrating from the dermal capillaries into the epidermis and generating subcorneal pustules on top of localised spongiform pustules of Kogoj, constitute a very mild psoriasiform hyperplasia. In the upper Malpighian layer of the epidermis, the pustules are situated between deteriorated and flattened keratinocytes. The spongiform pustule's neutrophils eventually move into the stratum corneum, much like in other variations, and take on the characteristics of a Munro microabscess. Dilated tortuous arteries and a superficial perivascular lympho/histiocytic infiltration are seen. (Figure 19,20). [33]

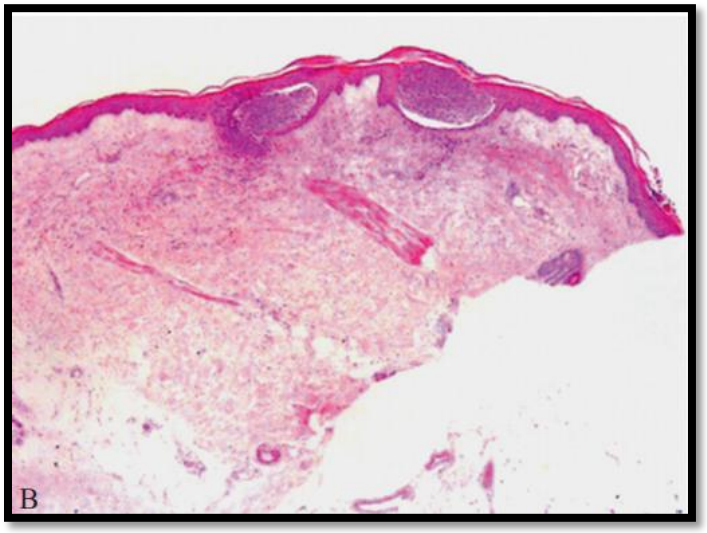


Figure 19: Histopathological photograph of pustular psoriasis

Slight epidermal hyperplasia, exocytosis of neutrophils migrating forming subcorneal pustules and large spongiform pustules of Kogoj; degenerated and flattened keratinocytes delimitate the collection of neutrophils; extravasation of erythrocytes between a lymphohistiocytic infiltrate and neutrophilic infiltrate in the dermis (H&E stain, 5×);

Adapted from[16]

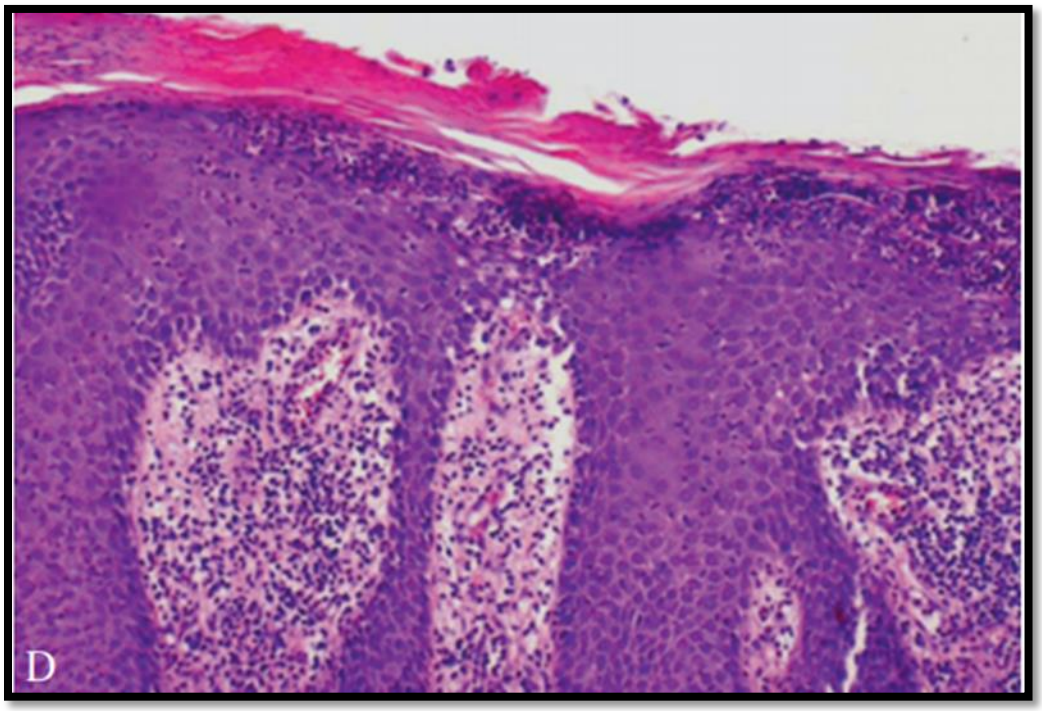


Figure 20: Histopathological photograph of pustular psoriasis

D) epidermal hyperplasia, elongation of the rete ridges and thinned suprapapillary plates, neutrophils aggregated in subcorneal collection; dermal papillae enlarged, occupied by tortuous vessels surrounded by lymphocytes (H&E stain, 60×).

Adapted from[16]

ERYTHRODERMIC PSORIASIS

The care of these patients with psoriatic erythroderma can be greatly aided by histological criteria indicating the psoriatic aetiology. The skin biopsy is required in these situations even though there are no histologic criteria that are uniformly specified for erythrodermic psoriasis. Wider dermal papillae, more consistent capillary dilatation, extravasated erythrocytes within edematous dermal papillae, perivascular and interstitial infiltration of lymphocytes and histiocytes, and the absence of the stratum corneum due to an extremely accelerated turnover rate are some characteristics that can be distinguishing and indicative of a psoriatic origin of the erythroderma. (Figure 21). [16]

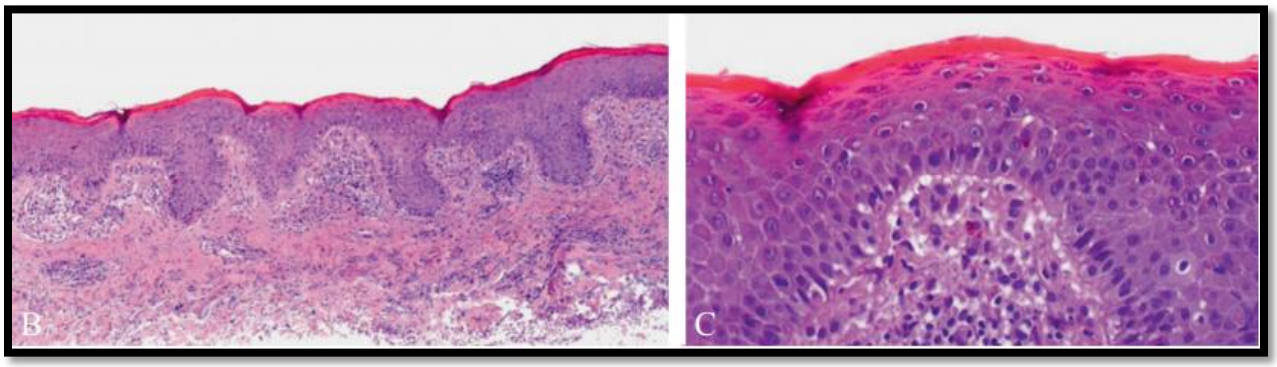


Figure 21: Histopathological photograph of erythrodermic psoriasis

Presence of wider dermal papillae with more consistent dilatation of capillaries, extravasated erythro- cytes within edematous dermal papillae associated with perivascular and interstitial infiltration of lymphocytes and histiocytes. The stratum corneum is almost completely absent (H&E stain, 10× and 60×).

Adapted From[16]

INVESTIGATIONS

The treatment of psoriasis is majorly directed towards its inflammatory and autoimmune nature, thus a clinician employees the use of cytotoxic & immunosuppressive drugs which require regular monitoring for toxicity, as the treatment given by the physician should be helpful to the patient and not harmful, following are the list of investigations done to monitor therapeutic toxicity in patients. [34]

Sl.No	**TABLE No. 2** : BASELINE INVESTIGATIONS
1.	COMPLETE AND THOROUGH PHYSICAL EXAMINATION
2.	COMPLETE BLOOD COUNT
3.	SERUM GLUTAMIC-OXALOACETIC TRANSAMINASE , SERUM GLUTAMIC PYRUVIC TRANSAMINASE , AND SERUM BILIRUBIN
4.	BLOOD UREA , SERUM CREATININE
5.	X-RAY CHEST
6.	CREATININE CLEARANCE FOR CYCLOSPORIN
7.	HIV (ELISA) IN “AT RISK” PATIENTS HEPATITIS B IN “AT RISK” PATIENTS
8.	URINE ROUTINE
Sl.No	FOLLOW-UP FOR FIRST 3 MONTHS: EVERY 2 WEEKS
1.	COMPLETE BLOOD COUNT
2.	BLOD UREA NITROGEN AND SERUM CREATININE
Sl.No	MONTHLY: EVERY 3 MONTHS
1.	COMPLETE BLOOD COUNT
2.	BLOD UREA NITROGEN AND SERUM CREATININE
3.	SERUM GLUTAMIC-OXALOACETIC TRANSAMINASE , SERUM GLUTAMIC PYRUVIC TRANSAMINASE , AND SERUM BILIRUBIN
4.	URINE ROUTINE AND MICROSCOPY
5.	CREATININE CLEARANCE FOR CYCLOSPORINE

METHOTREXATE

The drug has been successfully used in the treatment of skin diseases for the past several decades since 1951.363 MTX was found effective in the treatment of psoriasis first by Edmonson and Guy in 1958. The FDA approval for use in psoriasis was given in 1971.[35]

Hepatotoxicity is a major concern with an overall increased risk of severe fibrosis/cirrhosis. It is postulated that prolonged treatment with MTX leads to accumulation of polyglutamated form of MTX metabolite in hepatic cells, resulting in deficient nucleotide synthesis, thereby leading to hepatocyte injury.

Although, liver biopsy is the gold-standard investigation for detecting cirrhosis, because of its associated morbidity, other procedures are being evaluated. These include the following:

1. Liver function Tests (LFT): however, these may be normal even in the presence of severe liver disease.

2. Serum levels of amino-terminal pro-peptide of Type III pro-collagen (PIIINP)—The amino-terminal propeptide of type III collagen (PIIINP) is cleaved during collagen synthesis, which is upregulated in active fibrogenesis. It is a serum assay for products of matrix synthesis or degradation and the enzymes involved in the process could be markers of liver fibrosis. A large number of false-negative and false positive results may be seen, as this enzyme is not organ specific. Psoriatic patients having no arthritis but two elevated measurements of PIIINP are recommended to undergo liver biopsy. The number of liver biopsies can be limited to a minimum in patients with normal PIIINP. PIIINP assay should be performed three monthly and liver biopsy should then be considered for patients in whom it is persistently abnormal.

3. MRI and static radionuclide scanning have proved to be unreliable.

4. Liver ultrasonography can be a useful screening investigation if performed by an expert.

5. Dynamic hepatic scintigraphy measures any reduction in portal venous contribution to the total hepatic blood flow. It has a sensitivity of 83.3% and specificity of 81.5%, in detecting moderate to severe liver fibrosis.

6. Transient elastography (FibroScan): It is a new, non-invasive, rapid, and reproducible method allowing evaluation of liver fibrosis by measurement of liver stiffness. Fibroscan and shear wave elastography are two novel, non-invasive techniques that might be able to assess MTX induced hepatic fibrosis.

7. Proton magnetic resonance spectroscopy (HMRS) is able to measure liver fat content noninvasively. A combination of HMRS and 31 PMRS (which estimates cell membrane turnover and fibrosis) is the most suitable technique for monitoring MTX induced liver injury.[34]

APPROACH AND TREATMENT

APPROACH TO A PATIENT WITH PSORIASIS

A chronic condition like psoriasis can significantly lower quality of life. As a result, treating psoriasis requires addressing both the physical and mental elements of the condition.

The cutaneous psoriasis signs can be treated with a variety of topical and systemic treatments. Treatment options are selected based on the severity of the condition, any pertinent comorbidities, patient preference (including cost and convenience), effectiveness, and assessment of the response of each individual patient. Although pharmaceutical safety is a key factor in treatment decision-making, this must be evaluated against the danger of under-treating psoriasis, which could result in insufficient clinical improvement and unsatisfied patients.

The intended level of illness control and the patient's tolerance for particular treatments are two examples of factors that affect the desired treatment outcome, which varies for each patient. Patients who want their skin illness to go away completely should aim for minimum to no skin involvement with a well-tolerated treatment plan.

The target response for plaque psoriasis after six months is 1% body surface area, according to a panel of psoriasis experts assembled by the National Psoriasis Foundation. The acceptable response for plaque psoriasis after three months of treatment is either less than 3% body surface area involvement or 75% improvement over baseline. However, some patients' values and preferences favour tolerating a higher level of skin involvement and a less severe course of treatment. [36]

I. PSYCHOSOCIAL ASPECTS :

The clinician must be sympathetic and give the patient enough time. When appropriate, the doctor may find it beneficial to physically convey that the patient's psoriasis lesions are neither unattractive nor contagious by touching them with an ungloved hand.

Clinicians should clearly communicate to patients that controlling the condition is the main goal of treatment by outlining appropriate treatment goals. Psoriasis cannot be cured, despite the fact that treatment can significantly improve symptoms for sufferers.

A referral to a charity like the National Psoriasis Foundation is frequently beneficial, as is educating the patient about psoriasis.

Patients with minor skin conditions may nonetheless be severely psychosocially disabled. Psychoactive drug therapy and/or counselling may be helpful for some psoriasis sufferers. [36]

II. CHOICE OF THERAPY :

The initial therapeutic choice for the majority of patients will be between local (topical) and total body (phototherapy or systemic) therapy. Even patients receiving systemic therapy, nevertheless, will probably still require certain topical medications. Topical treatment may alleviate symptoms and reduce the amount of systemic medicine that must be used.

Patients may be divided into extensive (moderate to severe disease) and mild (or limited) illness categories for treatment planning purposes. Patients with mild to moderate skin conditions can frequently be treated with topical medications, while those with moderate to severe conditions may require systemic therapy or

phototherapy. The choice of therapy is also influenced by the location of the disease and the existence of psoriatic arthritis. Hand, foot, or face psoriasis can be severely disabling functionally or socially, and may require more extensive therapy.

More than 5 to 10 percent of the body's surface area, involvement of the face, palm, or sole, or a disease that is otherwise incapacitating are considered to be signs of moderate to severe psoriasis. Since using topical medications to a large area is typically not possible or acceptable for most patients, patients with more than 5% of their body surface area affected are typically candidates for phototherapy or systemic therapy. Topical medications alone rarely work to treat significant disease, and doing so can be expensive and frustrating for the patient-physician relationship. For patients receiving phototherapy or systemic medications for broad involvement, topical medicines are helpful adjuncts for recalcitrant, localized lesions.

The effectiveness of the more recent systemic medicines (biologics) is well established, although cost is a key factor in choosing these treatments. The treatment of moderate to severe plaque psoriasis still involves using tried-and-true methods like methotrexate and phototherapy.
Even for seasoned dermatologists, managing patients with extensive or resistant illness is a problem. However, the difficulty has been somewhat lessened by the availability of biologic drugs. [36]

III. LIMITED DISEASE

Topical corticosteroids and emollients work well to treat limited plaque psoriasis. Alternatives include tar, topical retinoids, and vitamin D analogues (such as calcipotriene and calcitriol) (tazarotene). Although relief might not be as quick as with powerful topical corticosteroids, topical tacrolimus or pimecrolimus

may be used as substitutes or as corticosteroid-sparing treatments for face or intertriginous areas. Another treatment option for recalcitrant diseases is localised phototherapy.

Dermatologists frequently recommend combinations of strong topical corticosteroids plus either calcipotriene, calcitriol, tazarotene, or UVB phototherapy. For immediate management, calcipotriene in conjunction with class I topical corticosteroids is quite successful. Then, for maintenance, calcipotriene alone may be used consistently and the combination with powerful corticosteroids may be used sporadically (on weekends). Combination products like calcipotriene-betamethasone and halobetasol-tazarotene are examples that are marketed for sale. Even though it may take many weeks to get the full advantages of topical therapy, with careful adherence, significant improvement can be noticed in as little as one week.

Because topical treatment adherence can be quite difficult, it is frequently advantageous to keep the treatment plan straightforward and employ delivery methods that the patient is comfortable with. [36]

IV. MODERATE TO SEVERE DISEASE

Phototherapy or systemic treatments such retinoids, methotrexate, cyclosporine, apremilast, or biologic immune-modifying drugs are required for severe psoriasis. Adalimumab, etanercept, infliximab, certolizumab pegol, anti-tumor necrosis factor (TNF) antibodies, anti-IL-12/IL-23 antibodies, anti-IL-17 antibodies, anti-IL-17 receptor antibodies, and anti-IL-23/IL-39 antibodies are among the biologics used to treat psoriasis. Other biologics include secukinumab, ixekizumab, Usually, improvements happen within a few weeks. Dermatologists typically treat people with severe psoriasis. [36]

TOPICAL THERAPIES

1. EMOLLIENTS

Emollients and hydration are effective and affordable psoriasis treatment adjuncts. Itching and soreness are reduced by maintaining soft, moist skin on those with psoriasis. Keeping your skin well hydrated can also help reduce the risk of irritation and eventual Koebnerization (development of new psoriatic lesions at sites of trauma).

The best products are thick creams or ointments like petroleum jelly, especially when used right away after a moisturising bath or shower. In reality, though, the moisturiser that the patient prefers may be the best option. [36]

2. CORTICOSTEROIDS

Despite the development of newer medications, topical corticosteroids continue to be the cornerstone of treatment for topical psoriasis. By altering gene transcription, corticosteroids have an anti-inflammatory, anti-proliferative, and immunosuppressive effect.

The application site, plaque thickness, the efficiency with which the active drug molecule is delivered by the vehicle, the efficiency with which the drug molecule activates corticosteroid receptors, and, perhaps most importantly, compliance all affect the efficacy/potency of a topical corticosteroid.

When selecting the most effective corticosteroid, the place of application must be taken into account to reduce side effects and increase compliance:

A. Potent corticosteroids in a solution vehicle, such as fluocinonide 0.05% or clobetasol propionate 0.05%, are usually recommended for use on the scalp or in the external ear canal. For scalp involvement, clobetasol0.05% shampoo, foam, or spray can be utilised. Patients may prefer an oil or ointment vehicle for scalp involvement if they regularly use scalp oils or ointments for general hair care (a typical practise among people with Afro-textured hair).

B. A low-potency ointment or cream (such as over-the-counter hydrocortisone 1% or prescription-strength 2.5%) is frequently sufficient on the face and intertriginous areas.

C. Strong preparations, such as betamethasone 0.05% or clobetasol propionate 0.05%, are frequently needed for thick plaques on extensor surfaces.

Topical corticosteroids are often applied twice day as part of a regimen. Most patients will get a quick reduction in inflammation with such treatment, but it is unclear whether skin will completely normalise or experience long-term remission. [35]

3. TOPICAL VITAMIN D ANALOGS

The topical vitamin D analogues calcipotriene (calcipotriol), calcitriol, and tacalcitol are used to treat psoriasis. A systematic study indicated that combination therapy with a topical corticosteroid is more successful than either medication alone, even if topical vitamin D analogues are helpful as monotherapy for some patients.

Calcipotriene is available as a cream, solution, ointment, or foam. It can also be found in combinations with betamethasone dipropionate in ointments, suspensions, and foams. In sensitive parts of the skin, calcitriol seems to cause less irritation than calcipotriene does. [36]

4. TAR

Despite newer (and less messy) therapeutic methods, the application of tar is still a well-established method for treating psoriasis. Evidently, the actions of tar are anti-inflammatory and anti-proliferative. As a supplement to topical corticosteroids, tar may be useful. Tar shampoos, creams, lotions, ointments, and oils are readily accessible over-the-counter. Two more recent products are a solution and a foam. Additionally, tar can be blended into lotions and ointments administered to each plaque twice day.[35]

One application per day of topical tar formulations, such as shampoos, lotions, and other products, is recommended. Patients need to be informed that tar products might leave stains on their skin, hair, and clothing. Because tar products are typically messy, it may be beneficial to apply them at night and wear inexpensive nightwear (such as old pyjamas). Patients might not like the way tar products smell.

Making sure the shampoo gets to the scalp should be the main concern. Before rinsing, allow the tar shampoo to sit for 5 to 10 minutes. [36]

5. TAZAROTENE

Two randomised, vehicle-controlled trials including 1303 psoriasis patients found that the topical retinoid tazarotene was both safe and efficient. The 0.05% cream was not as efficient as the 0.1% cream. In another trial, topical fluocinonide 0.05% was compared well with once-daily administration of tazarotene gel, 0.05% or 0.1%. Over the course of the 12-week research, there was little tazarotene absorption, indicating that systemic toxicity is unlikely under long-term medication. According to a tiny uncontrolled investigation on short contact tazarotene, a 20- minute application followed by washing looked to be less uncomfortable than usual use while yet appearing to be equally effective. The use of tazarotene is restricted by irritation; the irritation is diminished by concurrent treatment with a topical corticosteroid. [36]

6. TAPINAROF

Tapinarof is a topical aryl hydrocarbon receptor-modulating drug that may reduce psoriasis by normalisation of the skin barrier, antioxidant action, and modulation of T helper type 17 (Th17) cytokines like interleukin(IL) 17A and IL-17F. In 2022, the FDA approved the use of tapinarof 1% cream to treat adult plaque psoriasis. Once daily, the medication is applied to the affected areas. [36]

7. ROFLUMILAST

A topical phosphodiesterase 4 inhibitor is rolumilast. For the treatment of plaque psoriasis in adults 12 years of age and older, including psoriasis in intertriginous areas, the FDA authorised roflumilast 0.3% cream in 2022. The cream, which is used once daily on the affected areas, is projected to hit the market in 2022.[36]

8. ANTHRALIN

Topical anthralin, also known as dithranol, has been used as a successful psoriasis treatment since the early 20th century. Anthralinin psoriasis's mode of action is unclear, however it may entail anti-inflammatory actions and regulation of keratinocyte differentiation.[36]

9. ULTRAVIOLET LIGHT

Long established as useful for the management of psoriatic skin lesions, ultraviolet (UV) irradiation. UV light may have both anti-inflammatory and anti-proliferative effects (slowing keratinization) (inducing apoptosis of pathogenic T cells in psoriatic plaques). The potential for UV radiation to hasten photodamage and raise the risk of skin cancer must be taken into account while considering UV therapy.[36]

A. CONVENTIONAL MODALITIES :

Narrow band ultraviolet B (UVB) phototherapy, broadband UVB phototherapy, or oral or bath psoralen plus ultraviolet A (PUVA) photo-chemotherapy are all options for administering therapeutic levels of UV radiation. Broadband UVB and narrowband UVB both deliver UVB radiation at wavelengths between 290 and 320 nm. Treatment with a photosensitizer (either oral or bath psoralen) is followed by ultraviolet A (UVA) radiation in photo-chemotherapy (PUVA) (320 to 400 nm).[36]

B. HOME PHOTOTHERAPY

Utilizing a home UVB phototherapy unit that has been recommended by the treating physician is an alternative to office-based phototherapy. Patients who cannot easily access an office-based phototherapy facility, whose schedules do not allow frequent office visits, or for whom the expenses of in-office treatment are higher than those of a home phototherapy unit may prefer this option.[36]

C. EXCIMER LASER

A different option for treating small patches of psoriasis is the excimer laser, a UVB-emitting laser. Compared to conventional phototherapy, far larger doses of UVB can be given to psoriatic plaques during each treatment session since the 308 nm excimer laser exclusively treats affected skin.[36]

- **CANCER RISK**

An increased risk of nonmelanoma skin cancer and melanoma is a concern with PUVA. In patients who have received longer courses of PUVA, ongoing monitoring is recommended. Patients with a history of melanoma or severe nonmelanoma skin cancer should generally avoid phototherapy.[36]

10. SALTWATER BATHS

Psoriasis is improved by natural sunshine exposure. Psoriasis has also been treated using salt water baths and artificial UV exposure, as well as bathing in sea water and exposure to the sun (climatotherapy) (balneophototherapy).[36]

SYSTEMIC THERAPIES

Immunosuppressive or immunomodulatory medications such methotrexate, cyclosporine, apremilast, biologic medicines, and deucravacitinib are available as options for systemic therapy. Systemic retinoids are also used to treat psoriasis because of their positive effects on epidermal proliferation, differentiation, and immunomodulation.

The best treatments for moderate to severe psoriasis are biologic medicines. Their effectiveness is supported by network meta-analyses, which also show that the efficacy of the various biologic therapies varies. In a network meta-analysis of Psoriasis Area and Severity Index (PASI) response data from randomised trials, biologic treatments for psoriasis etanercept, adalimumab, certolizumab pegol, infliximab, ustekinumab, secukinumab, ixekizumab, brodalumab, tildrakizumab[36,37]

1. **Methotrexate**

For more than 50 years, psoriasis has been successfully treated with the folic acid antagonist methotrexate. Additionally, it is successful in treating psoriatic arthritis and psoriatic nail disease. Initial theories on the mechanism of action focused on the anti-proliferative effects of methotrexate on DNA synthesis in

epidermal cells; recent research has supported the idea that the mechanism of action of methotrexate is its immunosuppressive effects on activated T lymphocytes. [36]

HEPATOTOXICITY

Use of an alternative systemic medication should be taken into consideration for patients who have one or more risk factors for methotrexate-induced hepatotoxicity. History of alcohol use greater than moderate is a risk factor for methotrexate-induced hepatotoxicity. persistently abnormal results from liver function tests, liver disease in the past, such as chronic hepatitis B or C, Diabetes mellitus, obesity, and a history of genetic liver illness (such as hemochromatosis) a history of having used medications or chemicals that are hepatotoxic, Hyperlipidemia.[36]

2. ACITRETIN

Patients with severe psoriasis, including pustular and erythrodermic types, as well as those with HIV-associated psoriasis, are treated with systemic retinoids (vitamin A derivatives). Acitretin is the preferred retinoid for psoriasis. In a pilot study, acitretin therapy produced good to exceptional results in 6 out of 11 individuals with psoriasis and HIV infection, with four of them completely curing their skin condition. The typical acitretin dosage ranges from 25 mg every other day to 50 mg daily. The entire benefit of acitretin could not become apparent for three to six months due to the comparatively late onset of impact.[38]

3. CYCLOSPORINE

Patients with severe psoriasis can benefit from the T cell suppressor cyclosporine. The typical oral dose ranges from 3 to 5 mg/kg each day. In most cases, progress is visible within four weeks. If a modified micro-emulsion version of cyclosporine that is more gradually absorbed is administered, lower doses (1 to 3 mg/kg per day) are more suitable.

Since renal toxicity and hypertension are frequent side effects that frequently prevent psoriasis patients from using cyclosporine over the long term, close monitoring is necessary.[36]

4. APREMILAST

Another oral medication for the treatment of plaque psoriasis is apremilast, a phosphodiesterase 4 inhibitor. The synthesis of many cytokines implicated in the development of psoriasis is decreased when phosphodiesterase 4 is inhibited. Apremilast is expensive, costing more than methotrexate but less than biologics. The medication may also be useful for treating psoriatic arthritis. [36]

5. BIOLOGIC AGENTS

Treatment options for moderate to severe plaque type psoriasis include biologic medicines. The biologic treatments for psoriasis that are currently available offer outstanding short- and long-term efficacy as well as good tolerability. Etanercept, infliximab, adalimumab, ustekinumab, secukinumab, ixekizumab, brodalumab, guselkumab, tildrakizumab, risankizumab, and certolizumab pegol are a few examples of biologic therapy.

A. TNF-ALPHA INHIBITORS: Etanercept, infliximab, adalimumab, and certolizumab pegol are biologic tumour necrosis factor (TNF)-alpha inhibitors used to treat psoriasis.

B. INHIBITORS OF THE IL-17 PATHWAY: Among the medications used to treat psoriasis include secukinumab, ixekizumab, brodalumab, and bimekizumab, which are inhibitors of the interleukin (IL) 17 pathway.

C. INHIBITORS OF IL-23 AND RELATED CYTOKINES : Ustekinumab, Guselkumab, Tildrakizumab, and Risankizumab are anti-interleukin (IL) 23 active antipsoriatic medications.

D. **OTHER**: In India, psoriasis can be treated with itolizumab, a biologic drug that is a monoclonal antibody against the T cell costimulator CD6.

E. **TYROSINE KINASE INHIBITOR**: Deucravacitinib is an oral selective tyrosine kinase 2 (TKY2) inhibitor. This kinase controls the signalling of cytokines involved in the pathogenesis of psoriasis, namely IL-23. Deucravacitinib was given FDA approval in 2022 to treat people with moderate to severe plaque psoriasis who are also suitable for systemic therapy or phototherapy. [19]

6. EMERGING THERAPIES

A. THERAPIES TARGETING THE TH17 PATHWAY : Interleukins (ILs) in the T helper type 17 (Th17) pathway, including IL-23 and IL-17, are still being studied as potential therapeutic targets because of their critical roles in the pathogenesis of psoriasis. A humanised monoclonal IL-17 antibody called vunakizumab has shown promise in a phase 2 trial.

B. SMALL MOLECULES: Other prospective treatments include a range of tiny compounds that aim to block cellular signalling, which is crucial for the spread of the inflammatory response. Small compounds that inhibit Janus kinases (JAKs), lipids, protein kinase C inhibitors, selective tyrosine kinase 2 (TYK2) inhibitors, and the topical phosphodiesterase 4 inhibitor crisaborole are some examples of small molecules being investigated for the treatment of psoriasis. For a few examples of tiny compounds, see topical crisaborole, oral tofacitinib, and baricitinib.[36]

MULTIMODALITY THERAPEUTIC STRATEGIES

To increase the benefits of systemic drugs and reduce the serious side effects, multimodality therapeutic strategies are use like as follows.

1. COMBINATION THERAPY

Two therapeutic agents are used simultaneously, in smaller doses to obtain better results with reduced toxicities. One of them is an "accelerator," for example, cyclosporin, UVB or methotrexate ; while the other agent is the "maintainer," for example, psoralen plus ultraviolet A radiation or acitretin. The dose of the accelerator is tapered with obtaining maximal therapeutic response, while the maintainer is continued. After the clearance of psoriasis, usually one agent is discontinued and the safer of the two is used as maintenance therapy.

2. ROTATIONAL THERAPY

The therapeutic agents are rotated at regular intervals (2 years), from one agent to another to prevent cumulative toxicity of individual drugs. The transition between medications may involve a brief period of overlap. In rotational therapy, different treatment regimens are rotated before significant toxicity to individual drug develops. The therapeutic agent is used for specified period (usually 1–2 years) after which an alternative drug is started. This allows long-term treatment, minimizes chronic toxicity and also decreases resistance to the drug.

3. SEQUENTIAL THERAPY

Taking advantage of the fact that some therapeutic agents produce fast results while others are best suited for maintaining remission; the drugs are used in a deliberate sequence, moving gradually from one therapy to another with a brief period of overlap. It involves three steps: clearing or quick-fix phase, transitional phase, and maintenance phase. Sequential therapy regimen is applicable for both topical and systemic therapies. The aim is to produce a fast remission minimizing long-term toxicity and maintaining a prolonged disease free state.[39]

SHEAR WAVE ULTRASOUND ELASTOGRAPHY

A common medical imaging method with numerous clinical uses is ultrasound. It has been used in clinical practise for more than 40 years and is well-known for being simple to use, real-time capable, portable, and affordable. It allows for the construction of morphological images of organs based on the propagation of mechanical waves, and more specifically on high frequency compressional waves, or ultrasound, but it lacks fundamental and quantitative data on tissue elastic properties. In fact, the bulk modulus that controls the propagation of ultrasound is almost homogeneous in different biological tissues and is independent of tissue elasticity. [40]

The goal of elastography, whose research began roughly 20 years ago, is to image tissue stiffness, which offers extra information that is therapeutically pertinent. It is possible to map the stiffness either by imaging shear waves, mechanical waves whose propagation is controlled by the tissue stiffness rather than its bulk modulus (quasi-static methods), or by analysing the strain in the tissue under a stress.[41]

Elastography tries to quantitatively photograph the Young's E modulus, the physical parameter associated to stiffness, from a physics perspective. This has two significant benefits:[42]

1. The Young's modulus, indicated E, shows significant variances across various biological tissues, making it perfect for the distinction of various tissues with excellent contrast;

2. The stiffness of a tissue is defined by the Young's modulus, which is an accurate quantitative representation of a clinician's palpation and has useful diagnostic value.

ULTRASOUND ELASTOGRAPHY PHYSICS

Elastography measures tissue elasticity, which is a tissue's propensity to resist deformation when subjected to a force or to regain its original shape when the force is removed. Elasticity can be expressed by the following equation, assuming that a material is completely elastic and that its deformation has no time dependence (i.e. viscosity).[43]

- Hooke's Law: $\sigma=\Gamma\cdot\varepsilon$ (Eqn. 1)

where strain (ε) is the expansion per unit length with no dimensions (Figure 22, second row), stress (σ) is the force per unit area with kilopascals (i.e., N/m2), and the elastic modulus (Γ) connects the two with kilopascals (Figure 22, third row).

Young's modulus (E), shear modulus (G), and bulk modulus are the three categories of elastic moduli that are determined by the type of deformation (K). [42]

1. When a normal stress (n) causes a normal strain (n), where normal is perpendicular to the surface (Figure 22, first column), the following equation gives the definition of Young'smodulus E:
   - $\sigma_n = E\cdot\varepsilon_n$ (Eqn. 2)

2. When a shear stress (s) results in a shear strain (s), and the shear is perpendicular to the surface, the shear modulus G is given by the equation shown in the second column of Figure 22:
   - $\sigma_s = G\cdot\varepsilon_s$ (Eqn. 3)

3. 3. The following equation, which is shown in Figure 22, third column, describes the bulk modulus K when a normal inward force or pressure (B) results in a bulk strain or change in volume (B):
   - $\sigma_b = K\cdot\varepsilon_b$ (Eqn. 4)

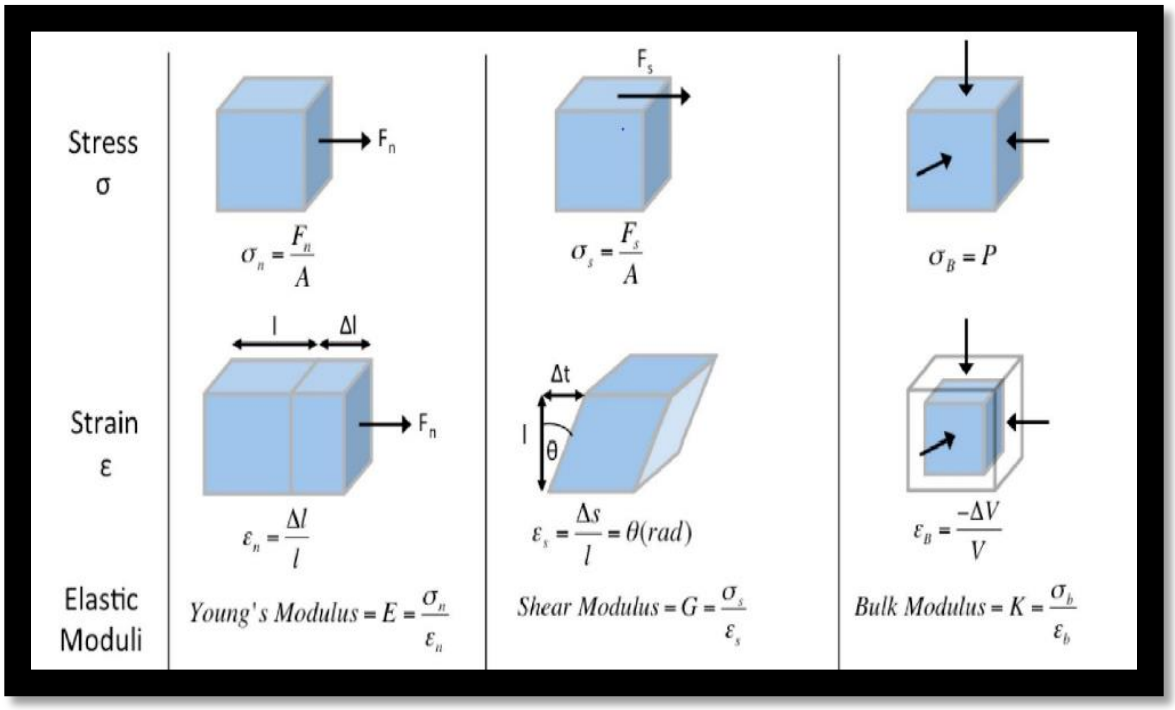


Figure 22 Physics of ultrasound elastography

Physics and theories for ultrasound elastography deformation Stress σ (force per unit area, top row), strain ε (expansion per unit length, middle row), and elastic modulus (bottom row) can all be used to characterise static deformations of completely elastic materials Γ (stress divided by strain, bottom row). This is used for the normal inward or pressure force used in ultrasound elastography, which is perpendicular to the surface in the first column, shear force, which is tangential to the surface in the second column, and bulk force.

Adapted: [42]

In ultrasonography, longitudinal waves and shear waves both propagate as waves.

1. Using the bulk modulus K, longitudinal waves are defined as having particle motion perpendicular to the direction of wave propagation (Figure 23c):

   - $C_L = \sqrt{(K/\rho)}$ (Eqn. 6)

where the average longitudinal wave speed (cL) in soft tissues is 1540 m/s. Even though longitudinal waves are employed in B-mode ultrasound, the comparatively minor variations in wave speed and, consequently, K between various soft tissues make it difficult to get sufficient tissue contrast for elastography measurements.

2. According to the shear modulus G, shear waves are characterised as having particle motion that is perpendicular to the direction of wave propagation (Figure 23b):

   - $C_L = \sqrt{(G/p)}$ (Eqn. 7)

where the shear wave speed (cS) in soft tissues is roughly 1 to 10 m/s. Soft tissues have low wave speed, allowing for large G variations between tissues, which provides enough tissue contrast for elastography studies.

As a solid seeks to maintain its original volume, the three different forms of deformations and elastic moduli are related rather than independent, with the effectiveness of this effort being shown by the Poisson's ratio (v). Young's modulus E and shear modulus G have the following relationship, albeit the proof is beyond the purview of this analysis:

- $E = 2(v + 1)G$ (Eqn. 8)

Soft tissue has a large water content, hence the Poisson's ratio v of an incompressible medium is close to 0.5, and E = 3G. Combining this with Equation 7 yields: [44]

- $E = 3G = 3pc_s^2$ (Eqn. 9)

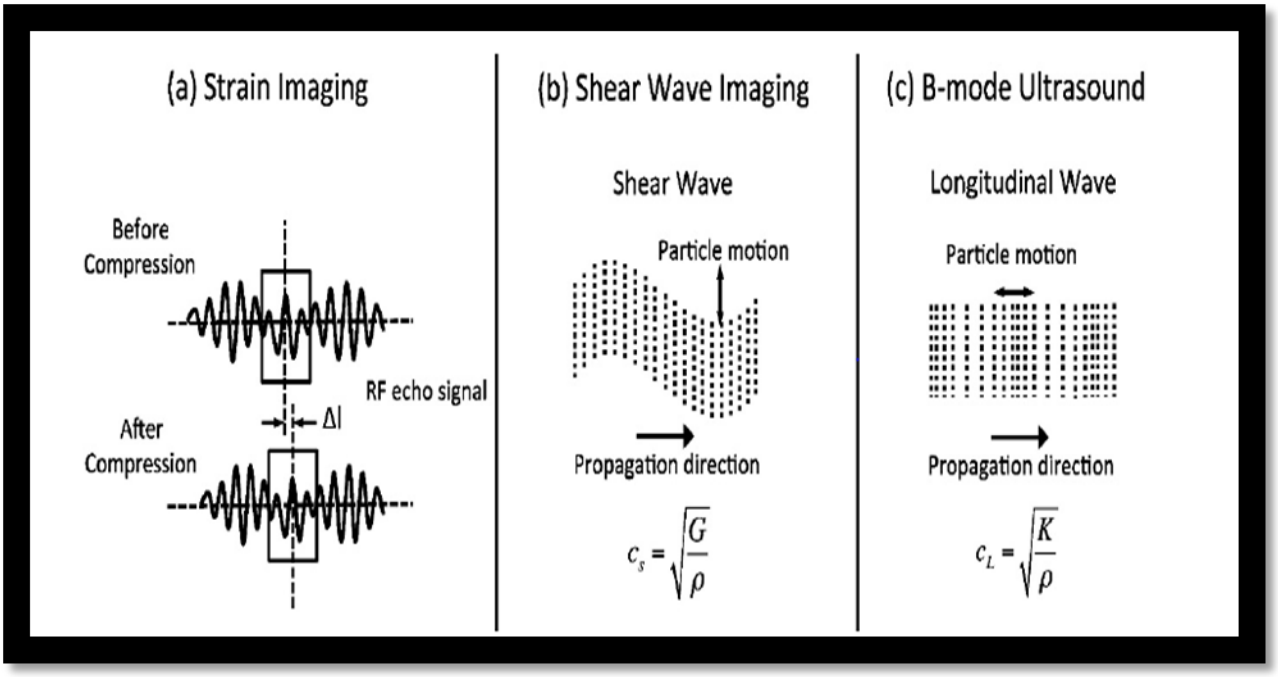


Figure 23: Physics and measuring techniques for ultrasound elastography.

The correlation of RF echo signals between search windows (boxes) in the states before and after compression is used in strain imaging (a) to measure tissue displacement. Shear wave speed cS and shear modulus G are connected in shear wave imaging (b), where particle motion is perpendicular to the direction of wave propagation. In B-mode ultrasound (c), the longitudinal wave speed cL and bulk modulus K are connected, and particle motion is parallel to the direction of wave propagation.

Adapted[42]

ULTRASOUND ELASTOGRAPHY TECHNIQUES

These principles allow us to categorise the many Ultrasound Elastography techniques that are now available according to the physical quantity that is being measured (Figure 24).

1. Strain imaging: Equation 2 is utilised to qualitatively assess the Young's modulus E. In this technique, a normal stress n is given to tissue, and the normal strain n is measured (Figure 22, first column).[42]

2. Shear wave imaging (SWI): In this method, tissue is subjected to a dynamic stress by means of an acoustic radiation force in point shear wave elastography (pSWE) and 2D shear wave elastography or a mechanical vibrating device in 1D transient elastography (TE) (2D-SWE). In order to determine the shear wave speed cs or the Young's modulus E, the excitation's shear waves are measured parallel to the 1D transient elastography excitation or perpendicular to the application of acoustic radiation force.[42]

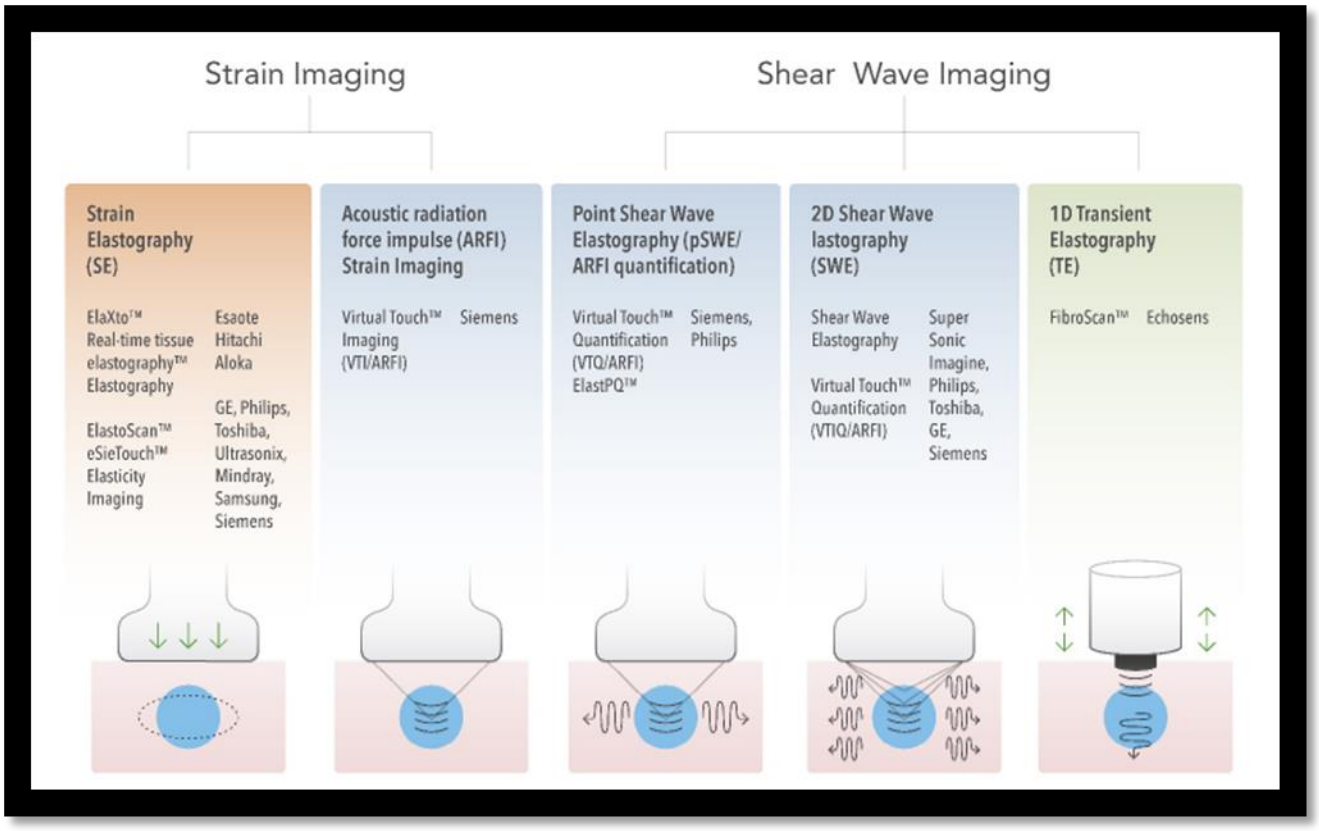


Figure 24: Techniques for ultrasound elastography.

By the physical quantity being measured, the following USE methods are currently available: 1) strain imaging (left), and 2) shear wave imaging (right). Methods of excitation include quasi-static mechanically induced displacement by active external compression or passively induced physiologic motion (orange), dynamic mechanically induced compression by "thumping" a transducer at the tissue's surface to produce shear waves (green), and dynamic ultrasound-induced tissue displacement and shear waves by acoustic radiation force impulse excitation (green) (blue) respectively.

Adapted[42]

SHEAR WAVE IMAGING

SWI uses a dynamic stress to produce shear waves in the parallel or perpendicular dimensions as opposed to strain imaging, which analyses physical tissue displacement parallel to the applied normal stress. Both qualitative and quantitative estimates of tissue elasticity can be obtained from the shear wave speed measurement. There are currently three technological methods for SWI:

(1) 1D-TE (1 Dimension Transient Elasticography),

(2) pSWE (2 Dimension Shear Wave Elasticography), and

(3) 2D-SWE (Figure 24). [42]

TWO-DIMENSIONAL (2D) SHEAR WAVE ELASTOGRAPHY

The most recent SWI technique that makes advantage of the acoustic radiation force is two-dimensional (2D) SWE. As opposed to ARFI strain imaging and pSWE, which use a single focal point, many focal zones are interrogated quickly, quicker than the shear wave speed. As a result, a nearly cylindrical shear wave cone is formed, enabling real-time 2D monitoring of shear waves for the development of quantitative elastograms as well as the measurement of shear wave speed or Young's modulus E. The 2D-SWE technology is currently used in the following commercially available systems: Acoustic Structure Quantification ^{TM} (ASQ) by Toshiba, Virtual Touch ^{TM} Imaging Quantification (VTIQ/ARFI) by Siemens, Shear Wave TM Elastography by Super Sonic Imagine (SSI), Shear Wave Elastography by Philips, and 2D-SWE by GE Healthcare. This method has the benefit of allowing the operator to be led by both anatomical and tissue stiffness information through the real-time display of a colour quantitative elastogram superimposed on a B-mode image.[45]

CLINICAL APPLICATIONS OF ULTRASOUND ELASTOGRAPHY IN LIVER

DIFFUSE LIVER DISEASE : A common pathway from the various causes of CLD, such as hepatitis viral disease, nonalcoholic fatty liver disease, alcoholic liver disease, and autoimmune liver disease, leads to liver fibrosis and ultimately cirrhosis, increasing the risk of hepatocellular carcinoma, portal hypertension (PH), and hepatic insufficiency. However, if the underlying cause of liver fibrosis is treated, the patient is given immunosuppressive, anti-inflammatory, or antiviral medications, or they receive new adjunctive anti-fibrotic treatments like antioxidants and angiotensin inhibitors, hepatic fibrosis can be reversed, stabilised, or prevented. The METAVIR score is the most popular histopathologic grading system, and liver biopsy is now the best reference standard for assessing and classifying stages of liver fibrosis/cirrhosis. The fibrosis stages, according to this system, are: F0 stands for a normal liver, F1 for slight fibrosis, F2 for moderate fibrosis, F3 for severe fibrosis, and F4 for cirrhosis.[46]

However, there are a few drawbacks to liver biopsy. It is invasive and, in around 20% of cases, might result in minor problems including brief discomfort. In 1.1% of liver biopsies, serious complications such bleeding, hemobilia, bile peritonitis, bacteremia, sepsis, pneumothorax, hemothorax, and even death take place. Undersampling limits liver biopsy as well; a typical biopsy core only represents around 1/50,000 of the total liver volume. The degree of disagreement between pathologists while grading liver fibrosis/cirrhosis ranges from 0.5 to 0.9, depending on the pathologist's level of experience. [42]

LIVER 2D SHEAR WAVE ELASTOGRAPHY

121 chronic HCV patients participated in the initial study comparing 2D-SWE (SSI) with 1D-TE, which used liver biopsy as the gold standard. In determining substantial fibrosis (F2), 2D-SWE performed better than 1D-TE (AUROC of 0.92 vs. 0.84; p=0.002). Using liver biopsy as the gold standard, an intra-individual prospective comparison study comparing 2D-SWE (SSI), pSWE (VTQ/ARFI), and 1D-TE (FibroscanTM) in 349 consecutive patients revealed that 2D-SWE had higher diagnostic accuracy than 1D-TE in the diagnosis of severe fibrosis (F3) and higher than pSWE in the diagnosis of significant fibrosis (F2) (AUROCs of 0.88 In a different investigation, the AUROCs for 2D-SWE, pSWE, and 1D-TE did not significantly differ from one another. [47]

The World Federation for Ultrasound in Medicine and Biology (WFUMB) guidelines only recommend using liver USE to distinguish between significant (F2) or advanced fibrosis (F3) from non-significant fibrosis (F0-F1) due to its current limitations in differentiating between individual fibrosis stages, despite the fact that the main clinical application of liver USE is to detect, stage, and monitor liver fibrosis in CLD patients. In a similar vein, the Society of Radiologists in Ultrasound Consensus Conference Statement suggests using liver USE to distinguish between patients with minimum or no fibrosis (F0-F1) and those with severe fibrosis or cirrhosis (F3-F4). Technical advancements to increase the precision of fibrosis stage distinction and standardisation of elastography techniques among vendors are two future initiatives to enhance the use of liver USE. These initiatives will enable comparison of results across studies from various sites**.** [42]

MATERIALS AND METHODS

MATERIALS AND METHODS

1. SOURCE OF DATA:

All patients diagnosed with Chronic plaque Psoriasis visiting clinic of Dermatology, Venereology and Leprosy in RL Jalappa Hospital and Research Centre, Kolar between January 2021 to July 2022.

2. STUDY DESIGN: CROSS SECTIONAL STUDY

3. SELECTION CRITERIA

- **INCLUSION CRITERIA**

  A. All patients presenting with Psoriasis

  B. Psoriasis patients already on methotrexate therapy.

- **EXCLUSION CRITERIA**

  A. Patients with Psoriasis meeting criteria for alcohol dependence syndrome and Hepatitis.

4. SAMPLE SIZE CALCULATION:

Sample size of the present study is estimated based on Sample size of the present study is estimated based on the sensitivity of 81% for detection of liver fibrosis in patients with psoriasis, 95% confidence interval considering an absolute error of 10%. The estimated sample size is 60.

$$\text{Sample size} = \frac{Z_{1-\alpha/2}{}^2 p(1-p)}{d^2}$$

Here

$Z_{1-\alpha/2}$ = Is standard normal variate (at 5% type 1 error ($P<0.05$) it is 1.96 and at 1% type 1 error ($P<0.01$) it is 2.58). As in majority of studies P values are considered significant below 0.05 hence 1.96 is used in formula.

p = Expected proportion in population based on previous studies or pilot studies.

d = Absolute error or precision – Has to be decided by researcher.

5. STATISTICAL ANALYSIS:

Collected data Will be coded and entered into an excel data base. All the quantitative measures will be presented by (mean $\pm$ SD) and confidence interval, qualitative measures by proportions and confidence interval. The significance of differences in proportions will be done using Chi square test /Fischer's exact test and P value<0.05 will be considered to be statistically significant.

6. METHOD OF COLLECTION OF DATA (INCLUDING SAMPLING PROCEDURE)

Sampling technique: OPD estimates 7 cases per month accounting for 126 cases for one and half years

and required sample size being 60, considering sample interval of 2, these 60 cases will be recruited by systematic random sampling technique.

Data will be collected after obtaining written informed consent from all patients who are willing to participate in the study. In every case detailed history and history of associated diseases will be noted down. Detection of liver fibrosis will be made by shear wave ultrasound elastography.

Quantification of liver fibrosis by shear wave elastography. All Ultrasound examinations will be performed using Philips EPIQ5 system equipped with shear wave point quantification using curvilinear broadband transducer (C5 - 1)

This technique generates shear waves inside the tissue using radiation force from a focused ultrasound beam. The ultrasound machine, monitoring the shear-wave propagation using a Doppler-like ultrasound technique, measures the speed of propagation, which is then used to compute tissue stiffness, also known as the Young modulus (YM) of elasticity, in kilopascals (kPa).

Liver stiffness: F1: 6.48–6.60 kPa, F2: 6.60–8.07 kPa, F3: 8.07–9.31 kPa, and F4: >9.31 kPa.

SWE will be performed by one sonographer. Each SWE acquisition comprises 10 sequential measurements of the liver which are obtained at a depth of 8cm from the skin surface. Patients will not sedate. Informed consent will be taken from the patients and this study will be conducted after Institution Ethical Committee clearance. Relevant laboratory investigations will be done. ICD 10 diagnostic criteria will be used to exclude alcohol dependent patients .The data thus collected will be entered in to a specially designed Case Record Form and subjected to statistical analysis like proportion and Chi-square test.

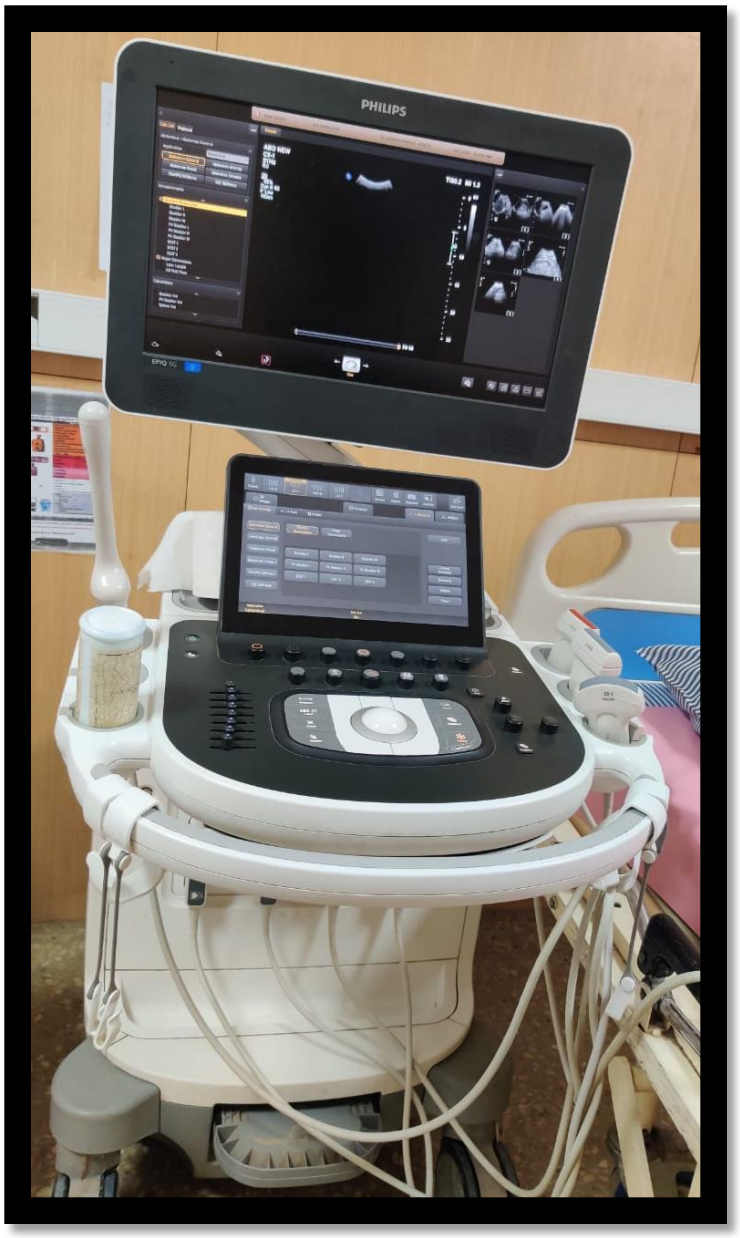


Figure 25: Philips EPIQ5 system equipped with shear wave point quantification using curvilinear broadband transducer (C5 - 1)

STATISTICAL ANALYSIS

Data was entered into Microsoft excel and analysed using SPSS version 26. Categorical data was presented as frequency and percentage, Continuous data was presented as mean and SD. Graphically data was presented as pie chart, bar diagram and Multiple bar diagram. Association of Non-alcoholic fatty liver disease score ultrasound shear wave elastography scores and BMI was done using Chi square. Spearman rank corelation was used to find the correlation between Non-alcoholic fatty liver disease score with other parameters. P value <0.05 is considered to be statistically significant.

RESULTS

Table 3: Distribution of study participants according to gender

Gender	Frequency	Percentage
Female	24	40.0
Male	36	60.0
Total	60	100.0

Out of 60 study participants, 24(40%) were female and remaining (60%) were males.

Figure 26: Pie Chart depicting distribution according to gender, n=60

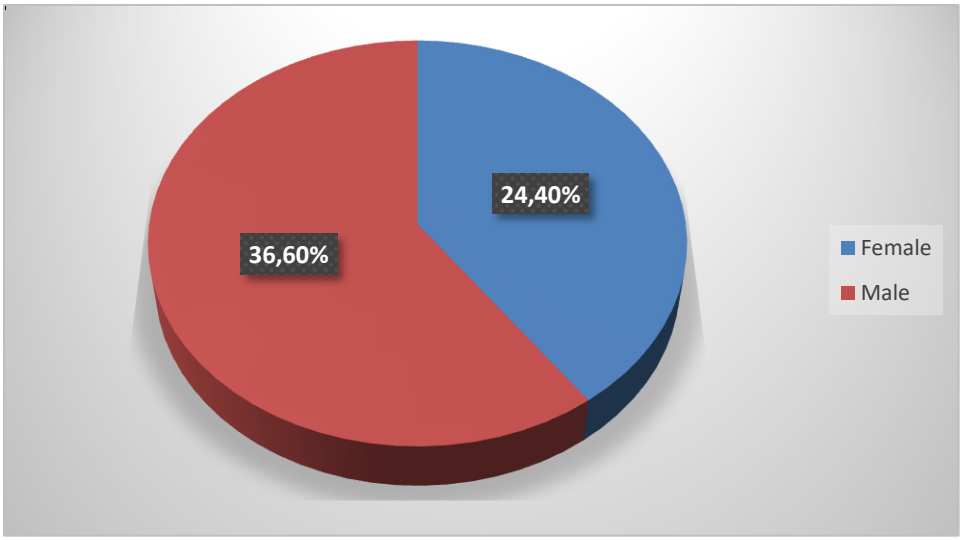


Table 4: Distribution of study participants according to age group

Age (in years)	Frequency	Percentage
12-29	14	23.3
30-39	18	30.0
40-49	12	20.0
50-59	9	15.0
60-69	6	10.0
70-79	1	1.7
Total	60	100.0

The mean age of the study participants was 40.63 with standard deviation of 13.802 years. The minimum age being 12 and maximum being 75 years. It is observed that 14(23.3%) belongs to age 1 to 29 years,18(30%) belongs to age 30 to 39 years, 12(20%) belongs to age group 40 to 49 years, 9(15%) belongs to age group 50 to 59 years and remaining belongs to age more than 60 years.

Figure 27: Bar diagram depicting distribution according age groups (in years)

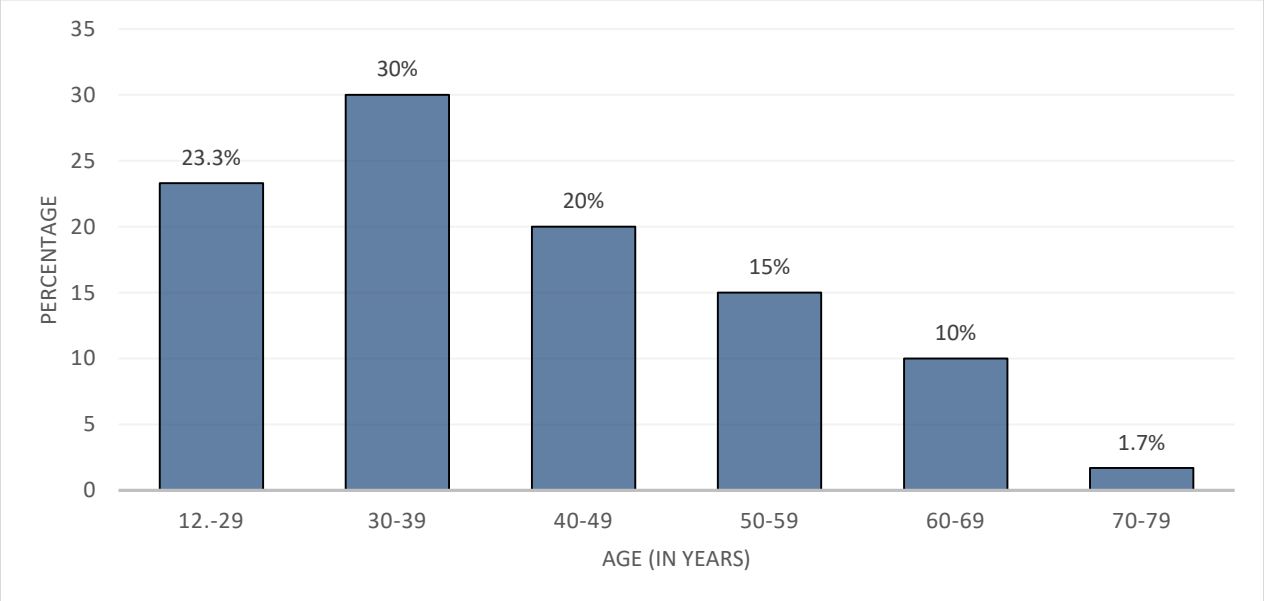


Table 5: Distribution of study participants according to variants

Variants**	Frequency	Percentage
Chronic Plaque Psoriasis	43	71.1
Psoriatic Arthritis	3	5.0
Guttate Psoriasis	1	1.7
Nail Psoriasis	1	1.7
Pustular Psoriasis	4	6.7
Palmo-Plantar Psoriasis	8	13.3
Scalp Psoriasis	3	5.0

**Multiple variants were observed

Table 3 shows the distribution of the study participants according to variants observed. Among few study participants multiple variants were seen. Most (71.1%) had Chronic Plaque Psoriasis followed by Palmo-Plantar Psoriasis (13.3%), Pustular Psoriasis (6.7%) Scalp Psoriasis and Psoriatic Arthritis (5%) each. 1.7% each had Guttate Psoriasis and Nail Psoriasis.

Figure 28: Bar diagram depicting distribution according variants

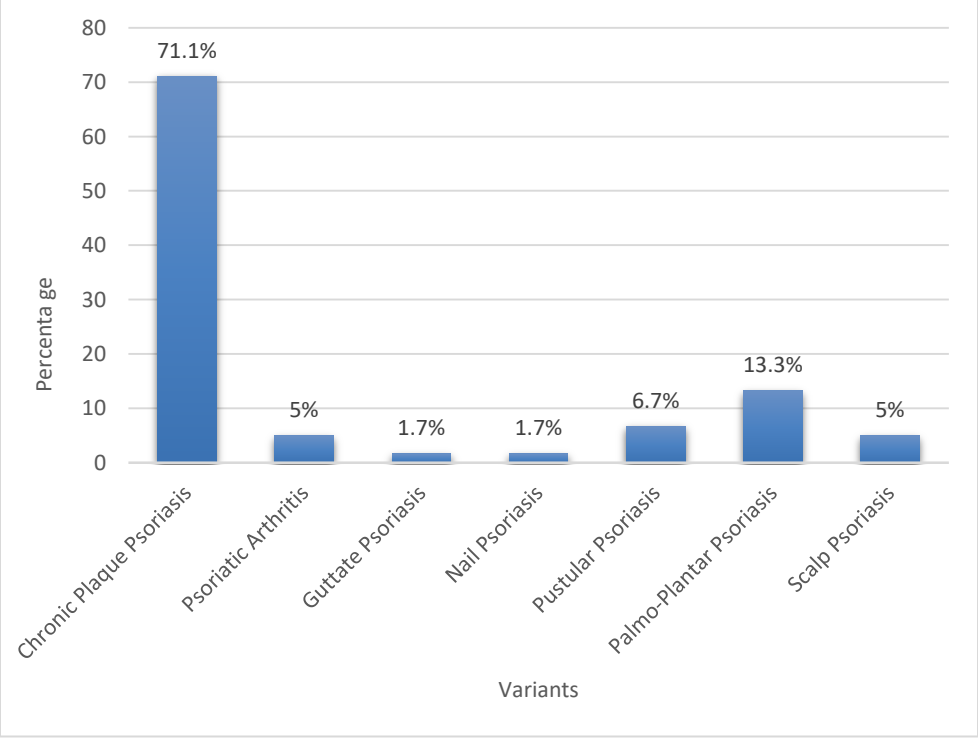


Table 6: Distribution of study participants according to comorbidities

Comorbidities **	Frequency	Percentage
Diabetes Mellitus	4	6.7
Hypertension	7	11.7
Obesity	4	6.7

**Multiple comorbidities were observed

Out of total, 11.7% had hypertension, 6.7% each had Diabetes Mellitus and Obesity.

Figure 29: Bar diagram depicting distribution according to comorbidities

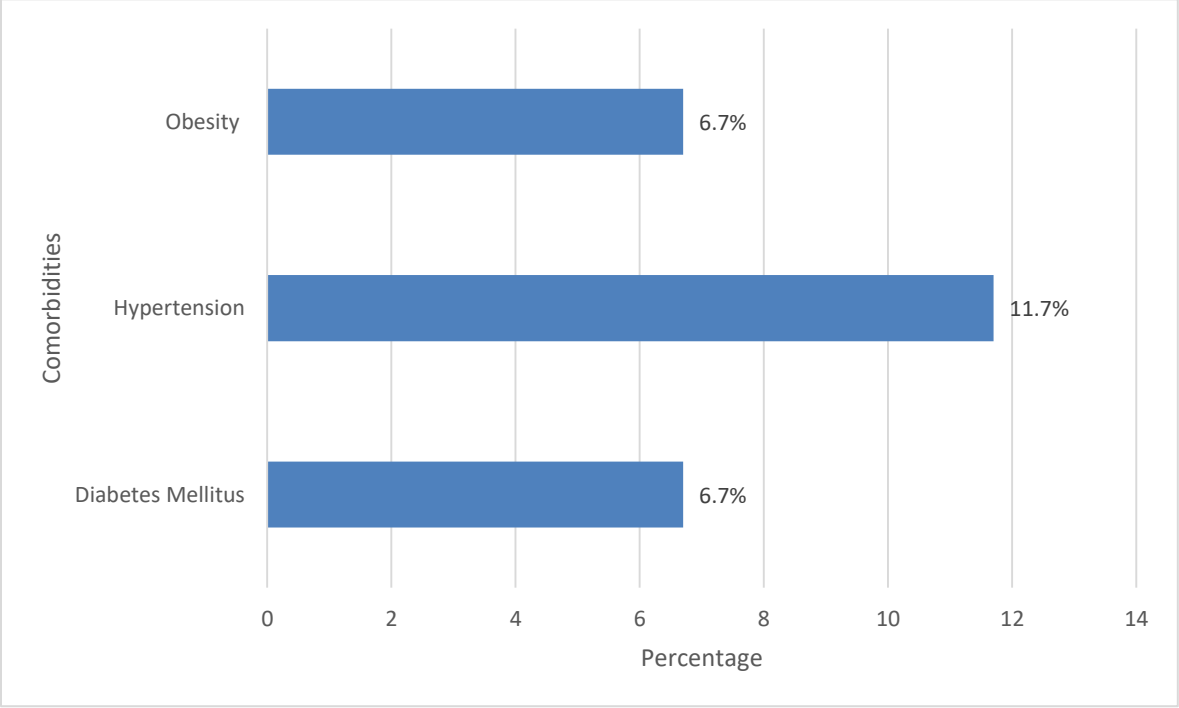


Table 7: Distribution of study participants according to BMI

BMI	Frequency	Percentage
Normal	17	28.3
Overweight	39	65.0
Obese	4	6
Total	60	100.0

It is observed that none were underweight. Most (65%) were overweight followed by normal (28.3) and obese (6%).

Figure 30: Pie Chart depicting distribution according to BMI, n=60

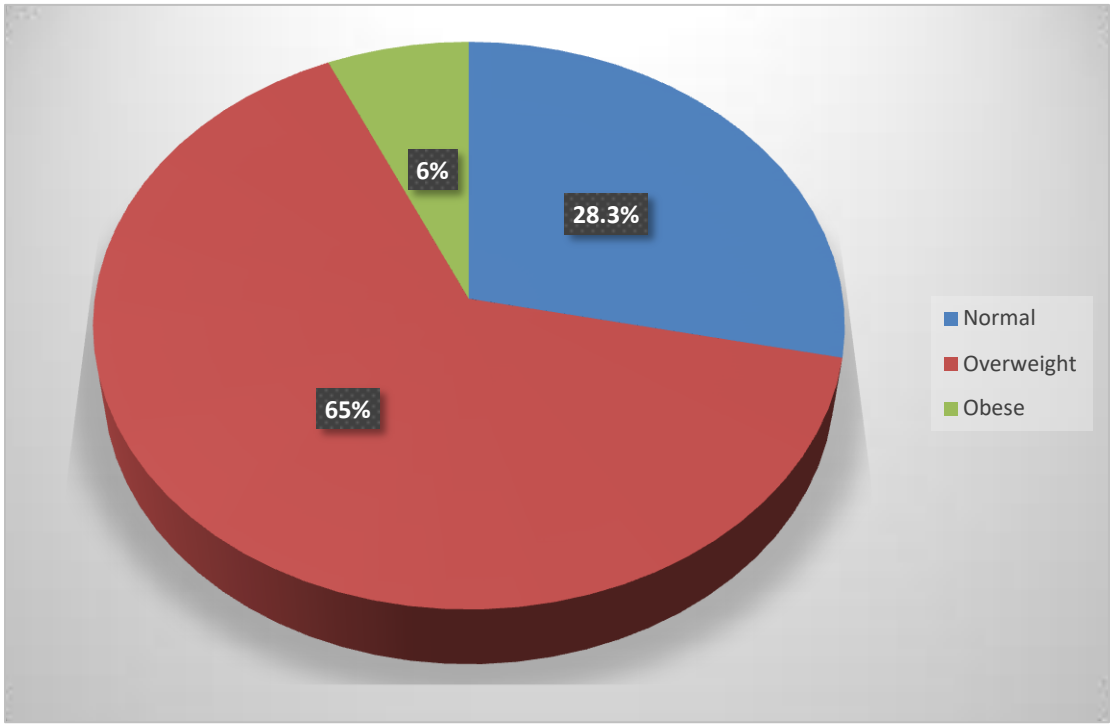


Table 8: Distribution according to ultrasound shear wave elastography at baseline

Ultrasound shear wave elastography(kp)	Frequency	Percentage
1-5	28	46.7
6-7	32	53.3
Total	60	100.0

At baseline, 46.7% had ultrasound shear wave elastography ranging between 1 to 5kp and remaining above 6kp **(**53.3%)

Figure 31: Pie Chart depicting distribution according to ultrasound shear wave elastography at baseline, n=60

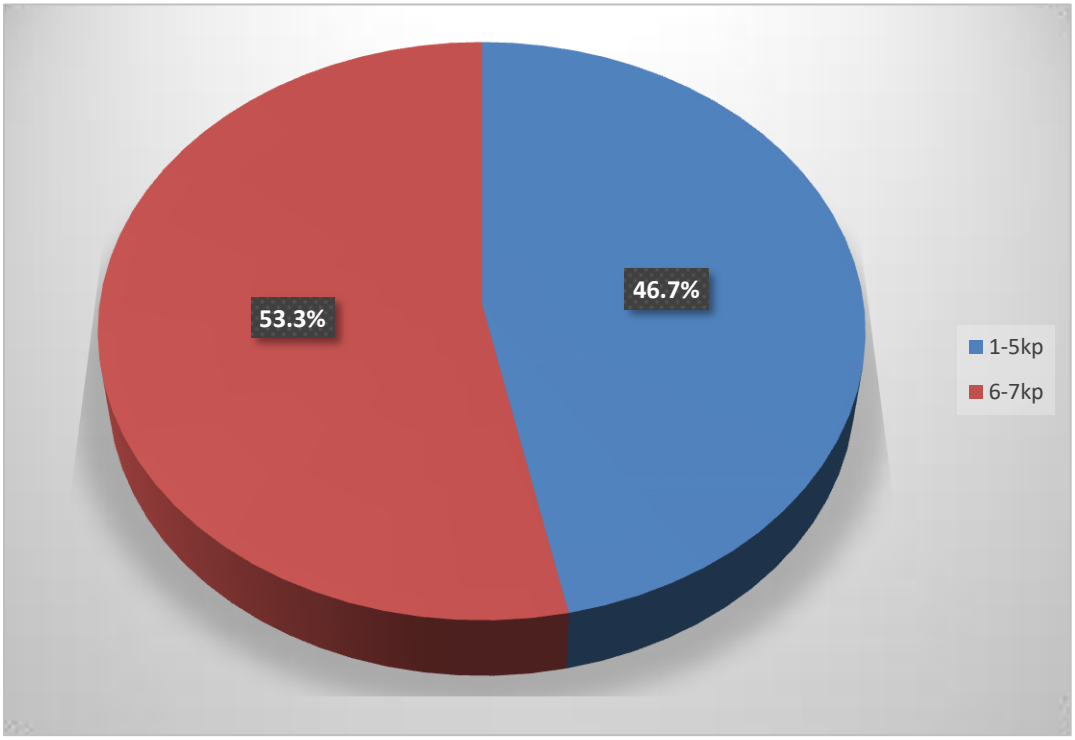


Table 9: Distribution according to ultrasound shear wave elastography at 6 months

ultrasound shear wave elastography (kp)	Frequency	Percentage
1-5	27	45.0
6-7	33	55.0
Total	60	100.0

At 6 months, 45% had ultrasound shear wave elastography ranging between 1 to 5kp and remaining above 6kp (55%).

Figure 32: Pie Chart depicting distribution according to ultrasound shear wave elastography at 6 months, n=60

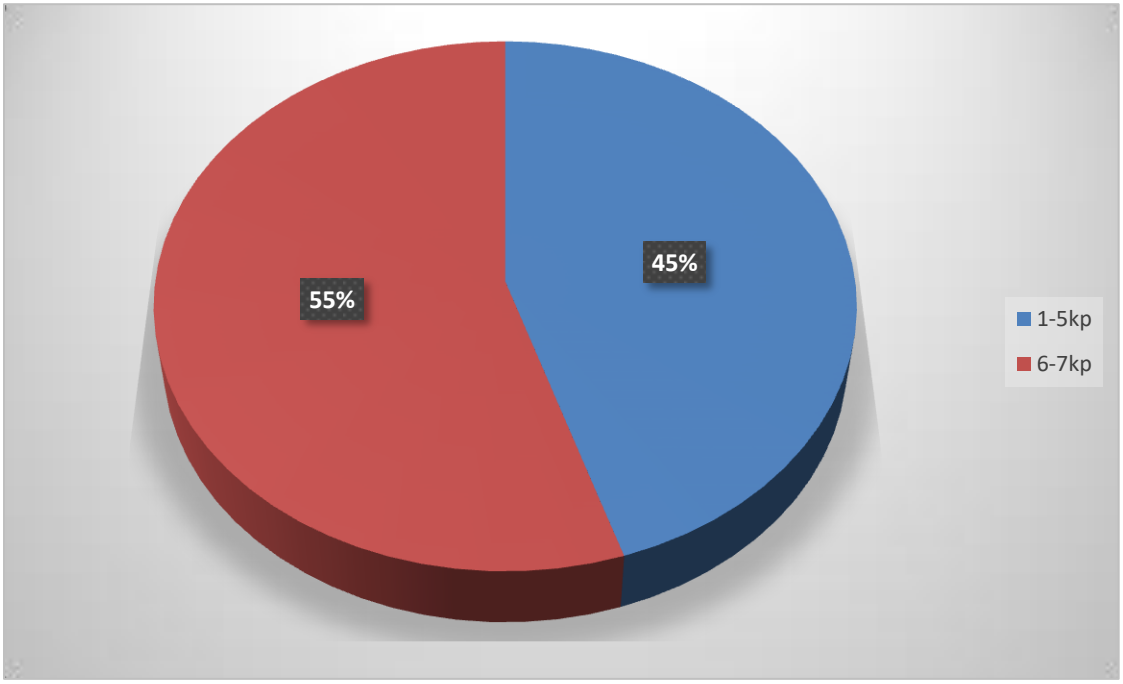


Table 10: Distribution according to Nonalcoholic fatty liver disease score at baseline

Non-alcoholic fatty liver disease score		Frequency	Percentage
Mild	< -1.455	31	51.7
Moderate	-1.455 to 0.676	29	48.3
Total		60	100.0

It is observed that almost half of the study participants had mild level of Non-alcoholic fatty liver disease score.

Figure 33: Pie Chart depicting distribution according Non-alcoholic fatty liver disease score, n=60

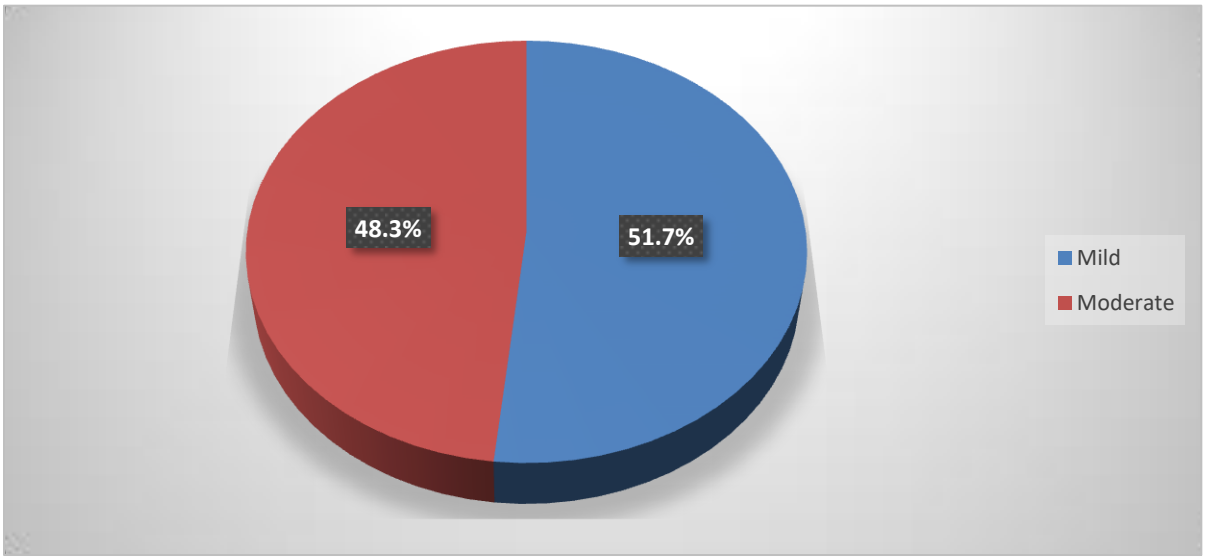


Table 11: Distribution according to Methotrexate cumulative dose

Methotrexate cumulative dose (Mg)	Frequency	Percentage
0-300	16	48.5
301-600	12	36.3
601-900	2	6.1
901-1200	2	6.1
>1200	1	3.0
Total	33	100.0

Table 11 shows 33 patients out of 60 were given Methotrexate. About 16 patients (48.5%) patients were given Methotrexate with cumulative dose of less than 300mg. 12 patients (36.3%) were given doses between 301to 600mg.

Figure 34: Bar diagram depicting distribution according to Methotrexate cumulative dose

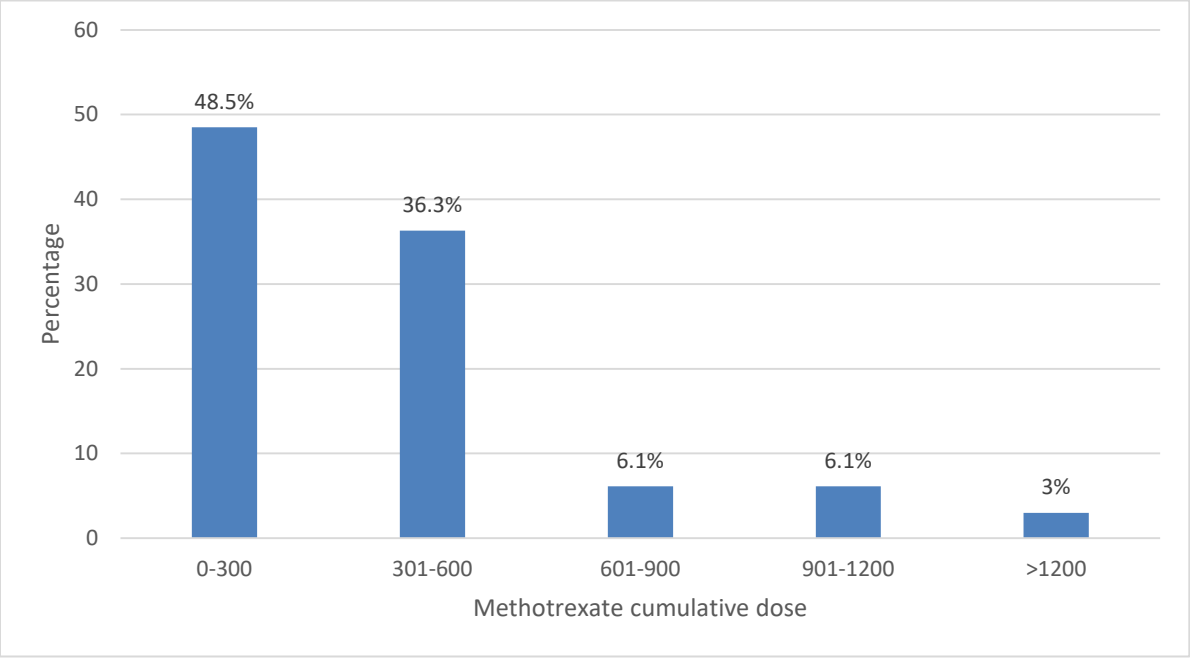


Table 12: Comparison of ultrasound shear wave elastography scores at baseline and 6 months

ultrasound shear wave elastography(kp) at baseline	ultrasound shear wave elastography(kp) at 6 months	
	1-5	**6-7**
1-5	27(100)	1(3.0)
6-7	0	32(97.0)
Total	27(100.0)	33(100.0)

*p value <0.05 is considered to be statistically significant

Statistical test used: McNemar test

The revealed that there was no significant difference in ultrasound shear wave elastography score at baseline and 6 months. (P value =1)

Table 13: Comparison of ultrasound shear wave elastography scores with Non-alcoholic fatty liver disease score

ultrasound shear wave elastography scores	Non-alcoholic fatty liver disease score		Total	P value
	Mild	**Moderate**		
1-5	24(40.0)	4(6.7)	28(46.7)	0.0001*
6-7	7(11.7)	25(41.7)	32(53.3)	
Total	31(51.7)	27(45.0)	60(100)	

*p value <0.05 is considered to be statistically significant

Test used : Chi square test

The study revealed that as ultrasound shear wave elastography scores is higher Non-alcoholic fatty liver disease score tends to be moderate (41.7%). The association was found to be statistically significant with p value <0.0001.

Figure 35: Pie chart depicting distribution according Non-alcoholic fatty liver disease score and ultrasound shear wave elastography scores

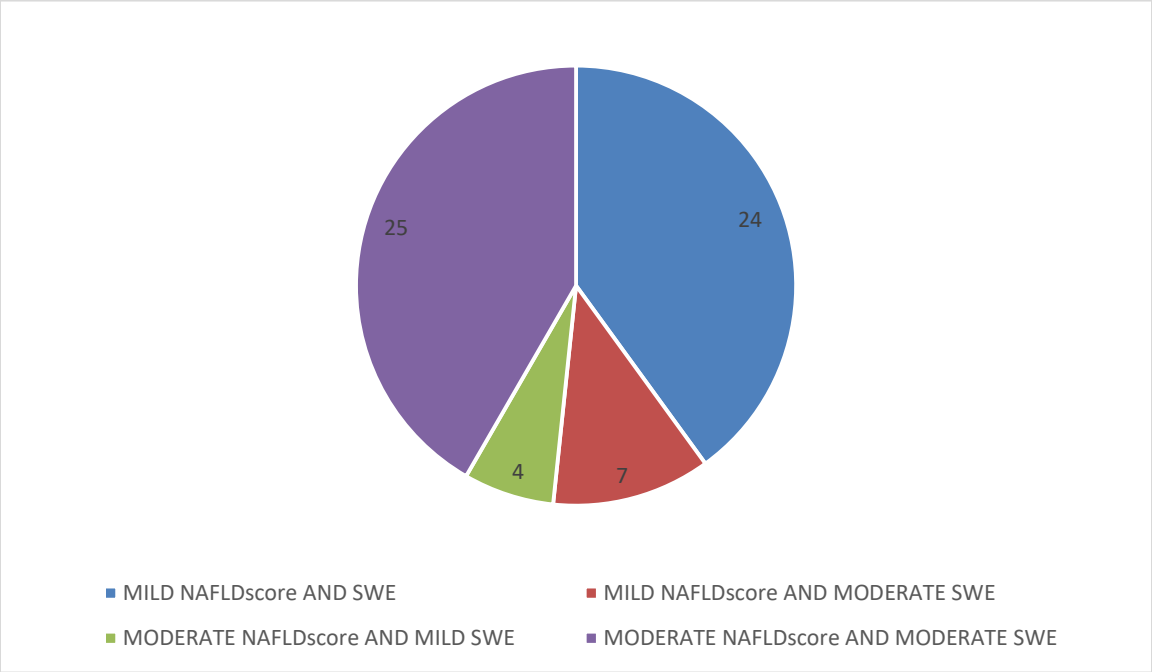


Table 14: Comparison of Non-alcoholic fatty liver disease score with BMI

BMI	Non-alcoholic fatty liver disease score		Total	P value
	Mild	Moderate		
Normal	4(6.7)	13(21.7)	17(28.3)	0.004
overweight	26(43.3)	13(21.7)	39(65.0)	
Obese	1(1.7)	3(5.0)	4(6.7)	
Total	31(51.7)	27(45.0)	60(100)	

*p value <0.05 is considered to be statistically significant

Test used : Fishers exact test

The study revealed that 5% had severe Non-alcoholic fatty liver disease score were obese. The association was found to be statistically significant with p value 0.004

Figure 36: Multiple bar diagram depicting distribution according Non-alcoholic fatty liver disease score and BMI

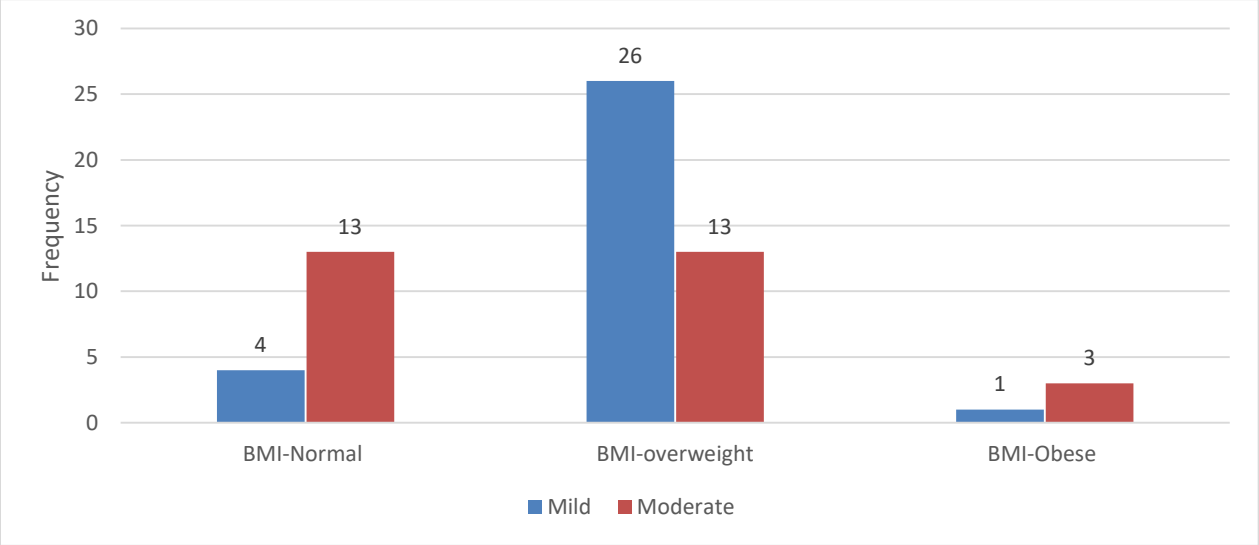


Table 15: correlation of Non-alcoholic fatty liver disease score with other parameters

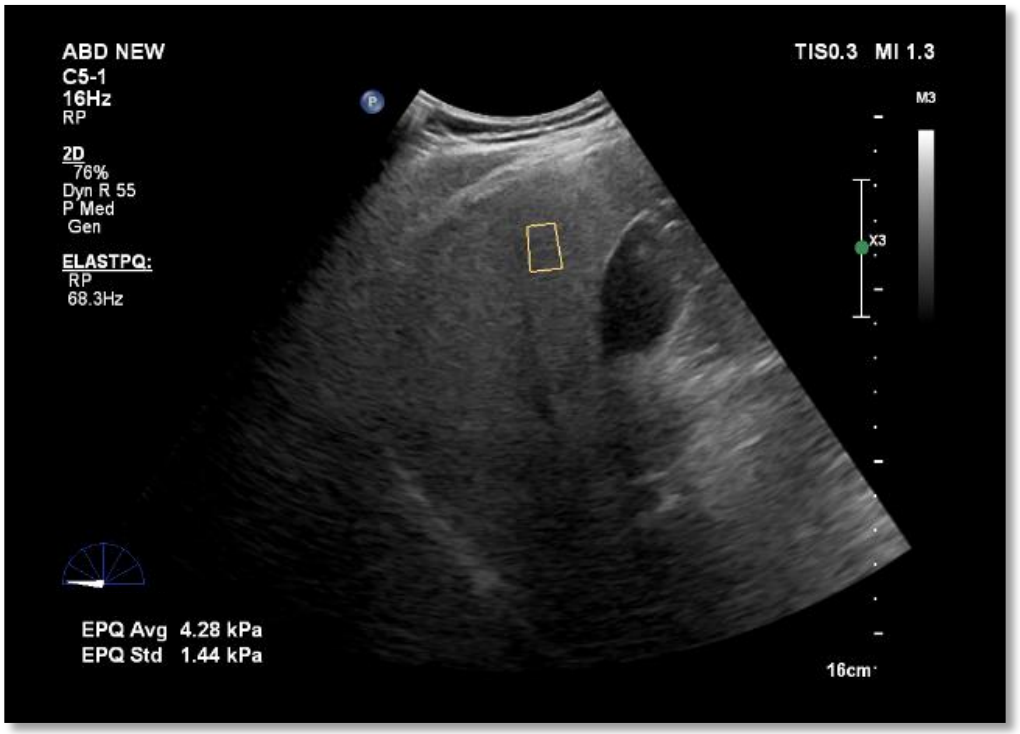
Study variables	Non-alcoholic fatty liver disease score		
	N	Corelation value (R)	P value
ultrasound shear wave elastography scores at baseline	60	0.551	0.0001*
BMI	60	0.269	0.038*
Methotrexate cumulative dose (mg)	33	0.163	0.426

*p value <0.05 is considered to be statistically significant
Statistical test used: spearman rank correlation

The study revealed that there is a moderate positive correlation between ultrasound shear wave elastography scores at baseline and Non-alcoholic fatty liver disease score (r=0.551, p value =0.0001). Further, The study revealed that there is a slight positive correlation between BMI and Non-alcoholic fatty liver disease score (r=0.269, p value =0.049).

ULTRASOUND SHEAR WAVE ELASTOGRAPHY IMAGING OF LIVER

A.



B.

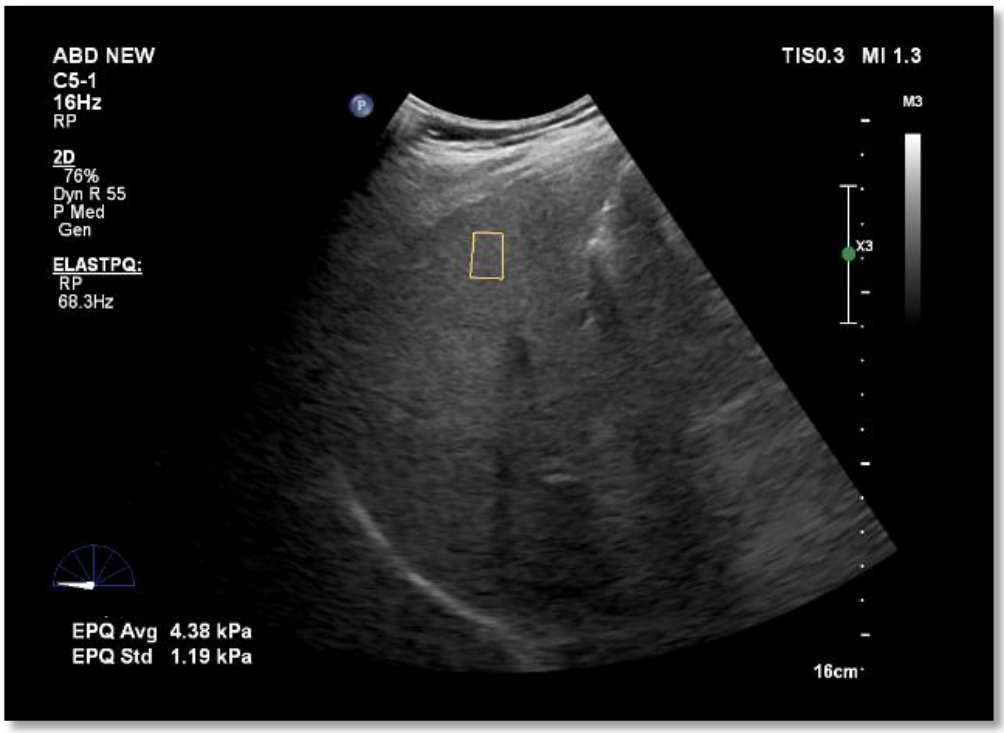
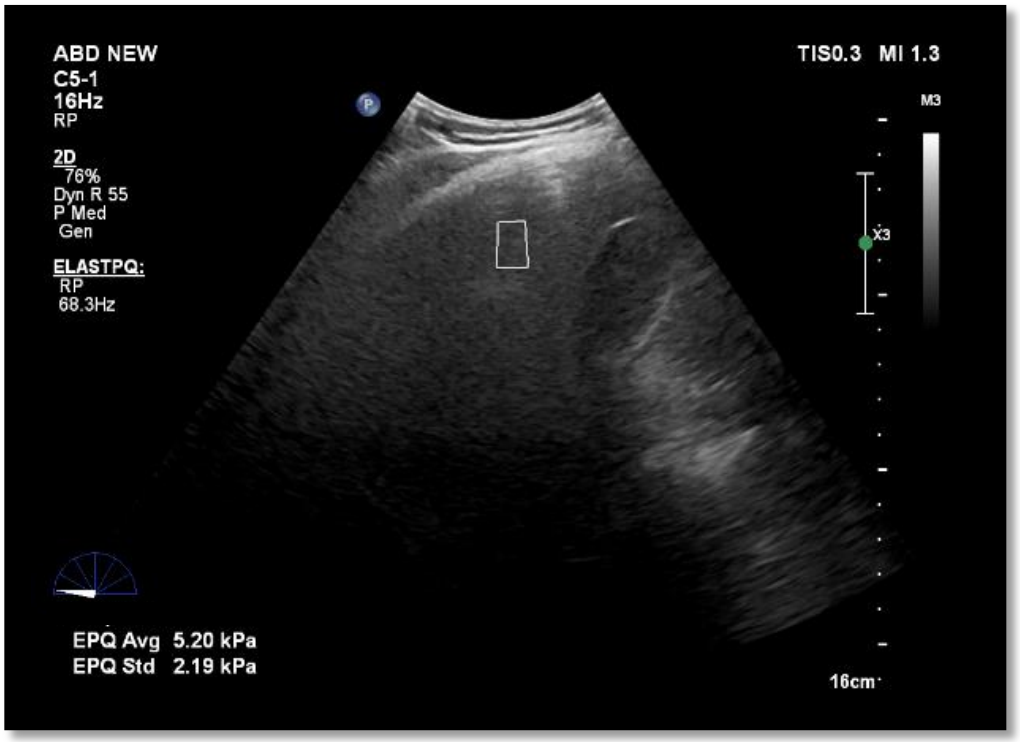


Figure 37: A. Patients baseline Shear Wave Elastography : EPQ Avg 4.28kPa.
B. Patients 6th month Shear Wave Elastography : EPQ Avg 4.38kPa.

ULTRASOUND SHEAR WAVE ELASTOGRAPHY IMAGING OF LIVER

A.



B.

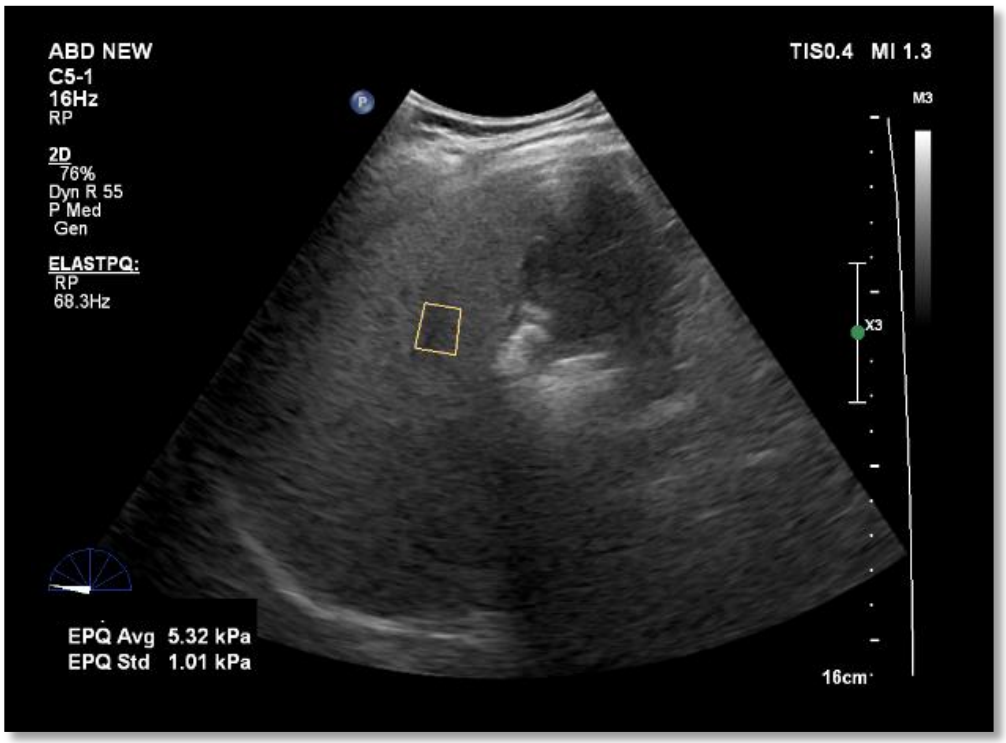
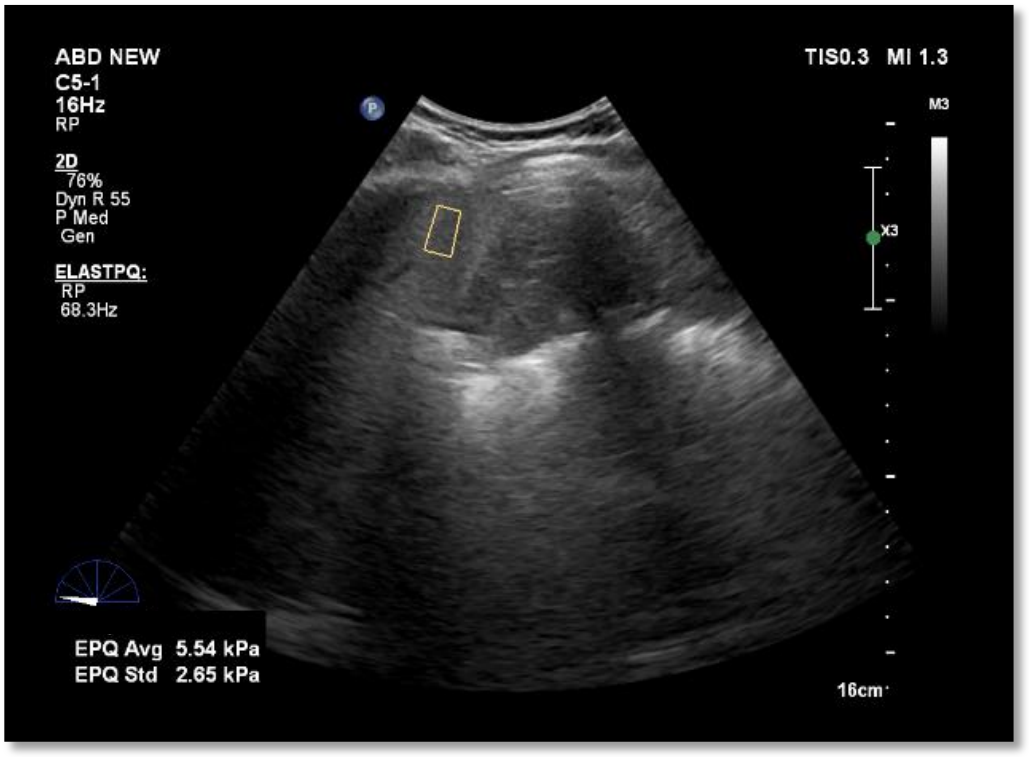


Figure 38 : **1.** Patients baseline Shear Wave Elastography : EPQ Avg 5.20kPa.
2. Patients 6th month Shear Wave Elastography : EPQ Avg 5.32kPa.

ULTRASOUND SHEAR WAVE ELASTOGRAPHY IMAGING OF LIVER

A.



B.

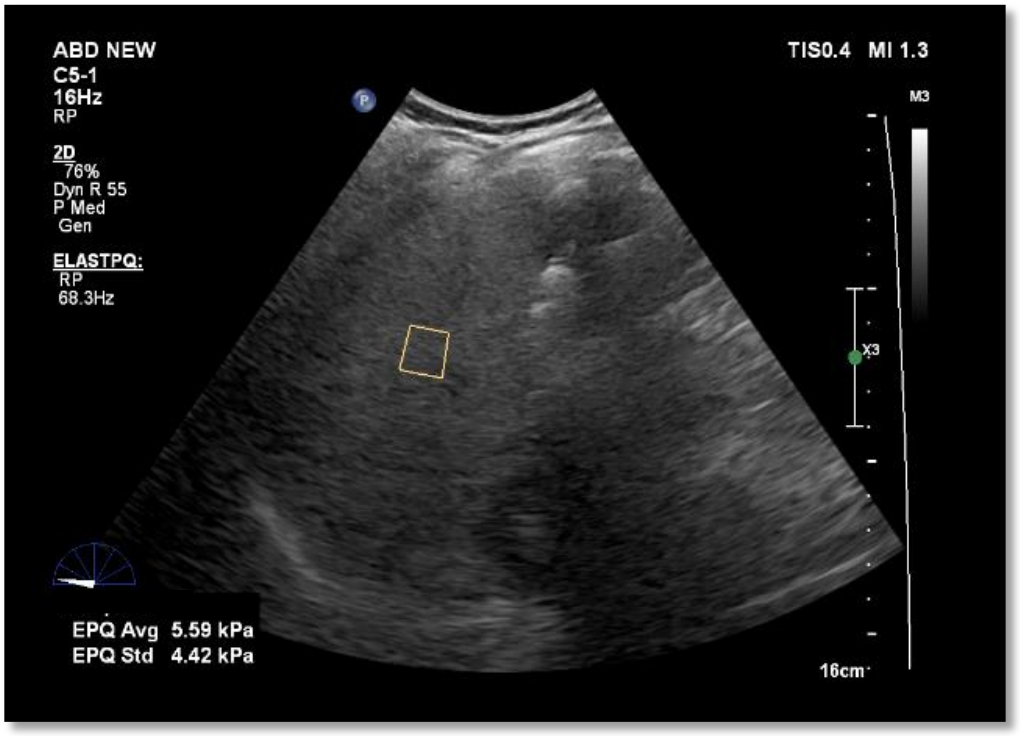
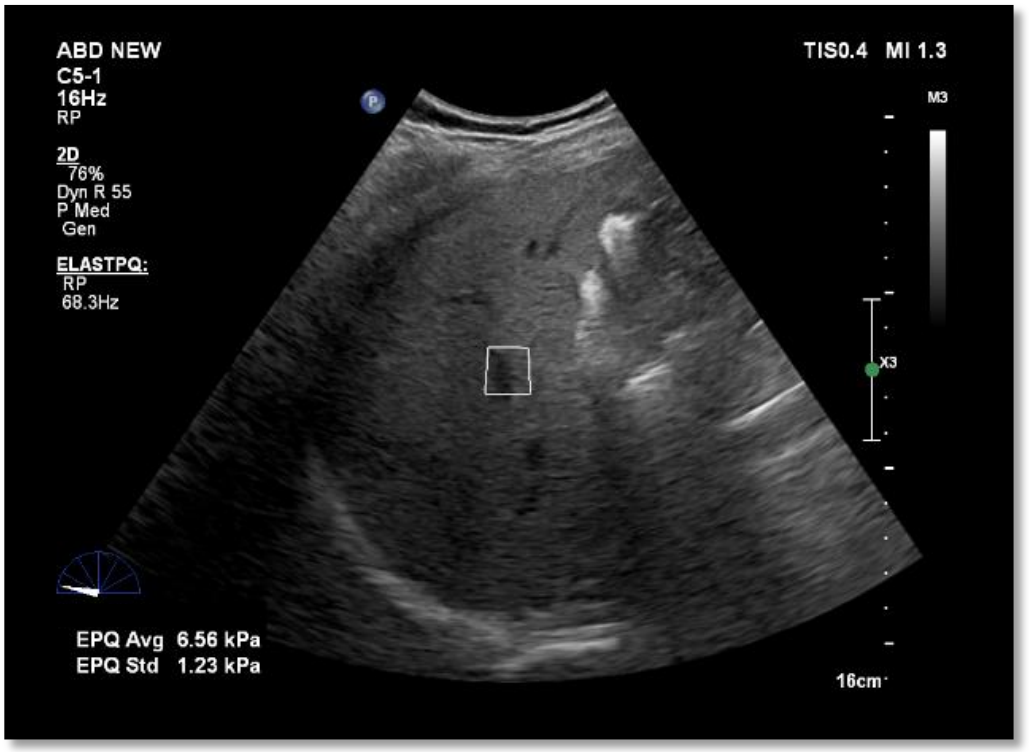


Figure 39 : **A.** Patients baseline Shear Wave Elastography : EPQ Avg 5.54kPa.
B. Patients 6th month Shear Wave Elastography : EPQ Avg 5.59kPa.

ULTRASOUND SHEAR WAVE ELASTOGRAPHY IMAGING OF LIVER

A.



B.

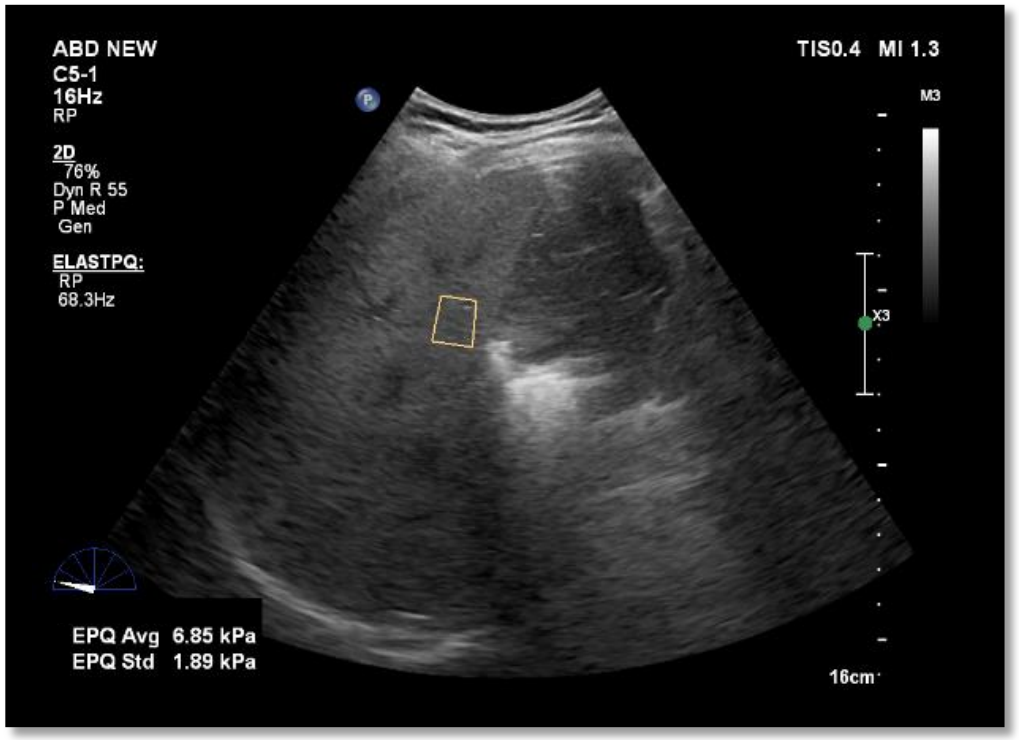


Figure 40 : **A.** Patients baseline Shear Wave Elastography : EPQ Avg 6.56kPa.
B. Patients 6th month Shear Wave Elastography : EPQ Avg 6.85kPa.

CLINICAL PHOTOGRAPHS

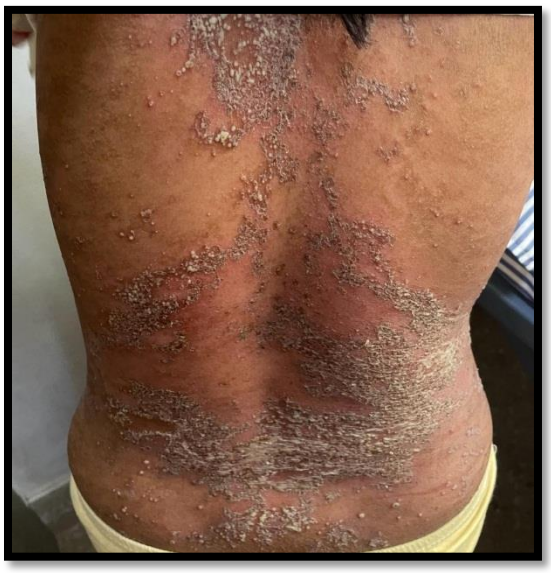


Figure 41a: Clinical Photograph of Pustular Psoriasis.

Multiple pustules over an erythematous base is seen over the upper back with scaling and many pustules coalescing to form lakes of pus over the lower back, flanks is seen

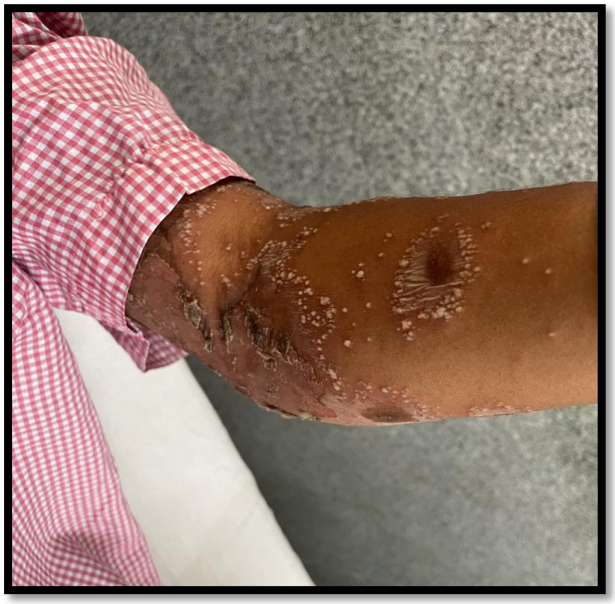


Figure 41b: Clinical Photograph of Pustular Psoriasis.

Multiple pinpoint pustules present around the dried-up lake of pus seen over the left arm and forearm.

CLINICAL PHOTOGRAPHS

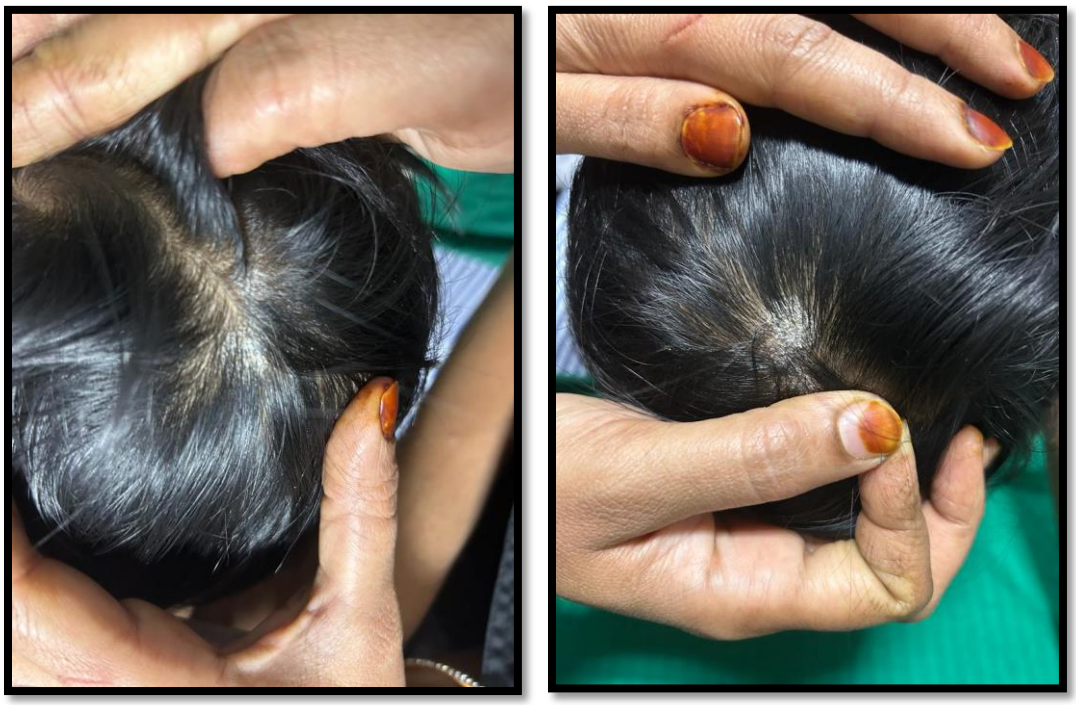


Figure 42: Clinical photograph of scalp psoriasis

A solitary well defined indurated plaque with silvery white scales seen over the vertex of the patient

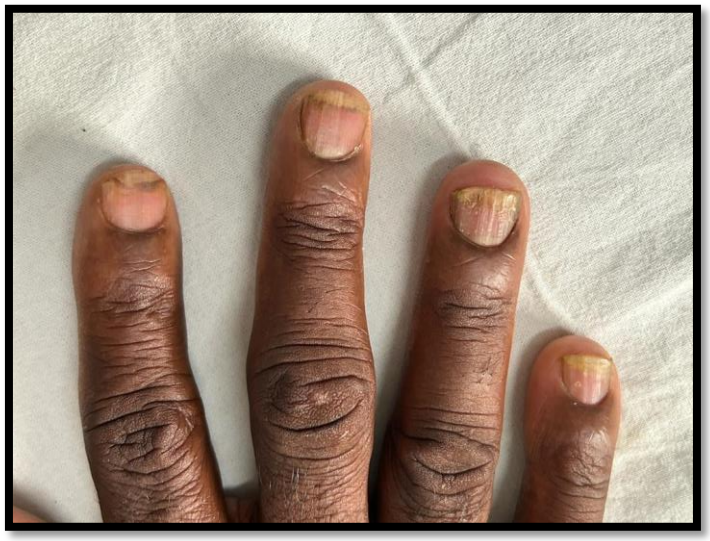


Figure 43a: Clinical photograph of Nail changes in psoriasis

Patients right hand 2^{nd},3^{rd}, 4^{th} & 5^{th} digits seen with lusterless nails, distal nail splitting Onychoschizia, coarse longitudinal ridging

CLINICAL PHOTOGRAPHS

Figure 43b: Clinical photograph of Nail changes in psoriasis

Patients right foot 1st, 2nd, 3rd, 4th & 5th digits seen with lusterless and brittle nails, with subungual hyperkeratosis with coarse pitting over the great toe.

Figure 43c: Clinical photograph of Nail changes in psoriasis

Patients right and left 1st digits seen with lusterless and brittle nails, with subungual hyperkeratosis with coarse pitting and transverse ridging.

CLINICAL PHOTOGRAPHS

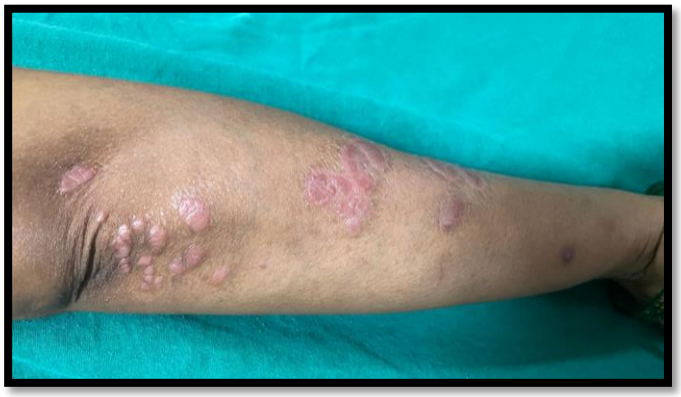


Figure 44: Clinical photograph of Chronic plaque psoriasis

Multiple well defined erythematous indurated plaques with mild scaling present over the extensor aspect of forearm and elbow.

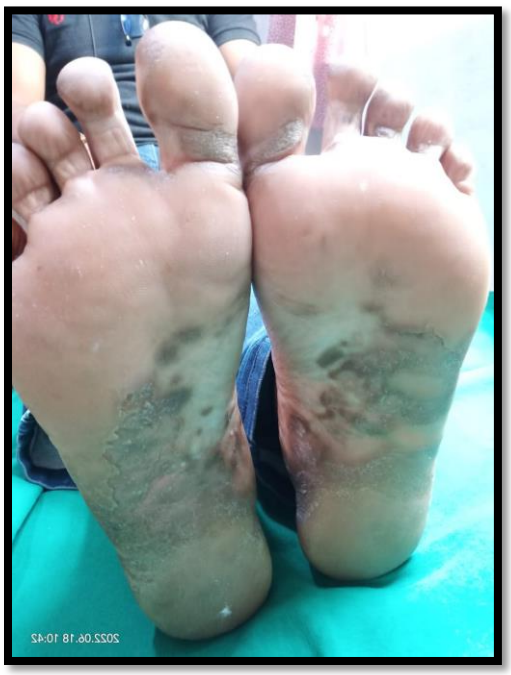


Figure 45: Clinical photograph of palmo-plantar psoriasis

Multiple well defined Hyperpigmented, hyperkeratotic plaques with scaling present over the medial aspect extending to the lateral aspect of both feet on the volar aspect.

CLINICAL PHOTOGRAPHS

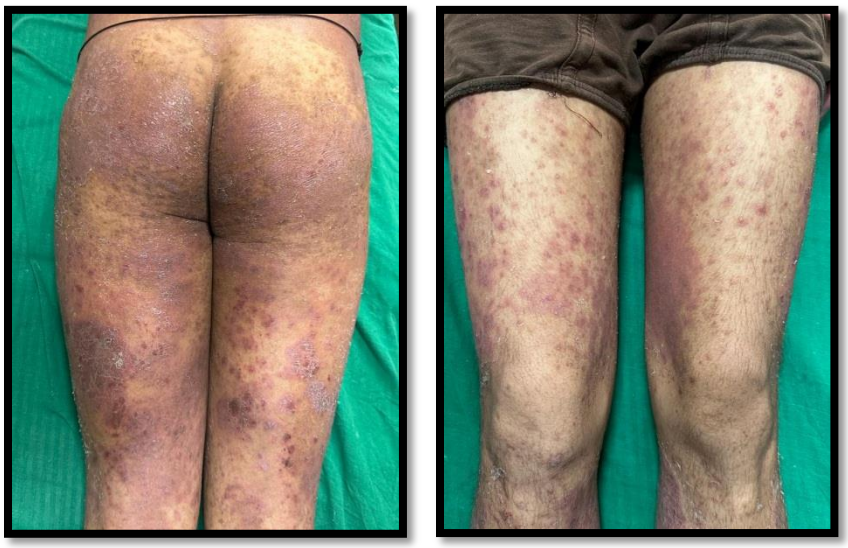


Figure 46a: Clinical photograph of Chronic plaque psoriasis

Multiple well defined erythematous indurated plaques with scaling present over the gluteal area and anterior and posterior aspect of the thighs.

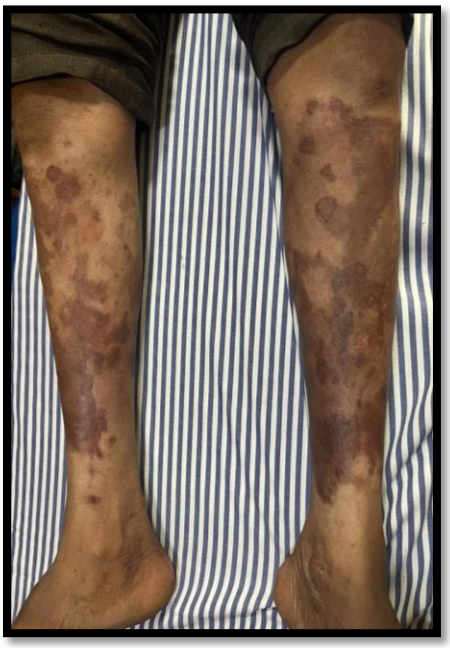


Figure 46b: Clinical photograph of Chronic plaque psoriasis

Multiples post-inflammatory hyper-pigmented macules noted over both the legs with development of new plaques over it .

DISCUSSION

DISCUSSION

Psoriasis is a lifelong immune-mediated inflammatory disease that primarily affects the skin, associated with physical and psychological morbidities. Psoriasis is associated with multiple comorbidities majorly affecting the Hepatic, cardiovascular and renal system either due to the disease itself or due to the medications used in the treatment.

The World Health Organization has recognized psoriasis as a serious non-communicable disease and highlighted the distress related to misdiagnosis, inadequate treatment and stigmatization of this disease. Hence this study is aimed at assessing and monitoring patients with psoriasis who are at higher risk of developing comorbidities.[4]

The present study is cross-sectional study involving 60 psoriatic patients of whom 24 (40%) were female and 36 (60%) were males was similar to Ican M et al, Vena GA et al. this could be due to the fact that our tertiary care center is placed in a rural area where women are less likely to and delay in seeking treatment than compared to males Ehsanul Huq KATM et al.[48,49,50]

The present study we found that majority of patients were in the age group of 30 to 39 (18, 30%) and there was only 1 (12, 1.7%) patient below the age of 19, and only 1 (75, 1.7%) patient above the age of 70. Similar to that of Parisi R et al, Ican M et al. as it was seen that prevalence of psoriasis was low with young age 1st, 2nd and after 6th decade of life.[48,51]

We found that our study showed Chronic plaque psoriasis or Psoriasis vulgaris (43, 71.1%) as the most common variant similar to Ogawa K et al, Ican M et al. followed by Palmo-plantar psoriasis (8, 13.3%) similar to Merola, Li, et al, the least common were Guttate psoriasis (1, 1.7%) which is in contradiction to Ican M et al and Nail psoriasis (1,1.7%) in contrasts to Merola, Li, et al as in our study nail psoriasis was taken as a sole manifestation and not nail changes seen in patients with psoriasis, in our study pustular psoriasis (4, 6.7%) which is in contrast to Mohd A A et al, in our study we generalized pustular psoriasis was seen in all 4 patients of which 2 patients went into erythroderma.[48,52,53,54]

In our study we found that the most common comorbidity was hypertension [7, (11.7%)] followed by Diabetes mellitus (4,6.7%) and Obesity (4,6.7%) with 15, 25% patients having comorbidities which was similar to Alajimi RS et al, in contrast to Fatas-Lalana B et al although similar finding of hypertension being the commonest comorbidity among psoriatic patients was noted in our study.[55,56]

It was seen in our study that majority of the study subjects were having body mass index (BMI) of Overweight (39, 65%) followed by normal (17,28.3%) and obese (4, 6%) it is seen that patients with psoriasis are at a higher risk of developing obesity from that of the general population although our study was in contrast to Mohd A A et al, Zafiriou E et al, but majority of our patients were overweight, the lack of obesity in this study population could be attributed to the fact that majority of the patients are from rural areas who are daily wage laborers and farmers who do not lead a sedentary lifestyle. [54,57]

In our study we found that majority of the patients had mild score (31, 51.7%) followed by moderate score (29,48.3%) Two cut-offs are present, one to exclude advanced fibrosis (<−1.455) (stage 0–2) and other indicates the presence of advanced fibrosis (>0.676) (stage >3). It was seen most of our patients had a score of less than -1.455 and 0.676, as such most patients were in range of 0 to stage 2 of liver fibrosis.[58]

In the study we found that majority of patients had a shear wave elastorgapyhy finding of 6-7kp (32, 53.3%) and 1-5kp (28,46.7%) at the 1st sitting in correlation with Mahajan R et al. [59]

In the study we found that majority of patients had a shear wave elastorgapyhy finding of 6-7kp (33, 55%) and 1-5kp (27,45%) at the 2nd sitting. We didn't find any significant correlation between 1st and 2nd sitting of shear wave elastography. In our study we found positive correlation between baseline Shear wave ultrasound elastography and non-alcoholic fatty liver disease with P value of 0.0001. In our study we found no positive correlation between baseline and 2nd sitting of shear wave ultrasound elastography. With P value of 1. In our study we found no positive correlation between cumulative dose of injection methotrexate and NFLD score P value 0.426. In our study we found positive correlation between Body mass index and NFLD score P value 0.038.

LIMITATION

Although Ultrasound shear wave Elastography and NAFLD score are good and reliant tools to assess liver fibrosis in patients with psoriasis it is not specific to psoriasis as it cannot differentiate the fibrosis caused by psoriasis and that caused by systemic comorbidities that aid in the causation of liver fibrosis in psoriatic patients.

CONCLUSION

CONCLUSION

Baseline non-invasive Ultrasound shear wave Elastography findings in patients with psoriasis showed positive correlation with Clinically assessed NAFLD score (*P* value 0.0001). We also found that NAFLD score had positive correlation with BMI (*P* value 0.038) in patients with psoriasis, we also found that there was no correlation between cumulative dose of methotrexate less than 1gm and NAFLD score (P value 0.426) The study suggests that Ultrasound Shear Wave Elastography and Non-alcoholic fatty liver disease score (NAFLDs) are both reliable methods to asses liver fibrosis.

Hence Ultrasound Shear Wave Elastography can be used as an ideal non-invasive technique as that compared to invasive liver biopsy in assessment and monitoring of liver fibrosis in psoriatic patients as a routine investigation.

Which can aid in the early detection of liver damage in patients and help in the formulation of treatment and care in these patients.

SUMMARY

SUMMARY

This is a cross sectional study of 60 psoriatic patients who were screened and evaluated as per the inclusion criteria and taken up for the study. All the patients underwent baseline and 6^{th} month follow-up Ultrasound shear wave Elastography performed by a well-trained sonographer using Philips EPIQ5 system equipped with shear wave point quantification with curvilinear broadband transducer (C5 - 1). The same patients also were graded as per the Non-alcoholic fatty liver disease score (NAFLD score).

In our study, 24(40%) were female and 36(60%) were males. The mean age of the study participants was 40.63 with standard deviation of 13.80 years. The minimum age being 12 and maximum being 75 years. It is observed that 14(23.3%) belongs to age 1 to 29 years,18(30%) belongs to age 30 to 39 years, 12(20%) belongs to age group 40 to 49 years, 9(15%) belongs to age group 50 to 59 years and remaining belongs to age more than 60 years.

Most (71.1%) had Chronic Plaque Psoriasis followed by Palmo-Plantar Psoriasis (13.3%), Pustular Psoriasis (6.7%) Scalp Psoriasis and Psoriatic Arthritis (5%) each. 1.7% each had Guttate Psoriasis and Nail Psoriasis.

Out of total, 11.7% had hypertension, 6.7% each had Diabetes Mellitus and Obesity. It is observed that none were underweight. Most (65%) were overweight followed by normal (28.3%) and obese (6%). At

baseline, 46.7% had ultrasound shear wave elastography ranging between 1 to 5kp and remaining above 6kp (53.3%).

At 6 months, 45% had ultrasound shear wave elastography ranging between 1 to 5kp and remaining above 6kp (55%). The study revealed that there is a moderate positive correlation between ultrasound shear wave elastography scores at baseline and Non-alcoholic fatty liver disease score ($r=0.551$, p value $=0.0001$). Further, The study revealed that there is a slight positive correlation between BMI and Non-alcoholic fatty liver disease score ($r=0.269$, p value $=0.049$).

Hence from this study it is evident that Ultrasound Shear Wave Elastography is an effective and alternative tool to rule out liver fibrosis in patients of psoriasis with or without methotrexate. It can be considered as an effective way to screen patients with psoriasis for liver fibrosis to rule out high risk patients prior to the start of cost effective methotrexate therapy.

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ANNEXURE I

PROFORMA

CASE NUMBER :

PATIENT PARTICULARS :

NAME:	**OP/IP NUMBER**
AGE& GENDER:	**DATE:**
ADDRESS:	**Occupation:**

CHIEF COMPLAINTS:

HISTORY OF PRESENT ILLNESS:

1. Age of Onset:
2. Site of onset:
3. Duration:
4. Any Associated Symptoms: itching/ burning/ pain
5. Mode of spread: static/ growing/ receding
6. Use of any drugs before onset of illness
7. Aggravating factors: Occupational/ hobbies/ trauma/ drug/ work/ sunlight/ emotional factors/ menstruation/ pregnancy/ food/ cosmetics/ chemicals/ any other:
8. Recovery: Some/ good/ poor/ no response

PAST HISTORY:

1. Associated systemic diseases: DM/ HTN/ Thyroid disease/ SLE/ Alopecia areata etc.
2. Associated cutaneous diseases:
3. H/o recent major surgery/ major trauma

FAMILY HISTORY:

1. Similar complaints:
2. Other skin problems:

PERSONAL HISTORY:

1. Diet: veg/ nonveg/ mixed
2. Bowel/ Bladder habits: regular/ altered.
3. Sleep- adequate/ disturbed
4. Appetite-
5. Habits: smoking/ tobacco chewing
6. H/o recent major surgery/ major trauma
7. Alcohol: IDC 10 diagnostic criteria more than 3 of the following.

A. Strong desire or sense of compulsion to take the substance.
B. Difficulties in controlling substance- taking behavior in terms of onset , termination or levels of use.
C. Physiological withdrawal state when substance use has ceased or been reduced.
D. Evidence of tolerance, such that increased doses of the psychoactive substance are required in order to achieve effects originally produced by lower dose
E. Progressive neglect of alternative pleasures or interests because of psychoactive substance use.
F. Persisting with substance use despite clear evidence of overtly harmful consequences.

TREATMENT HISTORY:

ON EXAMINATION:

GENERAL PHYSICAL EXAMINATION:

1. Built and Nourishment:
2. Pallor/ Icterus/ Clubbing/ Cyanosis/ Significant lymph node enlargement/ Edema
3. Vitals: Temperature-
    a. Pulse -
    b. Blood pressure-
    c. Respiratory rate-

SYSTEMIC EXAMINATION:

1. CVS
2. RS
3. PER ABDOMEN
4. CNS

CUTANEOUS EXAMINATION:

SITES OF INVOLVEMENT:

1. Face:
2. Upper limb:
3. Lower limb:
4. Trunk:

KOEBNERS PHENOMENON: Yes/ No

OTHER CUTANEOUS FINDINGS :

HAIR EXAMINATION:

NAIL EXAMINATION:

ORAL / MUCOSAL EXAMINATION:

PASI SCORE:

PASI: $0.1(E_H + I_H + D_H)A_H + 0.2(E_U + I_U + D_U)A_U + 0.3(E_T + I_T + D_T)A_T + 0.4(E_L + I_L + D_L)A_L$

E = Erythema, I = Induration, D = Desquamation, H = Head, U = Upper extremities T = Trunk, L = Lower extremities.

Severity scale 0 to 4 where 0 = nil, 1 = mild, 2 = moderate, 3 = severe, and 4 = very severe

BSA(Rule of nine) :

INVESTIGATIONS:

1. Complete haemogram:
2. RBS:
3. Liver Function test:
4. Hbs Ag:
5. Anti HCV:
6. Ultrasound abdomen:
7. Ultrasound shear wave elastography:

INVESTIGATIONS

CONVENTIONAL ULTRASOUND FEATURES:

1. Size:
2. Echogenicity:
3. Portal vein:
4. Spleen:
5. Ascites:

ULTRASOUND ELASTOGRAPHY FINDINGS:

1. ROI size:
2. ROI location:
3. Elastography values: / / / /
4. Average reading:

FINAL DIAGNOSIS:

ANNEXURE II

ENGLISH CONSENT

STUDY TITLE: CROSS-SECTIONAL STUDY OF LIVER FIBROSIS IN PSORIATIC PATIENTS USING ULTRASOUND SHEAR WAVE ELASTOGRAPHY

CHIEF RESEARCHER: DR. MADHU KIRAN C

UNDER THE GUIDANCE OF: DR. K. HANUMANTHAYYA

1. **NAME OF THE SUBJECT:** **AGE :**
2. **ADDRESS:**

a. I have been informed in my own vernacular language the purpose of the study, the necessity of relevant investigations to be carried out and photographs to be taken.
b. I understand that the medical information produced by this study will become part of institutional record and will be kept confidential by the said institute.
c. I understand that my participation is voluntary and may refuse to participate or may withdraw my consent and discontinue participation at any time without prejudice to my present or future care at this institution.
d. I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).
e. I confirm that _____ (chief researcher/ name of PG guide) has explained to me the purpose of research and the study procedure that I will undergo and the possible risks and discomforts that I may experience, in my own language. I hereby agree to give valid consent to participate as a subject in this research project.

Participant's signature

Signature of the witness: Date:

I have explained to _____ (subject) the purpose of the research, the possible risk and benefits to the best of my ability.

Chief Researcher/ Guide signature Date:

ಇಂಗ್ಲಿಷ್ ಒಪ್ಪಿಗೆ

ಅಧ್ಯಯನದ ಶೀರ್ಷಿಕೆ: ಅಲ್ಟ್ರಾಸೌಂಡ್ ಶಿಯರ್ ವೇವ್ ಎಲಾಸ್ಟೋಗ್ರಫಿಯನ್ನು ಬಳಸಿಕೊಂಡು ಸೋರಿಯಾಟಿಕ್ ರೋಗಿಗಳಲ್ಲಿ ಲಿವರ್ ಫೈಬ್ರೋಸಿಸ್ನ ಅಡ್ಡ-ವಿಭಾಗದ ಅಧ್ಯಯನ

ಮುಖ್ಯ ಸಂಶೋಧಕ: ಡಾ. ಮಧು ಕಿರಣ್ ಸಿ

ಮಾರ್ಗದರ್ಶನದಲ್ಲಿ: ಡಾ. ಕೆ.ಹನುಮಂತಯ್ಯ

1. ವಿಷಯದ ಹೆಸರು: ವಯಸ್ಸು:

2. ವಿಳಾಸ:

ಎ. ಅಧ್ಯಯನದ ಉದ್ದೇಶ, ಕೈಗೊಳ್ಳಬೇಕಾದ ಸಂಬಂಧಿತ ತನಿಖೆಗಳು ಮತ್ತು ಛಾಯಾಚಿತ್ರಗಳನ್ನು ತೆಗೆದುಕೊಳ್ಳಬೇಕಾದ ಅಗತ್ಯತೆಗಳನ್ನು ನನ್ನದೇ ಆದ ಸ್ಥಳೀಯ ಭಾಷೆಯಲ್ಲಿ ನನಗೆ ತಿಳಿಸಲಾಗಿದೆ.

ಬಿ. ಈ ಅಧ್ಯಯನದಿಂದ ಉತ್ಪತ್ತಿಯಾಗುವ ವೈದ್ಯಕೀಯ ಮಾಹಿತಿಯು ಸಾಂಸ್ಥಿಕ ದಾಖಲೆಯ ಭಾಗವಾಗುತ್ತದೆ ಮತ್ತು ಈ ಸಂಸ್ಥೆಯು ಗೌಪ್ಯವಾಗಿಡುತ್ತದೆ ಎಂದು ನಾನು ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ.

ಸಿ. ನನ್ನ ಭಾಗವಹಿಸುವಿಕೆಯು ಸ್ವಯಂಪ್ರೇರಿತವಾಗಿದೆ ಎಂದು ನಾನು ಅರ್ಥಮಾಡಿಕೊಂಡಿದ್ದೇನೆ ಮತ್ತು ಭಾಗವಹಿಸಲು ನಿರಾಕರಿಸಬಹುದು ಅಥವಾ ನನ್ನ ಒಪ್ಪಿಗೆಯನ್ನು ಹಿಂಪಡೆಯಬಹುದು ಮತ್ತು ಈ ಸಂಸ್ಥೆಯಲ್ಲಿ ನನ್ನ ಪ್ರಸ್ತುತ ಅಥವಾ ಭವಿಷ್ಯದ ಕಾಳಜಿಗೆ ಯಾವುದೇ ಪೂರ್ವಾಗ್ರಹವಿಲ್ಲದೆ ಭಾಗವಹಿಸುವಿಕೆಯನ್ನು ನಿಲ್ಲಿಸಬಹುದು.

ಡಿ. ಈ ಅಧ್ಯಯನದಿಂದ ಉಂಟಾಗುವ ಯಾವುದೇ ಡೇಟಾ ಅಥವಾ ಫಲಿತಾಂಶಗಳ ಬಳಕೆಯನ್ನು ನಿರ್ಬಂಧಿಸದಿರಲು ನಾನು ಸಮ್ಮತಿಸುತ್ತೇನೆ, ಅಂತಹ ಬಳಕೆಯನ್ನು ಕೇವಲ ವೈಜ್ಞಾನಿಕ ಉದ್ದೇಶ(ಗಳಿಗೆ)

ಇ. _____ (ಮುಖ್ಯ ಸಂಶೋಧಕರು/ಪಿಜಿ ಗೈಡ್‌ನ ಹೆಸರು) ನನಗೆ ಸಂಶೋಧನೆಯ ಉದ್ದೇಶ

ಮತ್ತು ನಾನು ಒಳಪಡುವ ಅಧ್ಯಯನ ವಿಧಾನ ಮತ್ತು ನಾನು ಅನುಭವಿಸಬಹುದಾದ ಸಂಭವನೀಯ ಅಪಾಯಗಳು ಮತ್ತು ಅಸ್ವಸ್ಥತೆಗಳನ್ನು ನನ್ನ ಸ್ವಂತ ಭಾಷೆಯಲ್ಲಿ ವಿವರಿಸಿದ್ದೇನೆ ಎಂದು ನಾನು ದೃಢೀಕರಿಸುತ್ತೇನೆ. ಈ ಸಂಶೋಧನಾ ಯೋಜನೆಯಲ್ಲಿ ವಿಷಯವಾಗಿ ಭಾಗವಹಿಸಲು ಮಾನ್ಯವಾದ ಒಪ್ಪಿಗೆಯನ್ನು ನೀಡಲು ನಾನು ಈ ಮೂಲಕ ಒಪ್ಪುತ್ತೇನೆ.

ಭಾಗವಹಿಸುವವರ ಸಹಿ

ಸಾಕ್ಷಿ ಸಹಿ: ದಿನಾಂಕ:

ನಾನು _____ (ವಿಷಯ) ಗೆ ಸಂಶೋಧನೆಯ ಉದ್ದೇಶ, ಸಂಭವನೀಯ ಅಪಾಯ ಮತ್ತು ನನ್ನ ಸಾಮರ್ಥ್ಯದ ಅತ್ಯುತ್ತಮ ಪ್ರಯೋಜನಗಳನ್ನು ವಿವರಿಸಿದ್ದೇನೆ.

ಮುಖ್ಯ ಸಂಶೋಧಕ/ಮಾರ್ಗದರ್ಶಿ ಸಹಿ ದಿನಾಂಕ:

ANNEXURE III

PATIENT INFORMATION SHEET

Study title: CROSS-SECTIONAL STUDY OF LIVER FIBROSIS IN PSORIATIC PATIENTS USING ULTRASOUND SHEAR WAVE ELASTOGRAPHY

Study site: R.L Jalappa Hospital, Tamaka, Kolar.

Aim:

1. To assess the utility of shear wave ultrasound elastography in detecting liver fibrosis in patients with psoriasis.
2. To correlate shear wave ultrasound elastography findings with Non-alcoholic fatty liver disease score in patients with psoriasis.

Psoriasis is a chronic inflammatory papulosquamous disease characterized by multiple remissions and relapses with a spectrum of clinical phenotypes and results from the interplay of genetic, environmental, and immunological factors. Psoriasis has no cure and the disease waxes and wanes with flareups. Many patients with psoriasis develop depression as the quality of life is poor. It is not contagious and not transmitted from one person to another by touching, eating together, sharing clothes.
It has been shown that psoriasis patients have an association with non alcoholic fatty liver disease and metabolic syndrome, Other associated diseases can be diagnosed by clinical history, examination and blood test. Patients with psoriasis are at a higher risk of liver injury either by psoriasis itself or due to drugs used in the treatment of psoriasis. So early diagnosis of liver damage and an early intervention is worthful.
Please read the following information and discuss with your family members. You can ask any question regarding the study. If you agree to participate in this study we will collect information (as per proforma) from you. Relevant investigations will be carried out. This information collected will be used for dissertation and publication only.
All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. The expenses required for the above investigations will be funded by the study investigator. This study has been reviewed by the Institutional Ethics Committee and you are free to contact the member of the Institutional Ethics Committee. There is no compulsion to agree to this study. The care you will get will not change if you don't wish to participate. You are required to sign/ provide thumb impression only if you voluntarily agree to participate in this study.

For any further clarification you can contact the study investigator:

Dr. MADHU KIRAN C

Mobile no: 7760508809

E-mail id: drmadhukirancmalur@gmail.com

ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆ

ಅಧ್ಯಯನದ ಶೀರ್ಷಿಕೆ: ಅಲ್ಟ್ರಾಸೌಂಡ್ ಶಿಯರ್ ವೇವ್ ಎಲಾಸ್ಟೋಗ್ರಫಿಯನ್ನು ಬಳಸಿಕೊಂಡು ಸೋರಿಯಾಟಿಕ್ ರೋಗಿಗಳಲ್ಲಿ ಲಿವರ್ ಫೈಬ್ರೋಸಿಸ್ನ ಅಡ್ಡ-ವಿಭಾಗದ ಅಧ್ಯಯನ

ಅಧ್ಯಯನ ಸ್ಥಳ: ಆರ್.ಎಲ್ ಜಾಲಪ್ಪ ಆಸ್ಪತ್ರೆ, ಟಮಕ, ಕೋಲಾರ.

ಗುರಿ:

1. ಸೋರಿಯಾಸಿಸ್ ರೋಗಿಗಳಲ್ಲಿ ಯಕೃತ್ತಿನ ಫೈಬ್ರೋಸಿಸ್ ಅನ್ನು ಪತ್ತೆಹಚ್ಚುವಲ್ಲಿ ಶಿಯರ್ ವೇವ್ ಅಲ್ಟ್ರಾಸೌಂಡ್ ಎಲಾಸ್ಟೋಗ್ರಫಿಯ ಉಪಯುಕ್ತತೆಯನ್ನು ನಿರ್ಣಯಿಸಲು.
2. ಸೋರಿಯಾಸಿಸ್ ರೋಗಿಗಳಲ್ಲಿ ಆಲ್ಕೋಹಾಲಿಕ್ ಅಲ್ಲದ ಕೊಬ್ಬಿನ ಪಿತ್ತಜನಕಾಂಗದ ಕಾಯಿಲೆಯ ಅಂಕಗಳೊಂದಿಗೆ ಶಿಯರ್ ವೇವ್ ಅಲ್ಟ್ರಾಸೌಂಡ್ ಎಲಾಸ್ಟೋಗ್ರಫಿ ಸಂಶೋಧನೆಗಳನ್ನು ಪರಸ್ಪರ ಸಂಬಂಧಿಸಲು.

ಸೋರಿಯಾಸಿಸ್ ದೀರ್ಘಕಾಲದ ಉರಿಯೂತದ ಪಾಪುಲೋಸ್ಕ್ವಾಮಸ್ ಕಾಯಿಲೆಯಾಗಿದ್ದು, ಕ್ಲಿನಿಕಲ್ ಫಿನೋಟೈಪ್‌ಗಳ ವರ್ಣಪಟಲದೊಂದಿಗೆ ಬಹು ಉಪಶಮನಗಳು ಮತ್ತು ಮರುಕಳಿಸುವಿಕೆಯಿಂದ ನಿರೂಪಿಸಲ್ಪಟ್ಟಿದೆ ಮತ್ತು ಆನುವಂಶಿಕ, ಪರಿಸರ ಮತ್ತು ರೋಗನಿರೋಧಕ ಅಂಶಗಳ ಪರಸ್ಪರ ಕ್ರಿಯೆಯ ಫಲಿತಾಂಶಗಳು. ಸೋರಿಯಾಸಿಸ್‌ಗೆ ಯಾವುದೇ ಚಿಕಿತ್ಸೆ ಇಲ್ಲ ಮತ್ತು ರೋಗವು ಉಲ್ಬಣಗೊಳ್ಳುವುದರೊಂದಿಗೆ ಕ್ಷೀಣಿಸುತ್ತದೆ. ಜೀವನದ ಗುಣಮಟ್ಟವು ಕಳಪೆಯಾಗಿರುವುದರಿಂದ ಸೋರಿಯಾಸಿಸ್ ಹೊಂದಿರುವ ಅನೇಕ ರೋಗಿಗಳು ಖಿನ್ನತೆಯನ್ನು ಬೆಳೆಸಿಕೊಳ್ಳುತ್ತಾರೆ. ಇದು ಸಾಂಕ್ರಾಮಿಕವಲ್ಲ ಮತ್ತು ಒಬ್ಬರಿಂದ ಇನ್ನೊಬ್ಬರಿಗೆ ಮುಟ್ಟುವ, ಒಟ್ಟಿಗೆ ತಿನ್ನುವ, ಬಟ್ಟೆ ಹಂಚಿಕೊಳ್ಳುವ ಮೂಲಕ ಹರಡುವುದಿಲ್ಲ.

ಸೋರಿಯಾಸಿಸ್ ರೋಗಿಗಳು ಆಲ್ಕೊಹಾಲ್ಯುಕ್ತ ಕೊಬ್ಬಿನ ಪಿತ್ತಜನಕಾಂಗದ ಕಾಯಿಲೆ ಮತ್ತು ಮೆಟಾಬಾಲಿಕ್ ಸಿಂಡ್ರೋಮ್‌ನೊಂದಿಗೆ ಸಂಬಂಧವನ್ನು ಹೊಂದಿದ್ದಾರೆಂದು ತೋರಿಸಲಾಗಿದೆ, ಇತರ ಸಂಬಂಧಿತ ಕಾಯಿಲೆಗಳನ್ನು ಕ್ಲಿನಿಕಲ್ ಇತಿಹಾಸ, ಪರೀಕ್ಷೆ, ಮತ್ತು ರಕ್ತ ಪರೀಕ್ಷೆಯಿಂದ ನಿರ್ಣಯಿಸಬಹುದು. ಸೋರಿಯಾಸಿಸ್ ಹೊಂದಿರುವ ರೋಗಿಗಳು ಸೋರಿಯಾಸಿಸ್‌ನಿಂದ ಅಥವಾ ಸೋರಿಯಾಸಿಸ್ ಚಿಕಿತ್ಸೆಯಲ್ಲಿ ಬಳಸುವ ಔಷಧಿಗಳ ಕಾರಣದಿಂದಾಗಿ ಯಕೃತ್ತಿನ ಹಾನಿಯ ಹೆಚ್ಚಿನ ಅಪಾಯವನ್ನು ಹೊಂದಿರುತ್ತಾರೆ. ಆದ್ದರಿಂದ ಯಕೃತ್ತಿನ ಹಾನಿ ಮತ್ತು ಆರಂಭಿಕ ಹಸ್ತಕ್ಷೇಪದ ಆರಂಭಿಕ ರೋಗನಿರ್ಣಯವು ಯೋಗ್ಯವಾಗಿದೆ.

ದಯವಿಟ್ಟು ಕೆಳಗಿನ ಮಾಹಿತಿಯನ್ನು ಓದಿ ಮತ್ತು ನಿಮ್ಮ ಕುಟುಂಬದ ಸದಸ್ಯರೊಂದಿಗೆ ಚರ್ಚಿಸಿ. ಅಧ್ಯಯನಕ್ಕೆ ಸಂಬಂಧಿಸಿದಂತೆ ನೀವು ಯಾವುದೇ ಪ್ರಶ್ನೆಯನ್ನು ಕೇಳಬಹುದು. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನೀವು ಒಪ್ಪಿದರೆ ನಾವು ನಿಮ್ಮಿಂದ ಮಾಹಿತಿಯನ್ನು (ಪ್ರೊಫಾರ್ಮಾ ಪ್ರಕಾರ) ಸಂಗ್ರಹಿಸುತ್ತೇವೆ. ಸಂಬಂಧಿತ ತನಿಖೆ ನಡೆಸಲಾಗುವುದು. ಸಂಗ್ರಹಿಸಿದ ಈ ಮಾಹಿತಿಯನ್ನು ಪ್ರಬಂಧ ಮತ್ತು ಪ್ರಕಟಣೆಗೆ ಮಾತ್ರ ಬಳಸಲಾಗುತ್ತದೆ.

ನಿಮ್ಮಿಂದ ಸಂಗ್ರಹಿಸಲಾದ ಎಲ್ಲಾ ಮಾಹಿತಿಯನ್ನು ಗೌಪ್ಯವಾಗಿ ಇರಿಸಲಾಗುತ್ತದೆ ಮತ್ತು ಯಾವುದೇ ಹೊರಗಿನವರಿಗೆ ಬಹಿರಂಗಪಡಿಸಲಾಗುವುದಿಲ್ಲ. ನಿಮ್ಮ ಗುರುತನ್ನು ಬಹಿರಂಗಪಡಿಸಲಾಗುವುದಿಲ್ಲ. ಮೇಲಿನ ತನಿಖೆಗಳಿಗೆ ಅಗತ್ಯವಿರುವ ವೆಚ್ಚಗಳನ್ನು ಅಧ್ಯಯನ ತನಿಖಾಧಿಕಾರಿಗಳು ಧನಸಹಾಯ ಮಾಡುತ್ತಾರೆ. ಈ ಅಧ್ಯಯನವನ್ನು ಸಾಂಸ್ಥಿಕ ನೀತಿಶಾಸ್ತ್ರ ಸಮಿತಿಯು ಪರಿಶೀಲಿಸಿದೆ ಮತ್ತು ನೀವು ಸಾಂಸ್ಥಿಕ ನೀತಿಶಾಸ್ತ್ರ ಸಮಿತಿಯ ಸದಸ್ಯರನ್ನು ಸಂಪರ್ಕಿಸಲು ಮುಕ್ತರಾಗಿದ್ದೀರಿ. ಈ ಅಧ್ಯಯನವನ್ನು ಒಪ್ಪಿಕೊಳ್ಳಲು ಯಾವುದೇ ಒತ್ತಾಯವಿಲ್ಲ. ನೀವು ಭಾಗವಹಿಸಲು ಬಯಸದಿದ್ದರೆ ನೀವು ಪಡೆಯುವ ಕಾಳಜಿಯು ಬದಲಾಗುವುದಿಲ್ಲ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸಲು ನೀವು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಸಮ್ಮತಿಸಿದರೆ ಮಾತ್ರ ನೀವು ಸಹಿ/ಹೆಬ್ಬೆರಳಿನ ಗುರುತನ್ನು ಒದಗಿಸಬೇಕಾಗುತ್ತದೆ.

ಯಾವುದೇ ಹೆಚ್ಚಿನ ಸ್ಪಷ್ಟೀಕರಣಕ್ಕಾಗಿ ನೀವು ಅಧ್ಯಯನ ತನಿಖಾಧಿಕಾರಿಯನ್ನು ಸಂಪರ್ಕಿಸಬಹುದು:

ಡಾ. ಮಧು ಕಿರಣ್ ಸಿ

ಮೊಬೈಲ್ ಸಂಖ್ಯೆ: 7760508809

ಇ-ಮೇಲ್ ಐಡಿ: drmadhukirancmalur@gmail.com

ANNEXURE IV

LEGEND FOR MASTER CHART

Sl.No	FULL FORM	SHORT FORM
1.	Chronic Plaque Psoriasis	CPP
2.	Chronic Plaque Psoriasis with Psoriatic Arthritis	CPP+PA
3.	Palmo-Plantar Psoriasis	PPP
4.	Scalp Psoriasis	SP
5.	Pustular Psoriasis	PP
6.	Nail Psoriasis	NP
7.	Guttate Psoriasis	GP
8.	Palmo-Plantar Psoriasis with Psoriatic Arthritis	PPP+PA
9.	Diabetes Mellitus	DM
10.	Hypertension	HTN
11.	Obesity	O
12.	Ultra sound shear wave Elastography 1st reading	Epq Avg1
13.	Ultra sound shear wave Elastography 2st reading after 6 Months	Epq Avg2
14.	Body Mass Index	BMI