"A CROSS SECTIONAL STUDY OF SERUM LIPID PROFILE IN 40 PATIENTS OF PSORIASIS AND EQUAL NUMBER OF AGE AND GENDER MATCHED CONTROLS"

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LIST OF ABBREVIATIONS

ABCA1	→	ATP Binding Cassette A1
AcH	→	Acetylcholine
Apo	→	Apolipoprotein
ATP	→	Adenosine Triphosphate
ADP	→	Adenosine Diphosphate
APR	→	Acute Phase Reaction
APC's	→	Antigen Presenting Cells
BMI	→	Body Mass Index
cAMP	→	Cyclic Adenosine Monophosphate
CAD	→	Coronary Artery Disease
CE	→	Cholesteryl ester
CETP	→	Cholesterol Ester Transfer Protein
CRP	→	C- Reactive Protein
CVD	→	Cardiovascular Diseases
CO	→	Cholesterol Oxidase
EGF	→	Epithelial Growth Factor
G-6-P	→	Glucose-6-Phosphate
G-6-PDH	→	Glucose-6-Phosphate Dehydrogenase

GM-CSF	→	Granulocyte-Macrophage Colony Stimulating Factor
HDL-C	→	High Density Lipid Cholesterol
HK	→	Hexokinase
HLA	→	Human Leukocyte Antigen
HPO	→	Horseradish Peroxidase
HTGL	→	Hepatic Triglyceride Lipase
IDL	→	Intermediate Density Lipoproteins
IFN	→	Interferon
IL	→	Interleukin
LDL-C	→	Low density Lipid Cholesterol
LCAT	→	Lecithin Cholesteryl Acyl Transferase
LXR	→	Liver X receptors
MHC	→	Major Histocompatibility Complex
MCP	→	Metacarpophalangeal
NAD	→	Nicotinamide Adenine Dinucleotide
NADH	→	Nicotinamide Adenine Dinucleotide- Hydrogen
OSA	→	Obstructive Sleep Apnea
PASI	→	Psoriasis Area Severity Index
PAF-AH	→	Platelet activating factor acetyl hydrolase

pDC	→	Peripheral Dendritic Cells
PIP	→	Proximal interphalangeal
PMN	→	Polymorphonuclear
PLTP	→	Phospholipid Transfer Protein
PON	→	Paraoxonase
ROS	→	Reactive Oxygen Species
SP	→	Substance P
SR	→	Scavenger receptors
TC	→	Total Cholesterol
TCR	→	T cells expressing specific receptor
TG	→	Triglycerides
TH-1	→	T- helper 1
TNF	→	Tumor Necrosis Factor
Vβ	→	β chain variable
VEGF	→	Vascular Endothelial Growth Factor
VLDL	→	Very Low Density Lipoproteins

ABSTRACT

BACKGROUND

Psoriasis is a chronic inflammatory skin disease that is associated with an increased cardiovascular risk profile. The underlying pathogenic mechanisms remain unclear. Multiple factors including systemic inflammation, oxidative stress, aberrant lipid profile and concomitant cardiovascular risk factors have been associated. Psoriasis has been associated with abnormal plasma lipid metabolism and oxidative stress.

OBJECTIVES

1. To determine the serum lipid disturbances in psoriasis
2. To study the demographic and clinical data in psoriasis

METHODS

The study was conducted at Dr. Prabhakar Kore KLE Hospital and MRC, Belgaum. Forty subjects, of psoriasis in the age group of 20-70 years were considered as cases. Forty healthy subjects of comparable age and sex were chosen as controls. Cases with history of diabetes, hypertension, obesity, family history of hyperlipidemia, intake of systemic drugs like lipid lowering agents, alcohol and smoking were excluded from the study.

COLLECTION OF DATA

Blood and urine samples were collected after obtaining proper consent from all cases and controls. Serum lipids were measured by enzymatic methods. Serum

fasting blood sugar, blood urea, serum creatinine, urine sugar and proteins were also measured simultaneously using routine laboratory methods.

RESULTS

Serum TC, LDL-C, TC/HDL-C ratio and LDL-C/HDL-C ratio were significantly higher in psoriasis patients compared to controls. There was no statistically significant difference in serum TG, HDL-C and VLDL-C among cases and controls.

CONCLUSION

The psoriatic patients could be considered as a group with increased atherosclerotic risk because of susceptibility to lipid profile, lipoprotein content and increased oxidative stress. Dyslipidemia may be a factor contributing to increased coronary heart disease in patients with psoriasis. A pathogenic link may coexist between lipoprotein, oxidative stress and psoriatic pathophysiology. This provides valuable information for timely intervention.

KEY WORDS

Psoriasis, lipid profile, cardiovascular risk

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INTRODUCTION

Psoriasis is a common, chronic, inflammatory, papulosquamous, proliferative condition of the skin, in which both genetic and environmental influences have a critical role. The disease is enormously variable in duration, periodicity of flares and extent.[1]

Psoriasis is a multisystem disease affecting more than 2% of the population.[2] Its etiology is still unknown, while genetic, metabolic and immunological mechanisms have been recommended as its cause. Lipid metabolism maybe playing a role in the pathogenesis of psoriasis.[3] Many data point out to lipid metabolism abnormalities during the course of psoriasis, suggesting that the perturbation of lipid metabolism may be a generalized phenomenon in psoriasis.

Psoriasis can present at any age and can appear just after birth or in old age. There is bimodal age of onset; the first peak at 15-20 years and a second one at 55-60 years.[4]

The disease occurs equally in males and females, but there is a considerable geographical variability in its prevalence.[5]

It is characterized by sharply demarcated erythematous plaques covered by silvery white scales.[6] The loss of scales from the skin surface in the course of psoriasis may be related to lipid disorders in the epidermis and in blood serum.[7]

Multiple factors including aberrant lipid and lipoprotein profiles, increased oxidative stress, decreased antioxidant capacity and other established risk factors, such as hypertension, obesity and diabetes mellitus have been associated with psoriasis.[2]

In the recent years, psoriasis has been recognized as a systemic disease associated with numerous multiorgan abnormalities and complications. In psoriatic patients an increased risk of cardiovascular abnormalities, hypertension, dyslipidemia, atherosclerosis, diabetes mellitus type 2, obesity, chronic obstructive pulmonary disease, cerebral stroke, osteoporosis, cancer and depression was noticed.[8]

Almost half a century ago, Lea, Cornish and Block reported increased serum lipid concentrations in the patients with psoriasis. Since then much research has been performed in this area, most of which consistently points to a raised prevalence of lipid abnormalities in individuals diagnosed with psoriasis.[2]

Patients with psoriasis have been observed to show changes in plasma lipid and lipoprotein composition, with tendency for an increase in total cholesterol (TC) and triglycerides (TG) associated with very low density lipoprotein (VLDL) cholesterol, and a decrease in high density lipoprotein (HDL) cholesterol.[5,9]

AIMS AND OBJECTIVES

- To determine serum lipid disturbances in psoriasis
- To study the demographic and clinical data in psoriasis

REVIEW OF LITERATURE

HISTORICAL ASPECTS OF PSORIASIS

During 129-99 BC, the word 'psora' was first used by Galen to describe a skin disorder characterized by a scaliness of the eyelids, corners of the eyes and scrotum.[10]

The Greek physician Hippocrates (460-377 BC) was the first person in recorded history to write about psoriasis, at the beginning of medicine in Corpus Hippocraticum. Hippocrates used the term psora, meaning "to itch".[11] The Roman sage Aurelius Cornelius Celsus is credited with the first clinical description of psoriasis.[4]

In 1776 Joseph Plenck wrote about psoriasis as fitting into the group of scaly diseases. Robert Willan (1757-1812) an English dermatologist was the first to recognize psoriasis as its own disease. He broke psoriasis into two categories. Leprosa Graecorum was the term used to describe the condition when the skin had scales. Psora Leprosa was used to describe the condition when it became eruptive.[12]

Psoriasis was first recognized as a distinct disease as early as 1808.[13] Although Robert Willan (1809) was the first to give an accurate description of psoriasis; it was Hebra (in 1841) who definitively separated the clinical features of psoriasis from those of leprosy.[10]

In 1879, Heinrich Koebner described the appearance of psoriatic plaques in clinically uninvolved skin of psoriatic patients following skin injury. He designated this phenomenon as 'artificial production of the psoriatic lesion'.[10]

Psoriatic skin changes are well known since biblical times about 3000 years. The first documented description was found in the Old Testament in the third book of

Moses in the Book of Leviticus. Here the psoriasis is assumed behind the term "zaraath".[14, 15] Since then, the hypothesized causes of the disease have naturally evolved. Until the late 1970s, the cause of the disease was considered to be due to a dysfunctionally increased proliferation and altered differentiation of the keratinocytes was based on typical microscopic changes. In the 1980s and 1990s, observations were made by the researchers to assume that activated T cells have a dominant pathogenic role in the initiation and persistence of psoriasis.[15]

Epidemiology:

Incidence and Prevalence: The prevalence of psoriasis is said to be 2% of the world's population. However, in the US and Canada, prevalences as high as 4.6% and 4.7% have been reported, respectively. Whereas, the frequency in Africans, African-Americans, Norwegian Lapps and Asians is between 0.4% to 0.7%.[10] The estimated prevalence of psoriasis in India varies from 0.44 to 2.8%.[16]

Estimates of the occurrences of psoriasis in different parts of the world vary from 0.1% to 3%.[4] According to world psoriasis day consortium about 125 million people all over the world suffer from this disease.[17]

Age of onset: Psoriasis can manifest at any age from infancy to old age. It has bimodal age of onset, the first peak at 15 to 20 years and the second one at 55 to 60 years. Men and women have almost equal frequency. However, a higher prevalence has been noted in men in most Indian studies.[4]

Patients with early onset are more likely to show widespread and recurrent disease, positive family history and show a significantly higher frequency of HLA Cw6.[18] This led Christophers and Henseler to propose that psoriasis can be

differentiated into 2 distinct patterns: type 1 with early onset at age and frequent HLA Cw6 association and type 2 with late onset and lacking HLA association.[19]

Type 1 disease which is a hereditary form, accounts for more than 75% cases, is HLA associated like HLA-Cw6 (commonest), DR7, B13 and B57 with a positive family history, onset before the age of 40yrs and is more severe and recurrent. Type 2 disease is a sporadic form, which starts later in life, with no family history or HLA-Cw6 association.[4] Also, psoriatic arthritis appears more common in individuals with type-1 early onset psoriasis vulgaris.[1]

Etiology and Pathogenesis:

Scientists thought that psoriasis was a skin disease, but in the mid-1980's they realized it is caused by a breakdown in the immune system. Psoriatic skin tries to replace itself by generating new cells, but it does so seven times as fast as healthy skin. Mitotic activity of the basal keratinocytes is increased by as much as factor of 50 in psoriatic skin, so keratinocytes need only 3-5 days to move from basal layer to cornified layer.[6] The body cannot shed the skin cells fast enough and this process results in patches or lesions forming on the skin surface. The skin's normal 30 day shedding cycle speeds up to 3 days and plaques of dead skin are formed.

The pathogenesis of psoriasis is thought to depend on the activation of lesional and/or circulating immune cells and their secreted products such as cytokines, chemokines and growth factors, leading to keratinocyte hyperproliferation, epidermal thickening and angiogenesis with, marked ectasia of blood vessels. The first master cytokine with a key role in developing and established psoriasis lesions is tumor necrosis factor alpha (TNF-α). Lesional dendritic cells, macrophages and T cells are

the major sources of TNF-α. A new potential master cytokine in psoriasis is IL-23, mainly produced by lesional dendritic cells, impacting proliferation and interferon gamma (INF-γ) production of memory TH-1 cells.[20]

Psoriasis is characterized by 4 abnormalities (1) Vascular changes where the papillary blood vessels become dilated and tortuous. This results in redness or erythema, one hallmark of psoriasis. (2) Inflammation where polymorphonuclear leukocytes from the dermal vessels enter the epidermis. Lesions are also rich in $CD4^+$ and $CD8^+$ T cells that release proinflammatory cytokines. (3) Hyperproliferation of the keratinocytic layer (acanthosis). (4) Keratinocytes retain their nuclei in the cornified layer (parakeratosis) and the granular layer is lost. These changes in the epidermis result in scaling.[13]

Genetics of psoriasis: The genetic basis of psoriasis has been appreciated for nearly 100 years. Psoriasis being genetically conditioned is beyond doubt.[19] Population surveys, twin studies, other family analysis and HLA studies all indicates genetic predisposition but controversies exist over the mode of inheritance.

Twin studies provide some of the strongest evidence for genetic basis of psoriasis. Identical twins share all their alleles in common, whereas fraternal twins only share half. Twin studies have indicated that many of the clinical features observed in psoriasis are determined by genetic factors. Various studies have shown the concordance for psoriasis in monozygotic twins ranging from 35% to 73%.[19]

This view is based on three observations. First, with regard to child developing psoriasis when first-degree relatives suffer from the disease, the risk is about 41% if both parents are affected with psoriasis whereas if only one parent is affected the risk

is 14%; if one sibling were affected, the risk was 6% that the other will be affected too, compared with 2% were no parent or sibling is affected.[19]

Secondly, its association with Human Leukocyte Antigen (HLA). HLA associations with psoriasis were reported in 1972. HLA-Cw6 has consistently demonstrated the highest relative risk for psoriasis. Several other HLA loci and alleles are associated with psoriasis, including HLA-B13, -B37, -B46, -B57, -Cw1, -DR7 and –DQ9. Unlike HLA-Cw6, there is no evidence for an association between HLA-Cw1-B46 haplotype and guttate psoriasis.[19]

Thirdly, several psoriasis susceptibility loci (PSORS 1-10) have been described. Several linkage studies have consistently identified PSORS 1 in the Major histocompatibility complex (MHC) region on chromosome 6 (6p21.3).[19]

Immunopathogenesis: Until recently, psoriasis was considered a disorder of epidermal keratinocytes; however it is now recognized primarily as an immune-mediated disorder. Skin is a primary lymphoid organ with an effective immunological surveillance system equipped with antigen presenting cells, cytokines synthesizing keratinocytes, epidermotropic T cells, dermal capillary endothelial cells, draining nodes, mast cells, tissue macrophages, granulocytes, fibroblasts and non-Langerhans cells. Skin also has lymph nodes and circulating T cells. These cells communicate by means of cytokine secretion and respond accordingly via stimulation of bacteria, chemical, ultraviolet light and other irritating factors. The primary cytokine released in response to antigen presentation is TNF-α. This is a controlled process unless the insult to the skin is prolonged, in which case imbalanced cytokine production leads to a pathological state such as psoriasis.[21]

In psoriasis, it is the activity of the T cells that is the driving force for induction and maintenance of the skin lesions. T lymphocytes consist of functionally distinct populations of helper T cells and cytolytic T cells. For activation, T cells need antigen presenting cells (APCs) to process and present peptide fragments on the APC cell surface. T cells respond to only cell surface associated antigens. Helper T cells express CD4, while cytolytic and suppresser T cells express CD8.[22]

Activation of T cell requires 3 steps: binding; antigen specific activation, also known as signal 1; and non-antigen specific cell-cell interaction, known as signal 2.

1. **Binding:** T cell attaches to the antigen presenting cell through surface adhesion molecules which are located reciprocally on the surfaces of both T cells and APCs. In skin, the Langerhans cells are the most efficient antigen presenting cell.
2. **Antigen specific activation:** Once the T cell-APC binding has occurred, the T cell express the T cell receptor which recognizes the peptide antigen being presented by the APC. This antigen stimulated activation leads to conversion of the naïve T cell into a memory cell. This is called antigen specific activation.
3. **Non-antigen specific cell-cell interaction:** This is also known as co-stimulation. If co-stimulation by other cell surface molecules does not occur following antigen presentation, the cell will not respond to the antigen and will undergo apoptosis.

After activation, the next step is induction of inflammatory response and tissue changes leading to clinical picture of psoriasis. This step involves many cell types (T cells, macrophages, dendritic cells, vascular endothelium, and keratinocytes). These secrete various cytokines that promote and maintain tissue inflammation. The cytokines involved are granulocyte-macrophage colony stimulating factor (GMCSF),

epithelial growth factor (EGF), interleukins (IL8, IL12, IL1, IL6), interferon-gamma (INF-γ), tumour necrosis factor-alpha (TNF-α).[22]

Langerhans cells, a type of dendritic cell, recognizes and captures antigens, migrates to local lymph nodes and presents them to T cells. The activation of T lymphocytes releases pro-inflammatory cytokines such as TNF-α that lead to keratinocyte proliferation. This hyperproliferative response decreases epidermal transit time (the approximate time it takes for normal maturation of skin cells) from 28 days to 2-4 days and produces typical erythematous scaly plaques of psoriasis. Vascular endothelial growth factor (VEGF) and IL-8 released from keratinocytes contribute to vascularization seen in psoriasis.[15,20,21]

TNF-α plays a critical role in activation of innate and acquired immune responses leading to chronic inflammation, tissue damage and keratinocyte proliferation.[22]

Debate continues whether psoriasis is an autoimmune disorder or T helper 1 immune dysfunction. Initially, immature dendritic cells in the epidermis stimulate T-cells from lymph nodes in response to as yet unidentified antigen stimulation. The lymphocytic infiltrate in psoriasis is CD4 and CD8 T cells; this synthesizes mRNA for interleukin-2 (IL-2) resulting in a subsequent increase in IL-2 receptors.[15,21,23]

Psoriasis is considered a Th-1 dominant disease due to increase in cytokines of Th-1 pathway- interferon-gamma (INF-γ), IL-2 and IL-12, found in psoriatic plaques. These cytokines are responsible for differentiation, maturation and proliferation of T-cells into memory cells. T cells migrate to the skin and accumulate around dermal blood vessels, resulting in the formation of psoriatic lesion.[1,12]

FIG 1: IMMUNOPATHOGENESIS OF PSORIASIS

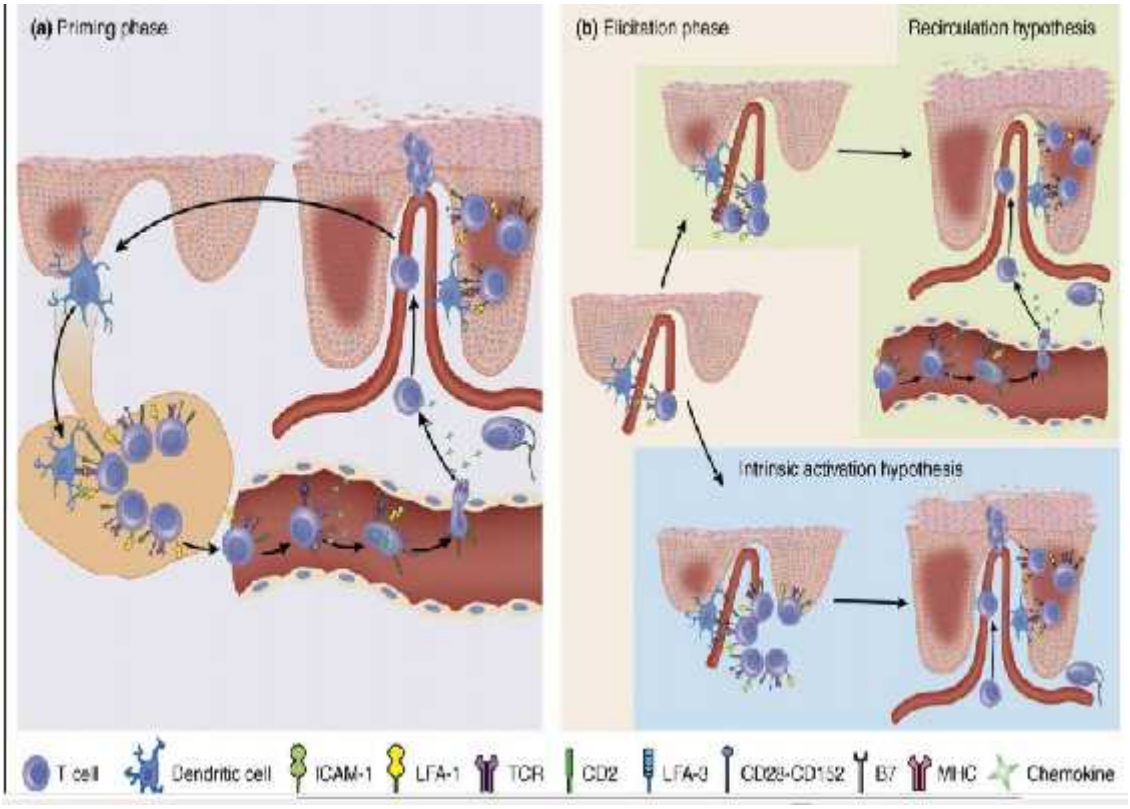


Figure 2. Two steps in the development of psoriasis: priming versus elicitation. The very first time a psoriasis patient experiences an outbreak of skin lesions can be considered the priming phase. Naïve T cells with autoimmune potential circulating through secondary lymphoid organs such as lymph nodes are activated by mature skin derived dendritic cells, clonally expanded and induced to upregulate adhesion molecules necessary for entrance into skin compartments. Upon recognition of the lesional inciting (auto-)antigen presented by lesional dendritic cells in a TNF-α-rich environment T cells will be activated, proliferate and secrete T helper (TH)-1 cytokines. Under normal circumstances inflammation is followed by resolution of the inflammatory process, however in the case of psoriasis a vicious circle begins involving a multitude of cellular and secreted components. This process culminates in the typical psoriatic tissue reaction featuring epidermal hyperproliferation, papillomatosis, activation and expansion of immune cells and an angiogenic tissue reaction. Infectious agents such as streptococci or human papilloma viruses, medications such as lithium or potentially stress might trigger these very first events of psoriasis. During the contraction phase of the autoimmune response and during tissue homeostasis memory T cells will be strategically positioned in skin ready to react to a new trigger event. Future flares (elicitation or recall phase) of psoriasis have a lower threshold and are triggered by events described above including physical stress leading to an activation of local T cells by skin derived antigen-presenting dendritic cells (intrinsic T-cell activation hypothesis). Local proliferation and expansion of T cells with consecutive secretion of TH-1 cytokines will again lead to downstream events including keratinocyte proliferation and an angiogenic tissue reaction. An alternative scenario involves selectin and integrin dependent recruitment of effector T cells along chemokines gradients into inflamed skin as predicted by the conventional immune surveillance concept (recirculation hypothesis).

Biochemical aspects

The biochemical changes found are associated with an increased cell turnover. There is a high concentration of lipids and phospholipids, an increase in acid mucopolysaccharides and alpha amino acids. Sulphydryl groups are also increased. Nuclear protein is increased as a result of epidermal proliferation. Enzymes, normally present in the granular layer, are displaced in parakeratotic keratin; acid phosphatase, nonspecific esterases, lipases and other enzymes not normally present orthokeratosis, are associated with the parakeratotic process. Serum and red cell folate and B12 levels are lowered because of increased utilization. Blood hydroxyproline is raised.[24]

Triggering factors

The present understanding favours a primarily immunological mechanism in which abnormal T lymphocytes affecting genetically susceptible keratinocytes under several environmental factors are recognized in triggering and exacerbating psoriasis.[12,25]

Trauma: Psoriasis lesion may appear as a consequence of injury to the uninvolved skin in psoriasis patients. This is known as "Koebner's phenomenon" and it was first described by a German dermatologist Heinrich Koebner in 1877. A wide range of injurious local stimuli including physical, chemical, electrical, surgical, infective and inflammatory injuries are known to elicit psoriatic lesions. The pathogenesis of Koebners phenomenon is attributed to the involvement of both epidermis and dermis. There is an increased influx of CD4 lymphocytes and local production of cytokines and adhesion molecules. Dermatosis resulting from the spread of an infective agent like molluscum or warts is termed as pseudo-Koebner phenomenon.[1] The Koebner

reaction usually occurs 7-14 days after the injury. Its incidence varies between 38 and 76% in patients with psoriasis. In a given patient it is an all-or-none phenomenon i.e. if psoriasis occurs at one site of injury it occurs at all sites of injury.[1,12] Clearing of the existing psoriasis lesion following injury has been observed and is termed Reverse Koebner Phenomenon.[1]

Infections: Several case reports have raised the hypothesis that subclinical streptococcal infection may play a role in exacerbation of chronic plaque psoriasis. In case of guttate psoriasis, studies suggest that respiratory infections, especially Streptococcus pyogenes, are strongly associated with the onset and flaring of this disease.[1,26] Guttate and chronic plaque psoriasis share strong HLA associations, particularly with HLA-Cw6.[1]

Study provides strong evidence that guttate psoriasis is triggered by streptococcal superantigens. "Superantigens" refers to a group of microbial antigens that cause the marked expansion of T cells expressing specific receptor (TCR) β chain variable (Vβ) gene segments. A recent report by Lewis et al described a marked overrepresentation of Vβ2+ T cells in the acute skin lesions of patients with guttate psoriasis. Superantigens stimulate T cells almost solely through the Vβ portion of the TCR and therefore induce an expression of both CD4+ and CD8+ T cells. This is markedly different from T cells activated by conventional peptide antigens which results in an expansion of only a subset of CD4+ or CD8+ Vβ-expressing cells with limited TCR junctional diversity.[27]

Severe exacerbation of psoriasis can be a manifestation of HIV infection and effectively treated with antiretroviral therapy. Like psoriasis, HIV-associated psoriasis has a strong association with HLA-Cw6. Interestingly; the prevalence of psoriasis in

HIV infection is no higher than in the general population (1-2% of patients) indicating that this infection is not a trigger for psoriasis but rather a modifying agent. Psoriasis is increasingly more severe with progression of immunodeficiency. This paradoxical exacerbation of psoriasis may be due to loss of regulatory T cells and increased activity of the CD8-T cells subset.[12]

Stress and Quality of life: Psychological stress or an abnormal response to stressors has been found to modify the evolution of skin disorders like psoriasis, and is associated with a variety of psychological problems, including poor self-esteem, sexual dysfunction, anxiety, depression and suicidal ideation. Estimates of the proportion of patients with psoriasis whose disease is affected by stressful events vary from 40-80%.

Psychological stress causes phenotypic changes in circulating lymphocytes and is regarded as an important trigger of the Th-1 cell-polarized inflammatory skin disease in psoriasis.

In a recent prospective study, the frequency of psychiatric disturbances decreased with improvement in clinical severity and symptom.

Considerable clinical evidence exists for the role of stress in onset and exacerbation of psoriasis. Psoriasis is associated with a lack of self-esteem and increased prevalence of mood disorders, including depression. Prevalence of depression in patients with psoriasis is about 24%.

The impact of psoriasis on quality of life can result in significant daily stress and psychological morbidity for the patient. The stress is largely secondary to the cosmetic disfigurement and social stigma associated with psoriasis. Because it is

cosmetically disfiguring skin condition, psoriasis can greatly affect an individual's body image and self-confidence. Symptoms like mild to intense itching "skin shedding", tightness; redness, dryness and bleeding all have a negative impact on the quality of life. Psoriasis can also have negative influence on the patient's desire for physical intimacy and causes decreased libido. Studies have shown that psoriasis interferes with sexual relations in 35-50% of patients.[28]

Alcohol consumption: To date, the data on alcohol as a risk factor for psoriasis have been conflicting. However, studies have suggested that psoriasis may lead to sustained drinking and alcohol may worsen psoriasis.[26]

A number of studies have shown the possible influence of alcohol on the severity, phenotype, course and prognosis of psoriasis, concluding that alcohol can not only trigger psoriasis but also exacerbate a preexisting disease. Heavy drinkers have a tendency to develop more severe, more extensive and more inflamed manifestations.

Alcohol consumption may adversely affect psoriasis through several mechanisms like altering aspects of immune response, predisposing drinkers to infections, enhancing mitogen-driven lymphocyte proliferation, upregulating proinflammatory cytokines, influencing keratinocyte proliferation and differentiation, and barrier function.

Ethanol metabolites, acetyldehyde (AcH) and acetone play role in the pathogenesis of psoriasis. AcH is a product of ethanol oxidation, through the action of alcohol dehydrogenase enzyme and through cytochrome p450 isoform 2E1, with production of reactive oxygen species. Acetone is formed by decarboxylation of

acetoacetic acid. Alcohol and its metabolites can promote production of proinflammatory cytokines in different cell types and may increase lymphocyte activation and proliferation.[29]

Smoking: Significant epidemiological evidence suggests an association between cigarette smoking and the development of psoriasis. Smoking increases oxidative damage, promotes inflammatory damage and enhances activation of genes associated with psoriasis. 'Oxidative damage' is caused by a series of reactions initiated by a highly reactive unpaired electron, referred to as free radical or reactive oxygen species (ROS). Free radicals are produced through natural metabolism and are normally detoxified by antioxidant molecules. However, prolonged free radical exposure can overwhelm an individual's antioxidant capacity. Cigarette smoke contains approximately 10^{15} free radicals per puff, and these can trigger a cascade of systemic reactions that lead to psoriasis. ROS, specifically O_2 and H_2O_2, are elevated in the lesional and nonlesional skin of patients with psoriasis, while dermal levels of antioxidants such as ascorbic acid are decreased.[30]

Smoking (more than 20 cigarettes daily) has also been associated with more than a twofold increased risk of severe psoriasis. Recently, a gene-environment interaction has been identified between low activity of the cytochrome P_{450} CYPA1A and smoking in psoriasis. Smoking has also been strongly associated with pustular psoriasis.[12,30]

Diet and obesity: Fatty tissue acts as an active endocrine tissue and gives rise to pro-inflammatory state which causes obesity in psoriasis. Diet rich in fresh fruits and vegetables are associated with lower prevalence of psoriasis. Dietary intake of Omega-3 and Omega-6 decrease the disease severity.[31]

Biopsy specimens of human adipose tissue have demonstrated increased levels of TNF-α mRNA in patients with a high percentage of body fat. Obesity has been shown to be associated with high levels of circulating TNF-α receptors in humans. Also TNF-α contributes to insulin resistance. Other inflammatory cytokines elevated in the serum of obese patients of psoriasis include IL-6, IL-1β, CCL2, CXCL8, CXCL9 and C-reactive protein.[32]

Climate: Psoriasis worsens in winter and improves in summer.[6] Low levels of vitamin D have important implications in the pathogenesis of psoriasis. Vitamin D deficiency is very frequent in patients with chronic plaque psoriasis and this finding is more common in winter. Vitamin D_3 not only acts on the vitamin D receptor to regulate keratinocyte growth and differentiation, but also has an influence on immune functions of dendritic cells and T lymphocytes. Vitamin D_3 inhibits the production of IL-2 and IL-6, blocks transcription of IFN-□ and granulocyte-macrophage colony stimulating factor mRNA and inhibits cytotoxic T cells and natural killer cell activity.[33]

Drugs: Medications that exacerbate psoriasis include anti-malarials, beta-blockers, lithium, NSAIDS, INF's (alpha and gamma), imiquimode, angiotensin- converting enzyme inhibitors and gemfibrosil. Withdrawal of potent topical or systemic steroids is associated with exacerbation of psoriasis. NSAIDS like oral phenylbutazone, oxyphenbutazone, indomethacin, diclofenac, meclofenamate and ibuprofen are reported to precipitate psoriasis. Imiquimod acts on pDCs and stimulates IFN-α production, which then strengthens both innate and Th1 immune responses.[1,12]

The precise mechanism of the influence of β-blockers on the course of psoriasis is unknown. Several hypotheses have been proposed like delayed-type

hypersensitivity, an immunological mechanism, impaired lymphocyte transformation, and a decrease in intraepidermal cAMP with consequent increase of epidermal cell proliferation. Therefore blockage of epidermal β-receptors may decrease the intraepidermal cAMP with consequent increase of epidermal cell turnover. Latency periods for β-blockers vary from several days to 12 months.

The first description of association between aggravation of psoriasis and treatment with lithium carbonate was carried out by Carter and lithium-provoked psoriasis was first reported by Bakker and Pepplinkhuizen. The latency period between starting lithium and the exacerbation of psoriasis is about 20 weeks. Lithium may induce a new onset of psoriasis; exacerbate pre-existing psoriasis; or cause nail changes, psoriasis pustulosa and erythroderma. Its incidence is reported to range from 3.4 to 45%. Recent studies have demonstrated that lithium affects cell communication between psoriatic keratinocytes through the "psoriatic cytokine network" by triggering the secretion of transformation growth factor (TGF)-α, IL-2, IL-6 and INF-γ. Decrease in cAMP and inositol causes low intracellular levels of calcium, leading to lack of differentiation and increased proliferation of keratinocytes, enhanced chemotaxis, and phagocytic activity of polymorphonuclear (PMN) leukocytosis.

Arachidonic acid can be metabolized to form either prostaglandins via the cycloxygenase pathway or leukotrienes via the 5-lipoxygenase pathway. NSAIDs inhibit the metabolism of arachidonic acid by the cycloxygenase pathway, leading to an accumulation of leukotrienes, which have postulated to aggravate psoriasis.[34]

Pregnancy: Psoriasis may remit during pregnancy. This is due to increased IL-10 levels in the circulation which is known type 1 immune response inhibitor.[4] During the third trimester of pregnancy, monocytic IL-12 production and TNF-α production

has been found to be lower than postpartum values, while, at the same time, urinary cortisol and norepinephrin excretion and serum levels of 1,25-dihydroxyvitamin were higher than postpartum values. These hormones are known to suppress IL-12 and TNF-α production by monocytes/macrophages.[35]

Serum and skin levels of TNF-α, INF-γ and IL-6 are increased in psoriasis and positively correlated with disease severity. A study has shown that greater risk of low birth weight infants observed among infants born to mothers with severe psoriasis is most likely attributed to the disease itself. The explanation given is that the cytokines have detrimental effects on the maternal placenta and thus lead to impaired fetal growth and low birth weight infants.[36]

Clinical features and classification of psoriasis:

Plaque psoriasis (Psoriasis vulgaris, chronic stationary psoriasis, nummular psoriasis): Psoriasis vulgaris is the most common form of psoriasis, seen in approximately 90% of patients. Lesions are erythematous, scaly, symmetrically distributed plaques with well defined edge covered with silvery white scales, characteristically localized to the extensor aspects of the extremities, particularly elbows and knees, along with scalp, lower lumbosacral, buttocks and genitalia.[12] Early lesions frequently start as small pinpoint papules, which, soon in their evolution, show scaling. Sometimes, lesions predominate on seborrheic areas (scalp and face). This is called as sebopsoriasis.[37] Under the scale, the skin has a glossy homogeneous erythema, and bleeding points appear when the scale is removed, traumatizing the dilated capillaries below (the Auspitz sign).[1,12] A white blanching ring, known as Woronoff's ring, may be observed in the skin surrounding a psoriatic plaque.[1,12,38] Several other varients of psoriasis include psoriasis geographica,

psoriasis gyrata, annular psoriasis, rupioid psoriasis, ostraceous psoriasis and elephantine psoriasis.[12]

Guttate (Eruptive) psoriasis: Guttate psoriasis (from the Latin gutta, meaning "a drop") is characterized by eruption of small papules over the upper trunk and proximal extremities. It typically manifests at an early age and as such is found frequently in young adults. This form of psoriasis has the strongest association to HLA-Cw6, and β haemolytic streptococcal throat infection frequently precedes or is concomitant with the onset or flare of guttate psoriasis.[12] Lesions are present over the upper trunk and proximal extremities. Lesions are from 2 or 3mm to 1 cm in diameter, round or slightly oval in shape.[1] The number of lesions may range from 5 or 10 to over 100. Guttate psoriasis accounts for 2% of total cases of psoriasis.[38] The disease is self-limiting; however, a proportion of affected individuals may progress to a more chronic form of plaque psoriasis.[37] The risk of developing a more chronic form of psoriasis after a first episode of guttate psoriasis has been estimated at 40%.[1,12,37]

Inverse psoriasis: Inverse psoriasis involves major skin folds including the axillae, genito-crural folds, submammary folds, gluteal folds and neck. Scaling is usually minimal or absent, and the lesions show a glossy sharply demarcated erythema.[12,38]

Erythrodermic psoriasis: Psoriatic erythroderma represents the unstable, generalized form of the disease that affects all body sites, including the face, hands, feet, nails, trunk, and extremities. Although all the symptoms of psoriasis are present, erythema is most prominent feature and superficial scaling is seen.[12] Whole skin is involved, patient is febrile and ill, the course is often prolonged, relapses are frequent and there is appreciable mortality.[1] Erythroderma may impair the thermoregulatory capacity of the skin, leading to hypothermia, high output cardiac failure, and metabolic changes

including hypoalbuminaemia, and anaemia due to loss of iron, vitamin B12, and folate.[38]

Pustular psoriasis: In pustular psoriasis, macroscopic lesions appear in and around the lesions and also on the uninvolved skin particularly over the flexor aspect of the thighs and arms. Pustular psoriasis can be either localized or generalized. Pustular psoriasis often occurs after abrupt withdrawal of corticosteroids.[12,38]

In one of the localized variant (Acrodermatitis continua of Hallopeau) also known as dermatitis repens, pustules involve the dorsal aspect of hands, forearms and feet. Whereas in palmoplantar pustulosis, clusters of pustules appear over the ventral aspect of hands and feet.[37]

In the generalized variant (von Zumbusch), pustules are distributed all over the body. The patient is pyrexial, with red, painful, inflamed skin studded with monomorphic, sterile pustules which may coalesce to form sheets.[12,38]

Nail changes in psoriasis: Nail changes are found in 20-50% of patients with psoriasis.[1] Fingernails are more commonly affected than toenails. Pitting is the most common nail change seen; other nail changes include yellowish discoloration, subungual hyperkeratosis, onycholysis, oil drop sign and splinter hemorrhages.[1,12,37] Orange-red areas may be present beneath the nail plates and are termed as “oil spots” or “oil drop sign”.[38]

Pits range from 0.5 to 2.0 mm in size and can be single or multiple. The proximal nail matrix forms the dorsal portion of the nail plate, and psoriatic involvement in this region results in pitting due to defective keratinization. Splinter haemorrhages result from capillary bleeding underneath the thin suprapapillary plate

of the psoriatic nail bed. Subungual hyperkeratosis is due to hyperkeratosis of the nail bed.[12]

Psoriatic arthritis: It is an inflammatory arthritis associated with psoriasis of skin and/or nails with a negative serological test for rheumatoid factor and the absence of rheumatoid nodules. Arthritis prevalence among psoriasis patients has been estimated at 2.6-7%. The peak onset for psoriatic arthritis is 4th decade. In juvenile onset form of psoriatic arthritis, the age of onset is between 9 and 12 years. Psoriatic arthritis appears more common in individuals with type 1 early-onset psoriasis vulgaris. A specific HLA association with psoriatic arthritis is HLA-B27, seen particularly in spondyloarthritis. It occurs in 5-30% of patients of cutaneous psoriasis.[1] Moll and Wright classification 5 clinical groups;

1. **Mono and asymmetric oligoarthritis (70%):** Inflammation of both distal and proximal interphalangeal joints of hands and feet is the most common presentation of psoriatic arthritis. It results in classical 'sausage' digits.
2. **Arthritis of distal interphalangeal joints (5%):** Involvement of distal interphalangeal joints is 'classic' but uncommon presentation of psoriatic arthritis.
3. **Rheumatoid arthritis-like presentation (15%):** There is symmetric polyarthritis involving small and medium-sized joints in particular the proximal interphalangeal joints (PIP), metacarpophalangeal joints (MCP), wrists, ankles and elbows. Patients are usually seronegative.
4. **Arthritis mutilans (5%):** This is the least common variant. Patients have severe, rapidly progressing, joint inflammation that results in destruction of the joints and permanent deformity. Digits become shorter, wider and softer because of osteolysis and telescoping phenomenon.

5. **Axial arthritis (5%):** The spondylitis resembles that seen in ankylosing spnodylitis, with axial arthritis as well as involvement of knees and sacroiliac joints.[10,39]

FIGURE 2: PLAQUE TYPE LESIONS DISTRIBUTED IN A SYMMETRICAL PATTERN OVER THE BACK

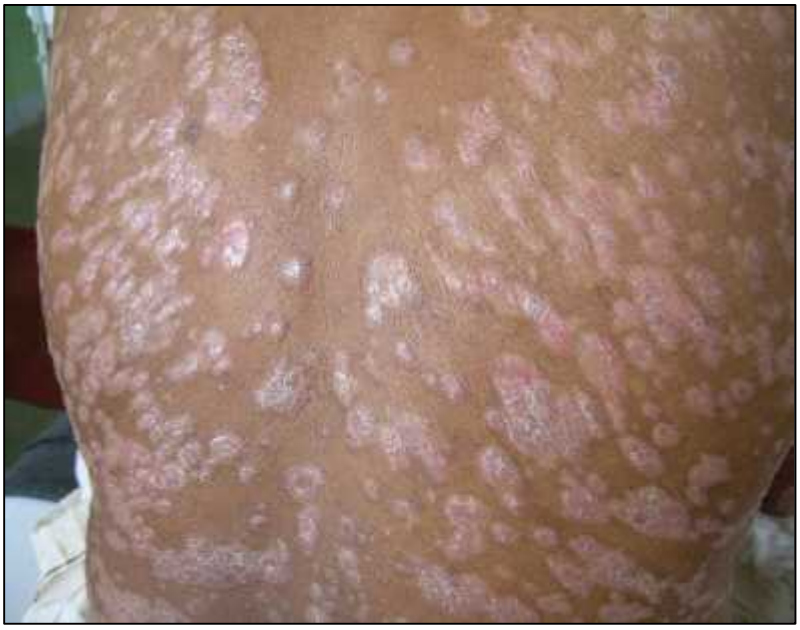


FIGURE 3: SINGLE PSORIATIC PLAQUE PRESENT OVER THE THIGH

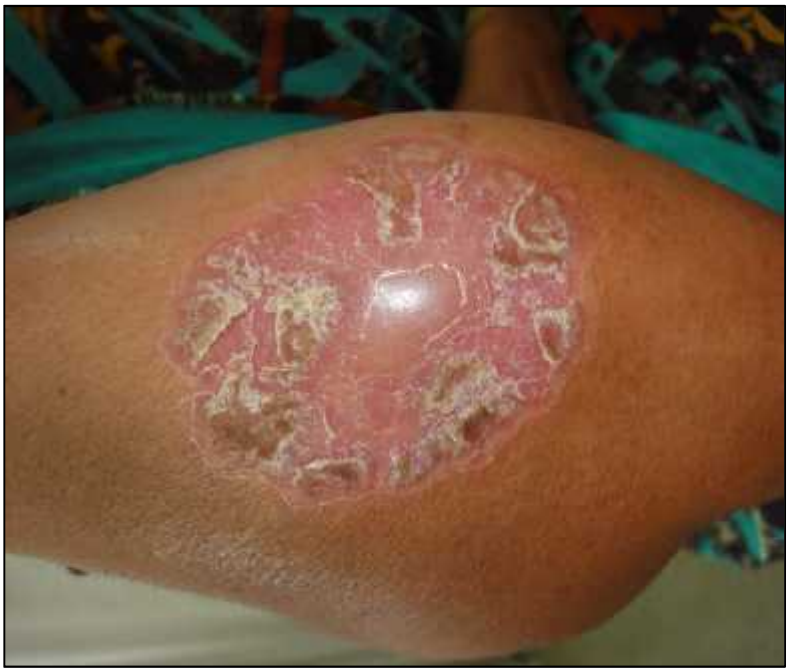


FIGURE 4: GUTTATE TYPE LESIONS OF PSORIASIS ON THE BACK

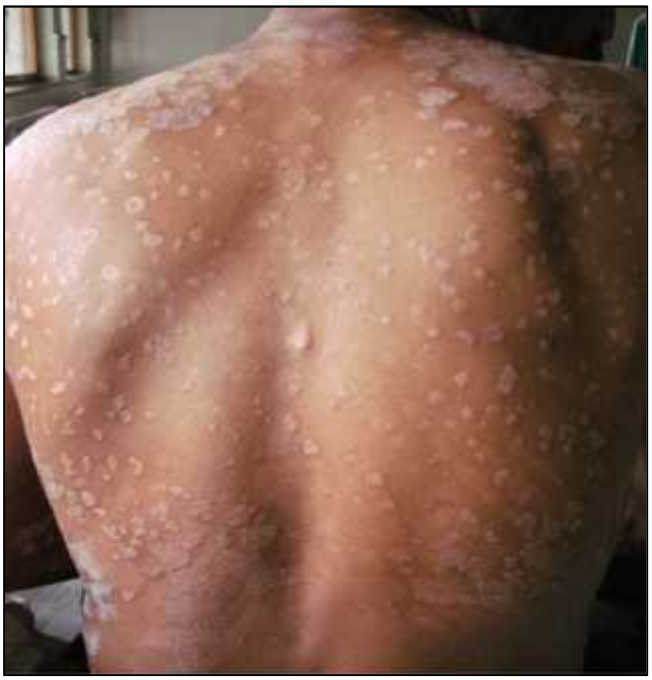


FIGURE 5: MULTIPLE, ERYTHEMATOUS, SCALY, SHINY PLAQUES PRESENT ON THE ABDOMEN AND UPPER LIMBS

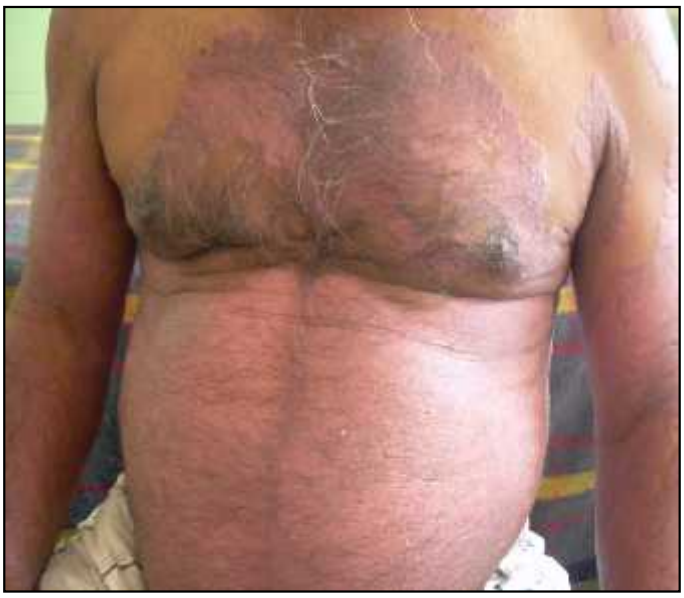


FIGURE 6: MULTIPLE NAIL PITS ON THE FINGER NAILS

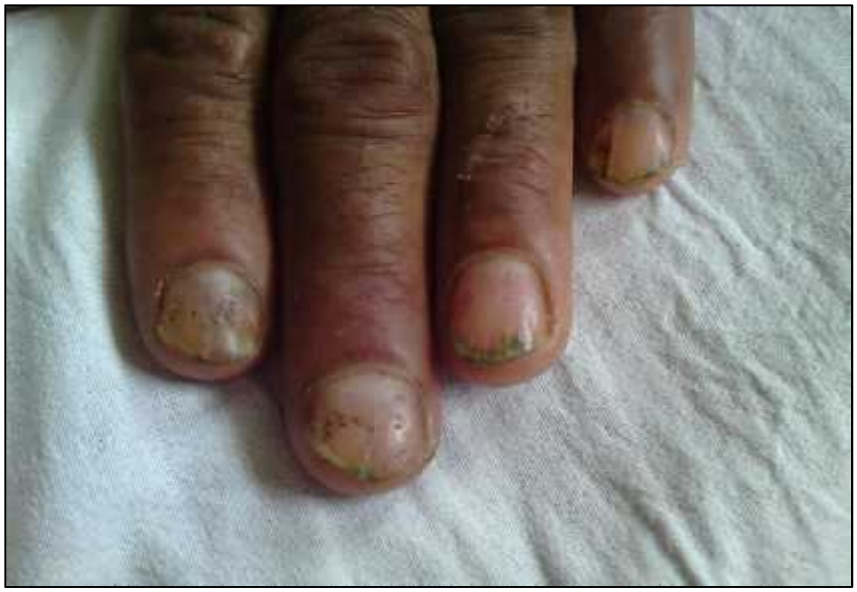


FIGURE 7: "OIL DROP SIGN" ON THE FINGER IN A PSORIASIS PATIENT

FIGURE 8: ARTHRITIS MUTILANS TYPE OF PSORIATIC ARTHRITIS IN THE HANDS IN A PATIENT

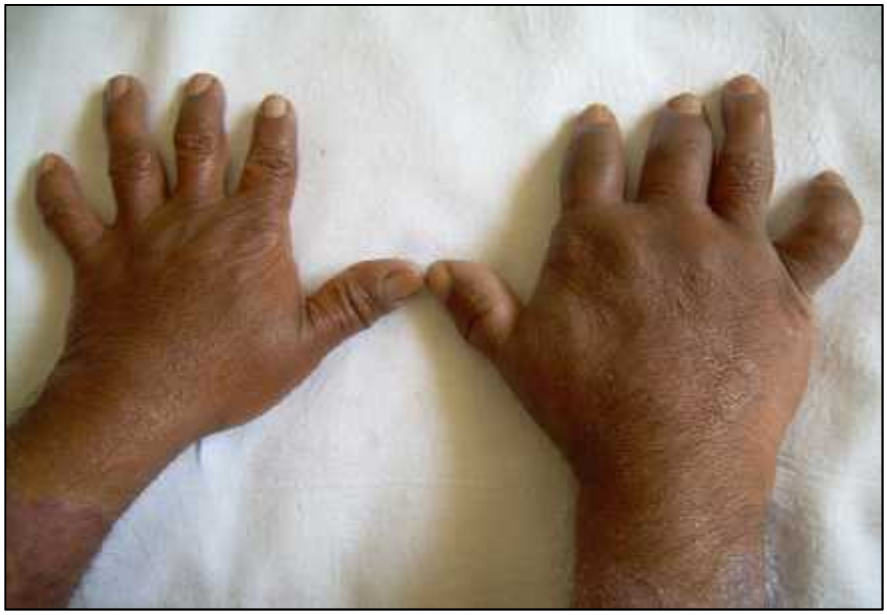
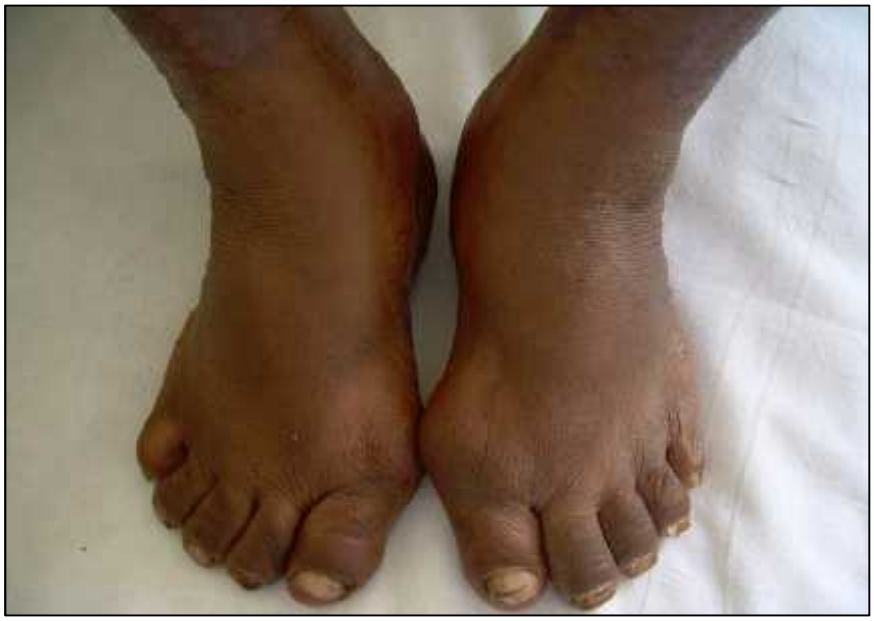


FIGURE 9: ARTHRITIS MUTILANS TYPE OF PSORIATIC ARTHRITIS IN THE FEET IN THE SAME PATIENT



Histopathology

Psoriasis is a dynamic dermatosis with morphological changes during the evolution of the individual lesion.

Early lesion: It consists of elongation and dilatation of blood vessels of papillary dermis, with associated edema and lymphocytic infiltrate (perivascular cuffing). Vessels are dilated and tortuous, with some neutrophils in the lumen. Lymphocytes and neutrophils emerge from the vessels reaching the epidermis ("squirting" papilla). Then there is thickening of epidermis with loss of granular cell layer and formation of moulds of parakeratosis. Scattered neutrophils are seen at the edge of moulds of parakeratosis which represents earliest manifestations of Munro's microabscesses.

Advanced stage: This is characterized by regular acanthosis (thickening of stratum spinosum) an epidermal "psoriasiform hyperplasia" with regular elongation of rete ridges and thinning of suprapapillary plates. Parakeratosis becomes confluent, with loss of granular layer. There is transmigration of inflammatory cells from epidermis into parakeratotic scales resulting in intracorneal collections of neutrophils, the so-called "Munro's microabscess". Similar accumulation in stratum spinosum is defined as "Spongiform pustule of Kogoj". Dermal inflammatory infiltrate is heavier than in early lesions, it is composed of T lymphocytes containing few Langerhans cells with occasional neutrophils.

Later lesions: There is orthokeratosis, an intact granular layer and mild exocytosis of inflammatory cells.[40]

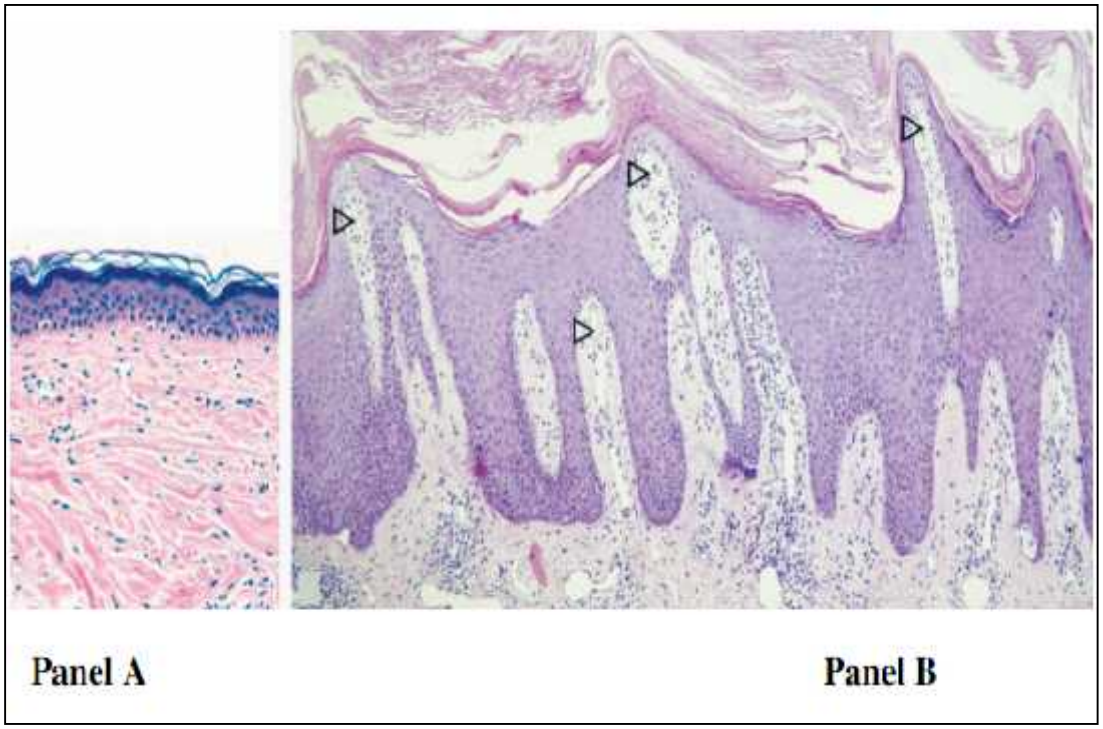
Histopathology based on the various forms of psoriasis:

Guttate Psoriasis: There is spongiosis and a superficial mononuclear infiltrate without the typical findings of epidermal thickening or neutrophilic microabscesses found in the well established lesions. There is marked edema in the upper papillary dermis.

Erythrodermic Psoriasis: The psoriasiform pattern is preserved, but there is near absence of parakeratosis, due to constant shedding of scales or desquamation. Extensive edema of the papillary dermis and some spongiosis is noted.

Pustular psoriasis: In the early stage, there is marked inflammatory infiltrate, predominantly of mononuclear cells with significant edema and spongiosis. A well developed pustular eruption will show a macropustule with large spongiotic intraepidermal or subcorneal space filled with aggregates of neutrophils and covered by a thick orthokeratotic stratum corneum. Focal acantholysis may be noted. Dermal changes show more edema and extravasated polymorphic neutrophils.[41]

FIGURE 10: HISTOPATHOLOGICAL ALTERATIONS IN PSORIATIC SKIN TISSUE



As compared with normal skin (Panel A), the epidermis in psoriatic skin (Panel B) is characterized by dramatic histopathological alterations, acanthosis with elongation of epidermal rete ridges (arrowheads), marked hyperkeratosis (thickening of the stratum corneum), loss of granular layer and parakeratosis (nuclei in the stratum corneum). In addition dermal blood vessels have increased in size and number (by both angiogenesis and dilatation); they are contorted and reach up to locations directly underneath the epidermis (arrows). Finally, mixture of leukocytic infiltrate in seen in both dermis and epidermis.

Comorbidities associated with psoriasis: Psoriasis has been associated with a number of behavioral and systemic comorbidities, including cardiovascular disease, Crohn's disease, hypertension, diabetis mellitus, obesity, depression, metabolic syndrome, hyperlipidemia, psoriatic arthritis, smoking, lymphomas, alcoholism, and anxiety. Epidemiological studies have shown that, in patients with psoriasis, associated disorders may occur more frequently than expected. Comorbidities often become clinically manifest years after onset of psoriasis and more frequently seen in severe disease. In particular, nonalcoholic fatty liver affects about 50%, Crohn's disease 0.5% and celiac disease 0.2 to 4.3% of psoriasis patients.[39]

Cardiovascular disease: Psoriasis is associated with traditional risk factors such as increased basal metabolic rate (BMI), hyperlipidemia, hypertension, type 2 DM, obesity and cigarette smoking. Elevated levels of C-reactive protein (CRP) are a risk factor for CVD and it can predict long term risk of cardiovascular events.[8] On the other hand, cardiovascular disease frequently develops in individuals with persistant hyperlipidemia. Risk factors like hypertension, vascular endothelial dysfunction, oxidative stress, hyperhomocysteinemia, diabetes, smoking, high alcohol consumption, obesity, metabolic syndrome and intra-abdominal adipose visceral tissue and their adipokines contribute to the formation of atherosclerosis which is hallmark of cardiovascular disease. The same factors are also implicated in psoriasis patients. The risk factors for cardiovascular disease as well as myocardial infarction occur with higher incidence in patients with psoriasis. The risk factors for cardiovascular disease as well as myocardial infarction occur with higher incidence in patients with severe psoriasis.[42]

Autoimmune diseases: The strongest link so far has been with inflammatory bowel disease, specifically Crohn's disease. Crohn's disease is mediated by an abnormal Th-1 immune response like psoriasis. Research has identified regions on chromosomes 16, 6, 4 and 3 where genetic markers are linked to both psoriasis and Crohn's disease.[26]

Studies suggest a possible link between psoriasis and multiple sclerosis, as psoriasis occurs more commonly in families with multiple sclerosis than in controls.[26]

Obesity: There is a positive association between psoriasis onset and body mass index.[26] Obesity is also associated with a state of chronic, low-grade inflammation and inflammatory markers such as C-reactive protein and fibrinogen, which have been associated with elevated cardiovascular risk. Obesity and low physical activity are more common among patients with psoriasis than control subjects.[43]

Quality of life (QOL): Patients with psoriasis have a reduction in their quality of life similar to or worse than patients with other chronic diseases such as ischaemic heart diseases and diabetes.[38]

Sleep disturbances can cause significant quality-of-life impairment. Direct and indirect evidence demonstrates that sleep quality in patients with psoriasis can be adversely affected by pruritus, depression, pain, obstructive sleep apnea (OSA) or a combination of these. TNF, IL-6 and substance P (SP) are mediators involved in psoriasis, pruritus, depression, pain and OSA that may also affect sleep.[44]

Metabolic syndrome: Metabolic syndrome is a constellation of disorders including obesity, dyslipidemia, hypertension and glucose intolerance that increases the risk of cardiovascular disease and diabetes. Several reports indicate the association between

psoriasis and metabolic syndrome. Among the inflammatory cytokines, TNF-α plays a pivotal role in both psoriasis and metabolic syndrome.[45]

Malignancies: Several studies have investigated the risk of cancer in patients with psoriasis. Psoriasis is associated with an increased risk of lymphoma, particularly Hodgkin's lymphoma and cutaneous T-cell lymphoma. Studies have reported increased risk of squamous cell carcinoma and melanomas as well.[25,26]

Psychiatric diseases: Wide ranges of psychological characteristics have been reported in psoriatic patients including depression, anxiety, obsessive behavior and difficulty expressing emotions such as anger. There is higher prevalence of depression in patients with psoriasis compared to controls. Increased rates of depression in patients may be another factor leading to increased risk of CVD. Depression may be so severe that patients may in fact contemplate suicide. In a study of 217 psoriatic patients, almost 10% reported a wish to be dead and 5.5% had active suicide ideation.[26]

Complications:

Patients with psoriasis have increased a morbidity and mortality from cardiovascular events, particularly MI, psychological stress, cancer, diabetes and hypertension. Secondary infection of psoriasis lesions with staphylococcus aureus may occur during topical steroid therapy under occlusive dressings. Nephritis and renal failure, hepatic failure, atypical pulmonary fibrosis, amyloidosis of the secondary type is a rare complication of arthropathic and generalized pustular psoriasis.[1]

Assessment tools used to evaluate psoriasis

The basic characteristics of psoriasis lesions- redness, thickness and scaliness- provide a means of assessing the severity of psoriasis. The current gold standard for assessment of extensive psoriasis has been psoriasis assessment severity index (PASI). The PASI is the measure of the average redness, thickness and scaliness of the lesions, weighted by the area of involvement. PASI along with physician global assessment and quality of life measures, provide a completement of measures for studies of moderate to severe psoriasis.[46]

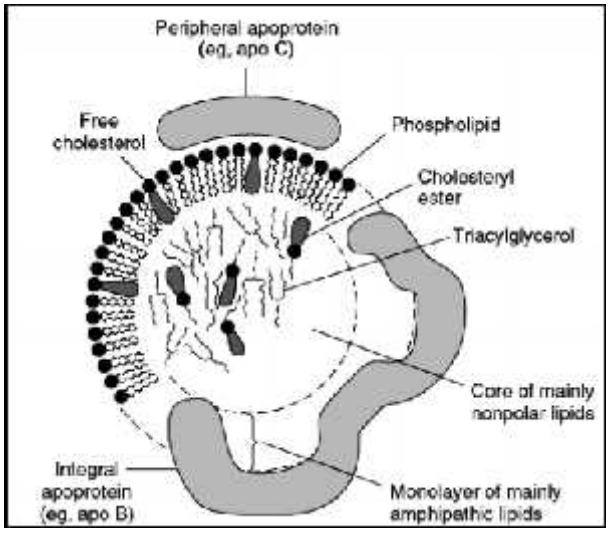
Health-related quality of life (HRQL) refers to patient's perceived distress and disability. It emphasizes physical functioning, emotional functioning, social functioning, occupational functioning, and leisure functioning. Dermatology Life quality index (DLQI) measures symptoms and feelings, daily activities, leisure, work and school, personal relationship and bother with treatment. It has been used widely in research and has good reliability, validity and sensitivity to change. Lattice system – Physicians Global Index relies on global rating of scale, erythema and lesion thickness to determine an overall rating for the patient.[47]

Certain combination outcome measures such as National Psoriasis Foundation – Psoriasis Score and Salford Psoriasis Index incorporate both physical measures of disease burden and quality of life outcomes.[4]

LIPOPROTEIN METABOLISM

Lipoproteins are large macromolecular complexes that transport hydrophobic lipids particularly triglycerides and cholesterol in the plasma, to and from tissues. Lipoproteins are spherical molecules made of lipids and protein molecules.[48,49] Triglycerides and esterified form of cholesterol (cholesterol esters) are non-polar lipids that are insoluble in aqueous environment and comprise the core of lipoprotein. Phospholipids and a small quantity of free cholesterols which are soluble in both lipids and aqueous environment cover the surface of particles; where they act as an interface between plasma and core components.[48,50,51]

FIGURE 11: STRUCTURE OF LIPOPROTEINS



The proteins associated with lipoproteins, called apolipoproteins facilitate assembly, structure and function of lipoproteins. Apolipoproteins activate enzymes important in lipoprotein metabolism and act as ligands for cell surface receptors. They serve as an additional interface between the lipids and aqueous environment, thus facilitating transport of hydrophobic lipids in aqueous media.[48,50]

The plasma lipoproteins are classified into 5 major classes based on their relative density; chylomicrons, very low density lipoproteins (VLDL), intermediate-density lipoproteins (IDL), low density lipoproteins (LDL) and high density lipoproteins (HDL). Each lipoprotein class comprises of a family of particles that varies in density, size, migration during electrophoresis and protein composition.[49,50] The physicochemical properties are summarized in the table below:

TABLE 1: CHARACTERISTICS OF MAJOR LIPOPROTEINS CLASSES

Lipoproteins	Chylomicrons	VLDL	IDL	LDL	HDL
Density (g/ml)	<0.95	0.95-1.006	1.006-1.019	1.019-1.063	1.063-1.210
Electrophoretic Mobility	Origin	Pre-β	Between β & Pre-β	Beta(β)	Alpha(α)
Molecular weight (Daltons)	$0.4\text{-}30X10^9$	$5\text{-}10X10^6$	$3.9\text{-}4.8\ X10^6$	$2.75X10^6$	$1.8\text{-}3.6X10^5$
Diameter (nm)	>70	25-70	22-24	19-23	4-10
Lipid Protein ratio	99:1	90:10	85:15	80:20	50:50
Major lipids	Exogenous TG	Endogenous TG	Endogenous TG & cholesterol esters	Cholesterol ester	Phospholipids
Major Proteins	A-1, B-48, CI,CII,CIII	B-100, CI, CII, CIII, E	B-100, E	B-100	AI, AII
Triglycerides	80-95	55-80	20-50	5-15	5-10
Cholesterol	2-7	5-15	20-40	40-50	15-25
Phospholipids	3-9	10-20	15-25	20-25	20-30
Proteins	1-2	7-10	11	21	50

Enzymes involved in lipid metabolism

1. **Lipoprotein lipase (LPL):** LPL is a glycoprotein synthesized by adipocytes and muscle cells. After secretion from these cells, LPL is transported across endothelial cells and binds to the capillary lumen via proteoglycan chains of heparin sulphate. LPL is present in adipose tissue, muscle and heart but not in

the liver. Apo C-II present in chylomicrons, VLDL and IDL activates LPL, it hydrolysis TG and liberates fatty acids that are taken up by muscle or adipose tissue.

2. **Hepatic Triglyceride lipase (HTGL):** It belongs to the same family of lipase as LPL. HTGL is synthesized in liver and binds to the luminal surface of the endothelial cells in the hepatic sinusoids. It plays a role in the metabolism of chylomicron, VLDL and IDL. HTGL also helps in the conversion of HDL_2 to HDL_3 in the liver by hydrolyzing the TG's and phospholipids in the HDL.

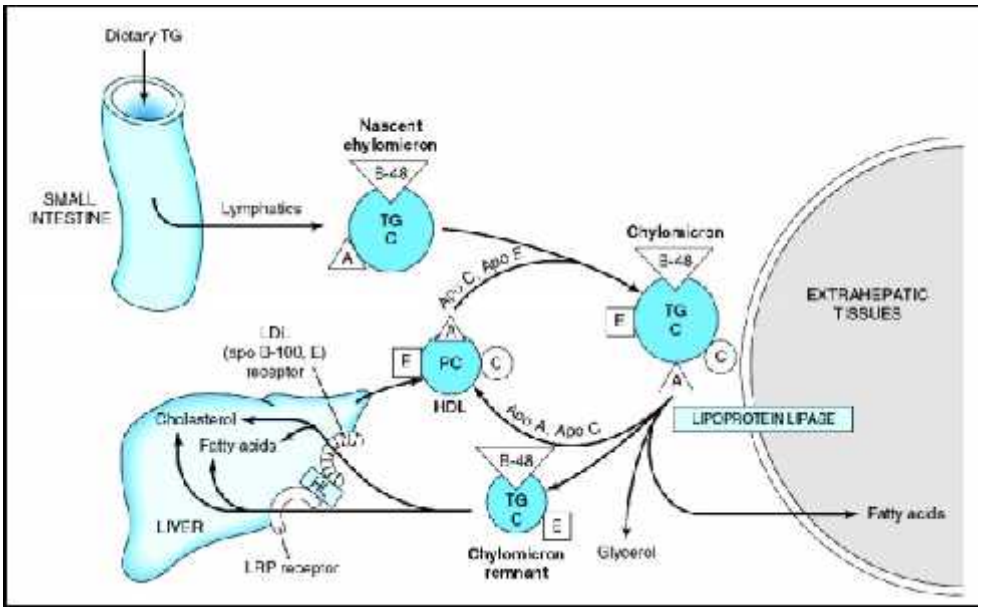
3. **Lecithin Cholesteryl Acyl Transferase (LCAT):** LCAT is synthesized in the liver. It forms cholesteryl ester by the transfer of linoleate to free cholesterol in plasma. Apo A-I is a factor for LCAT esterification of free cholesterol. LCAT is the main constituent of reverse cholesterol transport.

Lipoprotein metabolism: The pathways of lipid metabolism can be divided into exogenous, endogenous pathways (based on whether they carry lipids of dietary or hepatic origin), the intracellular LDL receptor pathway and HDL reverse cholesterol pathway.[48,49]

Exogenous pathway: Nascent chylomicrons are formed from dietary cholesterol and TG in the enterocytes and packed in the secretory vesicles in the golgi apparatus. They contain mainly TG (98% by mass), apo B-48 and apo A-1. Chylomicrons are formed after acquiring apo C and apo E from HDL in circulation. Apo-C activates lipoprotein lipase attached to luminal surface of endothelial cells and which hydrolyzes the TG to free fatty acids.

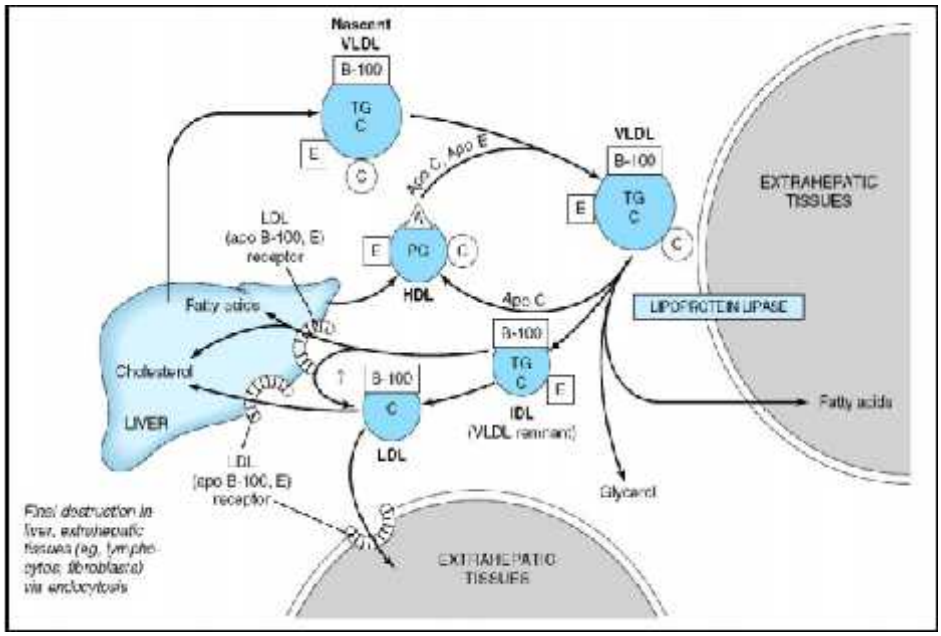
Simultaneously some of the phospholipids and apo-A are transferred to HDL. The newly formed chylomicron remnants contain 80-90% of TG content of original chylomicron, apo B-48 and apo E. This is recognized by hepatic apo E remnant receptors and then internalized by endocytosis later hydrolyzed in the lysosomes to fatty acids and cholesterol.[48,49]

Fig 12: EXOGENOUS PATHWAY – METABOLIC FATE OF CHYLOMICRONS



Endogenous pathway: Hepatocytes synthesize TG from carbohydrates and fatty acids, by activity of HMG-coA reductase when dietary cholesterol is insufficient. The endogenously made triglyceride and cholesterol are secreted as nascent VLDL similar to chylomicrons.

FIGURE 13: ENDOGENOUS PATHWAY – METABOLIC FATE OF VLDL AND PRODUCTION OF LDL



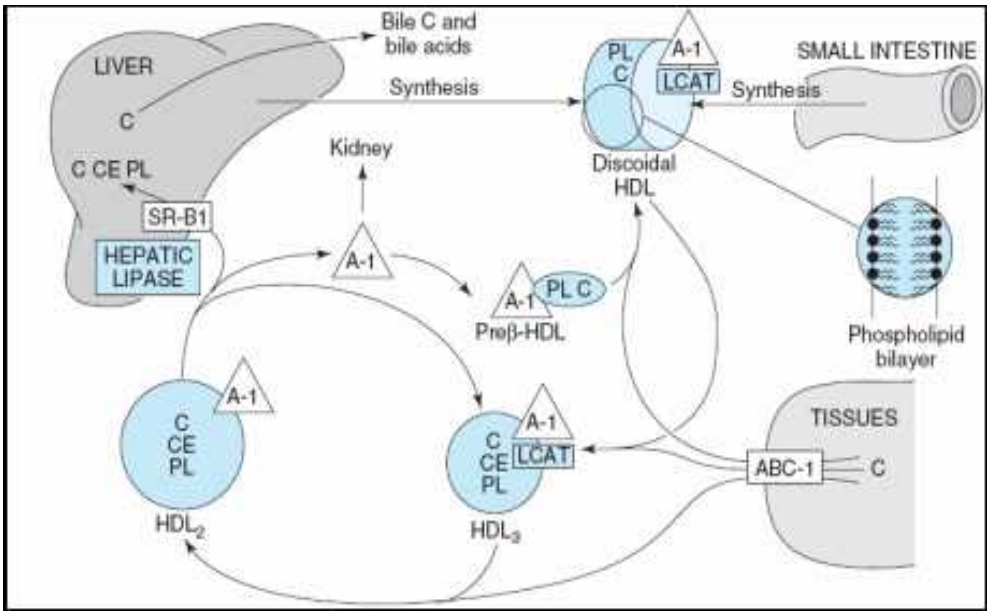
This TG rich particle (55% by mass) contains apo B-100, apo E and acquires apo C from circulating HDL to form VLDL. Apo C on the surface of the VLDL activates LPL, which hydrolyzes VLDL triglycerides and releases fatty acids. Then apo C particles are transferred back to LDL and forms VLDL remnant particles some of which are taken up by the liver and rest of them are converted into smaller denser particles called IDL. Large IDL particles which have several molecules of apo-E, bind to the hepatic remnant receptors and are removed from the circulation. Some IDL particles undergo a further hydrolysis in which triglycerides are removed and all lipoproteins except apo B-100 are transferred to HDL leading to formation of LDL.[48]

LDL receptor pathway: Specific receptors present in coated pits on the plasma membrane recognize and bind apo B-100 of LDL. The LDL particles are internalized in coated vesicles which then fuse to form an endosome; LDL dissociates from the receptor and migrates to the lysosome. Cholesteryl esters are also hydrolyzed and the

cholesterol is used for synthesis of cell membrane, steroid hormone and bile acids. Compared with VLDL and chylomicrons, LDL has a relatively long resistance time in the circulation. LDL can be taken up by the extrahepatic tissues through scavenger receptor or non-receptor-mediated pinocytosis and is unregulated. The non receptor mediated uptake becomes significant as plasma LDL concentration increases. Scavenger receptors are found in macrophages and other cells. Two third of LDL is normally removed by LDL receptors and remaining by the scavenger cell system.[48,50]

HDL reverse cholesterol pathway: HDL is secreted in the liver and intestine as disk shaped nascent particles that consists of phospholipids and apo A-I. through the extracellular addition of surface components of TG rich particle, such as phospholipids and cholesterol from cell membrane are transferred to nascent HDL.

FIGURE 14: HDL REVERSE CHOLESTEROL PATHWAY – METABOLISM OF HDL



Cholesterol is esterified by the action of LCAT in the presence of its co-factor apo A-I. The size of HDL particles depends strongly on the amount of accumulated CE and the activity of LCAT. The surface materials of TG rich particles that have been transferred to small circulating HDL_3 are subsequently esterified by LCAT to create larger CE rich HDL_2. HDL_2 is converted back to HDL_3 in the presence of hepatic LPL. A major function of LPL in lipoprotein metabolism is the transfer of excess cellular cholesterol to the liver. HDL cholesteryl esters are delivered to the liver by one of the following mechanism:

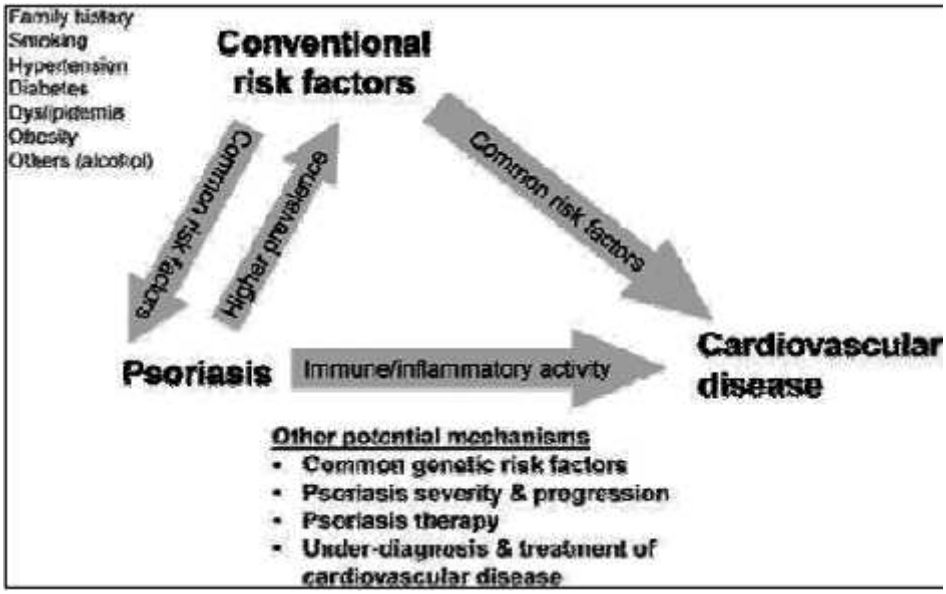
- CE are taken up from HDL by the hepatic HDL receptors
- CE are transferred from HDL to apo B-100 containing lipoproteins, a process mediated by cholesterol ester transfer protein (CETP) then taken up by liver via the specific LDL pathway.
- HDL apo E can be recognized by the hepatic remnant receptors.

These processes constitute the reverse cholesterol transport mechanism by which cellular and lipoprotein cholesterol is delivered back to the liver for reuse or disposal.[48,49,50]

DYSLIPIDEMIA AND CARDIOVASCULAR RISK IN PSORIASIS

Psoriasis is an immune disease characterized by inappropriate activation of cellular immune system directed against self antigens.[52] The link between psoriasis and cardiovascular disease (CVD) has been reported by several studies. Although the pathogenesis of increased cardiovascular events in patients with psoriasis remains to be established, there are several possible biological factors which may explain such a link.[43]

FIGURE 15: MECHANISM FOR THE RISK OF CARDIOVASCULAR DISEASE IN PSORIASIS



First, psoriasis may share common risk factors such as smoking and alcohol consumption (Figure-15). Second, patients with psoriasis may have a higher prevalence of conventional cardiovascular risk factors compared with those without psoriasis (eg, obesity, low physical activity). Third, medications commonly used to treat psoriasis may contribute to increased risk. Indeed, methotrexate use is associated

with hyperhomocysteinemia, a risk factor for CVD. Acitretin and cyclosporine use are associated with lipid abnormalities.[43]

Fourth, inflammatory activity in psoriasis act independently of conventional cardiovascular risk factors and medications to increase the risk through biological mechanisms. Another possible explanation is under diagnosis and under treatment of CVD in patients with psoriasis compared with those without psoriasis, similar to other chronic diseases. Finally, shared genetic mechanisms may play a role.

Molecular mechanisms that lead to atherosclerosis in patients with psoriasis are very complex and may involve multiple synergistic interactions among conventional cardiovascular risk factors, medications and underlying inflammatory autoimmune dysfunction and genetic makeup of the patients.[43]

CHRONIC INFLAMMATION AS A MECHANISM FOR RISK OF CORONARY ARTERY DISEASE IN PSORIASIS

Atherosclerosis shares many similarities other immune mediated diseases including psoriasis. Common traits include immunologic processes, cytokine profiles and the immunological cell types (Table 2). Inflammatory markers have been shown to be increased in both conditions, at local and systemic levels. Histologically both conditions involve monocytes, macrophages, mast cells, lymphocytes and connective tissue cells and the extracellular matrix.

TABLE 2: IMMUNOLOGICAL SIMILARITIES BETWEEN ATHEROSCLEROSIS AND PSORIASIS

	Psoriasis	Atherosclerosis
Cell activation Macrophages, Mast cells, T cells Circulating natural killer cells	 ↑ ↓	 ↑ ↓
Innate immunity Activation of nuclear factor-(kappa) B pathway Toll-like receptor expression	 Yes ↑	 Yes ↑
Adaptive immunity Cytokine profile(Th1/Th2 imbalance) CD40/CD40L signaling interaction and sCD40L levels	 Th1 ↑ ↑	 Th1 ↑ ↑
Chemokines ,Adhesion molecules , Endothelins, Super antigens Neoangiogenesis	↑ ↑ Yes	↑ ↑ Yes

Activation of T cells, mast cells and macrophages release several cytokines, matrix-degrading proteins and collagen-breaking enzyme, contributing to evolution of psoriatic lesion and destabilizing of atherosclerotic plaques. These striking histological and molecular similarities between psoriasis and atherosclerosis provide compelling evidence to suggest that the inflammatory processes in psoriasis can potentially contribute to high risk of atherosclerosis.[43]

Epidemiological data suggest a link between psoriasis and chronic infections and inflammatory conditions. For example, chronic bronchitis, rheumatoid arthritis, systemic lupus erythematosus and psoriasis have been associated with increased risk of atherosclerosis.[53] During inflammation, a wide range of alterations in metabolism occurs. These are part of body's reaction known as the acute phase reaction (APR).[52, 53] Atherosclerotic lesions in the arterial wall are characterized by lipid accumulation in macrophages resulting in foam cell formation. The development of lipid foam cells is primarily regulated by 2 determinants: lipid uptake and lipid removal.

Inflammation is associated with alterations in triglycerides and cholesterol metabolism, changes in circulating levels of lipoproteins and the composition of lipoproteins. Furthermore, there are changes in the level and activity in a variety of plasma proteins involved in the metabolism and function of these lipoproteins. (Table 3)[53]

TABLE 3: POTENTIAL PROATHEROGENIC CHANGES AND EFFECTS OF LIPOPROTEINS DURING INFECTION AND INFLAMMATION.[53]

Changes	Effects
VLDL	
Increased VLDL levels	Provides lipid substrates for macrophage uptake
Decreased LPL and HL	Decreases clearance of triglyceride-rich lipoproteins
Increased sphingolipid content	Decreases clearance of triglyceride-rich lipoproteins
Decreased tissue apo E expression	Decreases lipoprotein clearance
LDL	
Increased small dense LDL	Increases susceptibility to oxidation; increases LDL penetration through endothelium; increases interaction with arterial wall proteoglycans and LDL retention in arterial wall
Increased PAF-AH activity	Increases LPC production
Increased sPLA2	Releases polyunsaturated fatty acids from phospholipids that can become oxidized fatty acids
Increased sphingolipid content	Facilitates LDL aggregation and uptake into macrophages
Increased ceruloplasmin	Increases LDL oxidation
HDL	
Decreased HDL and apo A-I	Impairs apolipoprotein-mediated cholesterol removal from cells
Decreased LCAT	Impairs cholesterol removal from cells by diffusion mechanism
Decreased CETP	Impairs cholesterol transfer to TG-rich lipoproteins
Decreased HL	Reduces pre-β HDL generation
Decreased PLTP	Reduces pre β HDL generation; decreases HDL phospholipid content and impairs CH removal by increasing cholesterol flux from HDL into cells
Increased SAA	Decreases availability of ch in HDL to be metabolized by hepatocytes; increases ch uptake into macrophages
Increased sPLA2	Decreases HDL phospholipid content and impairs CH removal by increasing CH flux from HDL into cells
Increased PAF-AH activity	Increases LPC production
Decreased PON	Decreases ability of HDL to protect against LDL oxidation
Decreased transferrin	Impairs the ability of HDL to prevent LDL oxidation
Increased apo J	Induces smooth muscle cell differentiation in arterial wall

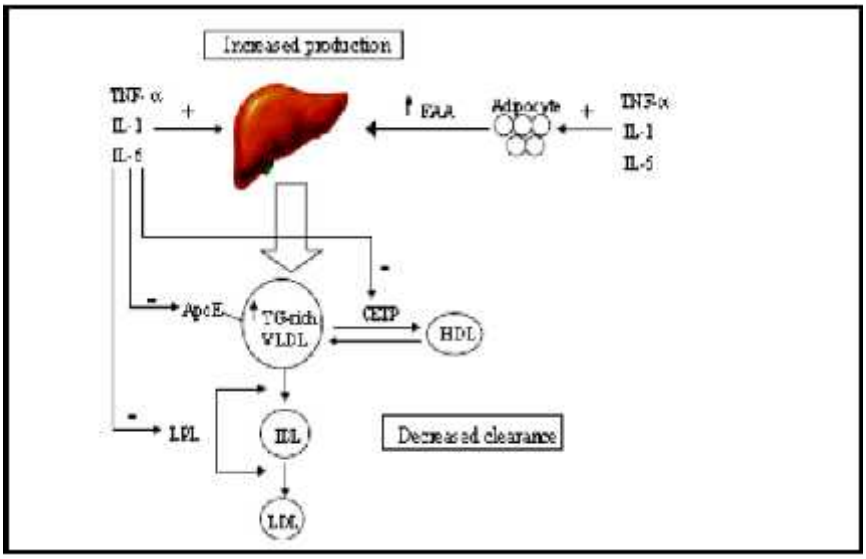
NOTE: CETP, cholesterol ester transfer protein; HL, hepatic lipase; LCAT, lecithin:cholesterol acyl transferase; LPC, lysophosphatidylcholine; PAF-AH, platelet-activating factor acetyl hydrolase; sPLA2, secretory phospholipase A2; SAA, serum amyloid A.

Changes in VLDL lipoprotein and TGs during inflammation

Hypertriglyceridemia-associated inflammation has been attributed to both decrease lipoprotein clearance and increase lipoprotein production. The increase in hepatic TG-rich particles production is secondary to an increase in re-esterification of plasma fatty acid arising from both enhanced lipolysis and increased "de-novo" fatty acid synthesis in the liver. Cytokines such as TNF-α, IL-1, IL-2, IL-6 and IFN-α increase plasma TGs by stimulating secretion of hepatic-rich TG, VLDL particles and TG synthesis in hepatic cells. TNF-α induces lipolysis and "de novo" fatty acid synthesis, IL-1 mainly stimulates "de novo" fatty acid synthesis. Increased lipolysis mediated by both hormone and non-hormone-sensitive-lipase results in a greater free fatty acid flux to the liver, thereby promoting lipoprotein VLDL secretion. Cytokines can also stimulate the synthesis of cortisol and catecholamines that lead to increased lipolysis.

Inflammation inhibits TG clearance by reducing LPL activity and VLDL-associated apo-E levels. Apo-E is essential for cellular uptake of TG-rich particles. TNF-α and IL-1 leads to hepatic and extrahepatic apoE RNA messenger, decreasing apoE secretion in the cultured cells.[54]

FIGURE 16: MECHANISM OF HYPERTRIGLYCERIDEMIA PRODUCTION ASSOCIATED TO INFLAMMATION



Changes in LDL lipoprotein and cholesterol during inflammation

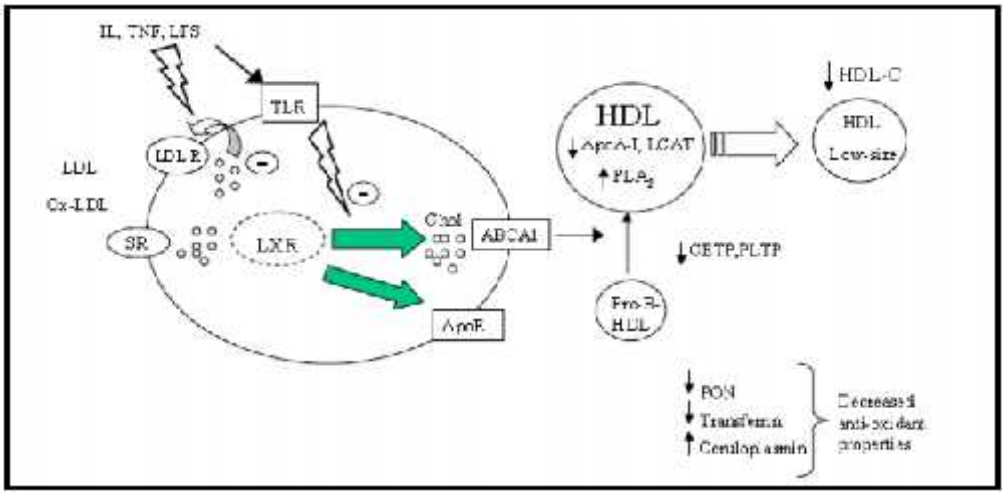
Inflammation causes dysregulation of LDL-R expression. TNF-α and IL-1 override the suppression of LDL-R induced by a high intracellular concentration of cholesterol. Inflammation also induces expression of scavenger receptors (SRs) and foam cell generation, by increasing SR gene promoter activity. Cholesterol accumulation by LDL-R dysregulation or SR pathways, in addition to decreasing ABCA1-dependent cholesterol efflux, leads to foam cell formation. These mechanisms of cholesterol cell accumulation lead to decrease in LDL during the APR. Higher TNF-α levels decrease LDL levels but increase the small and dense LDL. Small LDL particles show increased atherogenicity given their decrease affinity for LDL-Rs, higher capacity for oxidation and higher ability to cross over the intima artery wall and its increased uptake by foam cells.[54]

Changes in HDL lipoprotein during inflammation

Inflammation is associated with a decrease in HDL-C levels. HDL that circulates during inflammation (also termed acute phase HDL) are depleted in cholesterol ester but enriched in free cholesterol, triglycerides and sphingolipids. There are reductions in other plasma proteins proposed to play a major role in HDL metabolism and reverse cholesterol transport, including lecithin: cholesterolacyltransferase (LCAT), cholesterol ester transfer protein (CETP), hepatic lipase (HL) and phospholipid transfer protein (PLTP). One of the mechanisms by which HDL may be anti-atherogenic is its ability to protect LDL against oxidation. Several HDL-associated proteins have these anti-oxidant effects, including PAF-AH, paraoxonase (PON), ceruloplasmin and transferrin.[53,54]

HDL is an acceptor of cholesterol efflux. This process is passively facilitated by cholesterol dependent gradient diffusion of cholesterol to HDL and actively by the interaction of pre-β-HDL and ABCA1. ABCA1 is a cholesterol transporter membrane of ABC transporter super family. Liver X receptors (LXRs) are transcriptional regulators of cholesterol absorption, transport and elimination.[54]

FIGURE 17: MECHANISMS LEADING TO INTRACELLULAR LIPID LOADING, IMPAIRING REVERSE CHOLESTEROL TRANSPORT AND HDL ANTIOXIDANT CAPACITY



Decreases in hepati**c** lipase (HL) during APR contribute to the increase in the serum TG levels by (a) decreasing the removal of TGs from VLDL and chylomicrons and (b) the reduction in reverse cholesterol transport. Inflammation reduces the activity of LCAT, CETP and PLTP. These changes produce small HDL particles which have faster catabolism and elimination from the circulation.[54,55]

Paraoxonase (PON) protein protects LDL from oxidative stress. Depletion of PON results in the loss of anti-oxidant function of HDL. Cytokines stimulates the hepatic production and secretion of sPLA2. It hydrolyses HDL phospholipids and reduces HDL size without generating preβ-HDL, which induces their catabolism. Increased sPLA2 levels accelerate the development of atherosclerosis.[54] Study by Torkhovskaia., suggested the existence of changes in reverse cholesterol transport system in psoriasis, which may influence skin cell proliferation.[55]

Although there have been extensive studies of serum lipids and apolipoprotein levels in psoriasis, their importance in etiology or enhancement of the disease remains controversial.[56,57,58] Multiple studies have consistently shown an aberrant lipoprotein associated with psoriasis.[56,59,60]

Multiple cardiovascular risk factors are associated with psoriasis which is more strongly associated with severe psoriasis than with mild psoriasis.[55] These proatherogenic changes of lipoprotein during inflammation may be the potential mechanism that account for the epidemiologic observations linking inflammatory conditions and atherosclerosis.[3]

METHODOLOGY

The study was carried out on 40 psoriatic patients and its comparison with equal number of age and gender matched healthy controls who attended the inpatient and outpatients department of Dermatology at Dr. Prabhakar Kore KLE Hospital and MRC, Belgaum during the year 2010-2011. Ethical clearance was obtained before the study was started.

SOURCES OF DATA

Inclusion criteria: Cases of psoriasis in the age group 20-70yrs and those willing to give consent.

Exclusion criteria: Patients of the following conditions are excluded from the study. Diabetes, hypertension, hyperlipidemic, chronic alcoholics, history of lipid lowering drugs and retinoids.

Method of collection of data

Informed consent was taken from the patient and control subjects. A pre-structured and pre-tested proforma was used to collect the data. Baseline data including detailed medical history, including conventional risk factors, clinical examinations and relevant examinations were included as part of the methodology.

12 hours overnight fasting venous blood samples were collected from cases and controls and the samples were centrifuged for the estimation of fasting blood glucose, serum triglycerides and total cholesterol, LDL cholesterol, HDL cholesterol, VLDL cholesterol. Serum VLDL- Cholesterol is calculated using the formula, VLDL= S.TG/5. LDL-Cholesterol is calculated from the values of total cholesterol,

HDL cholesterol and triglycerides by applying Friedwald's equation. Total Ch/HDL and LDL-C/HDL-C ratio are determined.

Details of the different methods of estimation are as follows:

1. Estimation of Blood Glucose (Hexokinase-glucose-6-phosphate dehydrogenase method) [61,62]

Principle: Hexokinase (HK) catalyses the phosphorylation of glucose in the presence of adenosine-5'-triphosphate (ATP) and magnesium to form glucose-6-phosphate (G-6-P) and adenosinediphosphate (ADP). G-6-P is then oxidized by glucose-6-phosphate dehydrogenase (G-6-PDH) in the presence of nicotinamide adenine dinucleotide (NAD) to produce 6-phosphogluconate and NADH.

Reagent preparation: All reagents are liquid and ready to use.

Procedure: The assay was carried out using A25 biosystem auto analyzer

Reference range:

Normal serum level: FBS: 70-110 mg/dl PPBS: 80-140mg/dl

2. Estimation of Total cholesterol in serum (Enzymatic method- cholesterol oxidase/Horseradish peroxidase) [63,64]

Principle: Cholesterol esterase (CE) catalyzes the hydrolysis of cholesterol esters to produce free cholesterol which, along with pre-existing cholesterol, is oxidized in a reaction catalyzed by cholesterol oxidase (CO) to form cholest-4-ene-3-one and hydrogen peroxides. In the presence of horseradish peroxidase (HPO), the hydrogen peroxide thus formed is used to oxidize N, N diethylalanine-HCL/4-aminoantipyrine (DEA-HCL/AAP) to produce a chromophore that absorbs at 540 nm.

Reagent preparation: Hydrating, diluting and mixing are automatically performed by the instrument.

Procedure: The assay was carried out using A25 biosystem atoanalyzer

Reference range:

< 200 mg/dL: Desirable

200 – 239 mg/dL: Borderline high

> 240 mg/dL: High

3. Estimation of serum triglycerides[65]

Principle: Lipoprotein lipase (LPL) enzyme converts triglycerides into free glycerol and fatty acids. Glycerol kinase catalyses the phosphorylation of glycerol by adenosine-5-triphosphate (ATP) to glycerol-3-phosphate. Glycerol-3-phosphate-oxidase oxidizes glycerol-3-phosphate to dihydroxyacetone phosphate and hydrogen peroxide (H_2O_2). The catalytic action of peroxidase forms quinoneimine from H_2O_2, aminoantipyrine and 4-chlorophenol.

Reagent preparation: reagent and standard are provided ready to use.

Procedure: The assay was carried out using A25 biosystem auto analyzer

Reference values:

Normal: < 150 mg/dL

Borderline high: 150 – 199 mg/dl

High : 200 – 499 mg/dL

Very high: > 500 mg/dL

4. Estimation of Serum High-Density Lipoproteins – Cholesterol (Abell-Kendall method)[66]

Principle: Chylomicrons, VLDL and LDL form water soluble complexes with dextran sulfate in the presence of magnesium sulfate. These complexes are resistant to the polyethylene glycol (PEG) - modified cholesterol esterase and cholesterol oxidase that reacts with HDL cholesterol. In the presence of oxygen, the HDL cholesterol is oxidized to Δ4-cholestenone and hydrogen peroxide. The generated hydrogen peroxide then reacts with 4-aminoantipyrine and sodium N-(2-hydroxy-3-sulfopropyl)-3, 5-dimethoxyaniline (HSDA) in the presence of peroxidase to form a coloured dye. The color intensity of the dye is directly proportional to the serum HDL-C concentration.

Reagent preparation: All reagents are liquid and ready to use.

Procedure: The assay was carried out using A25 biosystem auto analyzer

Reference values:

< 40 mg/dL	Low HDL Cholesterol
> 60 mg/dL	High HDL Cholesterol

5. Estimation of Very Low Density Lipoprotein Cholesterol

Serum VLDL-C is calculated using the formula:

VLDL Cholesterol = Triglycerides /5

Reference range: 5 – 40mg/dL

6. Estimation of Low Density Lipoprotein Cholesterol

Serum LDL-C is calculated using the formula:

LDL Cholesterol = Serum Total Cholesterol – (HDL-C + LDL-C)

Reference range: 60 – 160 mg/dL

7. TC / HDL-C and LDL-C / HDL-C ratio are determined

RESULTS

The present study is undertaken to evaluate the significance of lipid levels in psoriasis. 40 psoriasis patients were considered for the study. 40 age and gender matched healthy individuals were chosen as controls.

Age, sex and body mass index (BMI)

The values of age, sex and BMI in controls and cases are presented in Table 4. The mean age in psoriatic cases compared to controls was not statistically significant, (p value =1) and is presented in Fig 18. Sex distribution in cases and controls is projected graphically in Fig 19.

The mean BMI values in cases as compared to controls was statistically not significant (p value=0.079). The BMI distribution in cases and controls is graphically depicted in Fig 20.

Lipid parameters

The mean value distribution of serum lipid parameters of the study groups are projected in Table 8. The mean serum total cholesterol levels are significantly (p value=0.003) higher in psoriatic cases, as compared to controls. Distribution of cases and controls according to serum total cholesterol levels are presented in Fig 21.

The mean serum triglyceride levels are lower among psoriatic cases as compared to controls. The difference is statistically not significant (p value=0.765). Distribution of cases and controls according to serum triglyceride levels is presented in Fig 22. The serum HDL-C levels are lowered in cases as compared to controls. This difference is statistically not significant with p value=0.896. Distribution of cases and controls according to serum HDL-C levels are pictured in Fig 23.

The mean serum LDL-C levels in psoriatic cases are higher as compared to controls. The difference is statistically significant (p value=0.010). Distribution of cases and controls according to serum LDL-C levels is presented in Fig 24. The mean serum VLDL-C levels are lowered in cases as compared to controls. The difference in statistically not significant with p value=0.366 and details are projected graphically in Fig 25.

Total cholesterol/HDL-C ratio is higher among psoriatic cases as compared to controls. The difference is statistically significant (p value=0.009). The data is pictorially presented in Fig 26. The LDL-C/HDL-C ratio is higher in cases as compared to controls. The difference is statistically significant with p value=0.019). These values are also pictured in Fig 27.

The comparison of hyperlipidemia with the duration of illness of psoriasis is depicted in Fig-28.

The comparison of PASI score in psoriasis patients with hyperlipidemia is depicted in Fig 29.

The comparison of nail changes in psoriasis with hyperlipidemia is plotted in Fig-30 and various types of nail changes in association with hyperlipidemia are depicted in Fig-31.

The comparison of joint involvement in psoriasis with hyperlipidemia is plotted in Fig-32 and various types of joint involvement in association with hyperlipidemia are depicted in Fig-33.

Various types of psoriasis in association with hyperlipidemia are depicted in Figures 34 and 35.

TABLES AND GRAPHS

TABLE 4: DISTRIBUTION OF AGE, GENDER AND BMI OF CASES AND CONTROLS

Basic characteristics	Cases	Controls	P value
Age (yrs)	40.9±13.47	40.9±13.47	1
Male:Female	33:7	33:7	---
BMI ($kg/m^{2)}$	23.6±2.11	22.8±1.81	>0.079

TABLE 5: AGE DISTRIBUTION OF CASES AND CONTROLS

Age (years)	Cases		Controls	
	No.	%	No.	%
21-30	12	30	12	30
31-40	7	17.5	7	17.5
41-50	14	35	14	35
51-60	3	7.5	3	7.5
61-70	4	10	4	10
Total	40	100	40	100

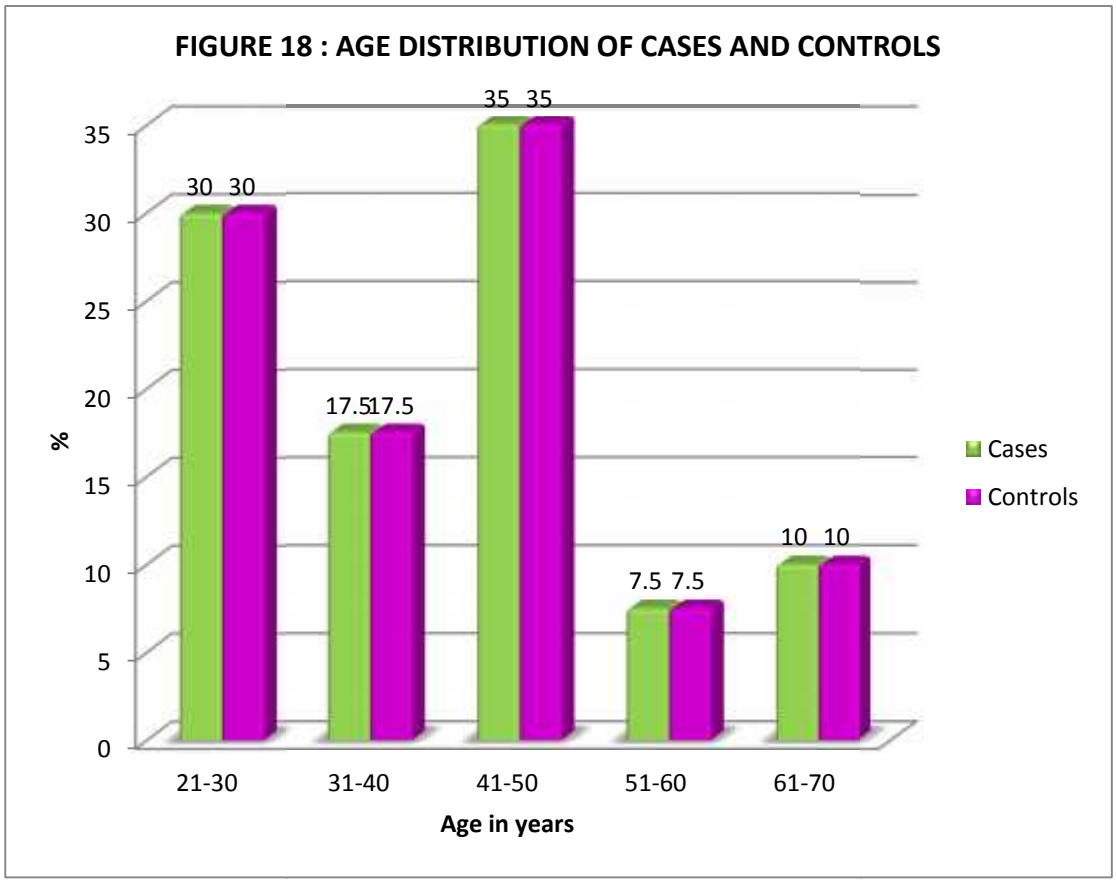


TABLE 6: SEX DISTRIBUTION OF CASES AND CONTROLS

Sex	Cases		Controls	
	No.	%	No	%
Male	33	82.5	33	82.5
Female	7	17.5	7	17.5
Total	40	100	40	100

FIGURE 19: GENDER DISTRIBUTION OF CASES AND CONTROLS

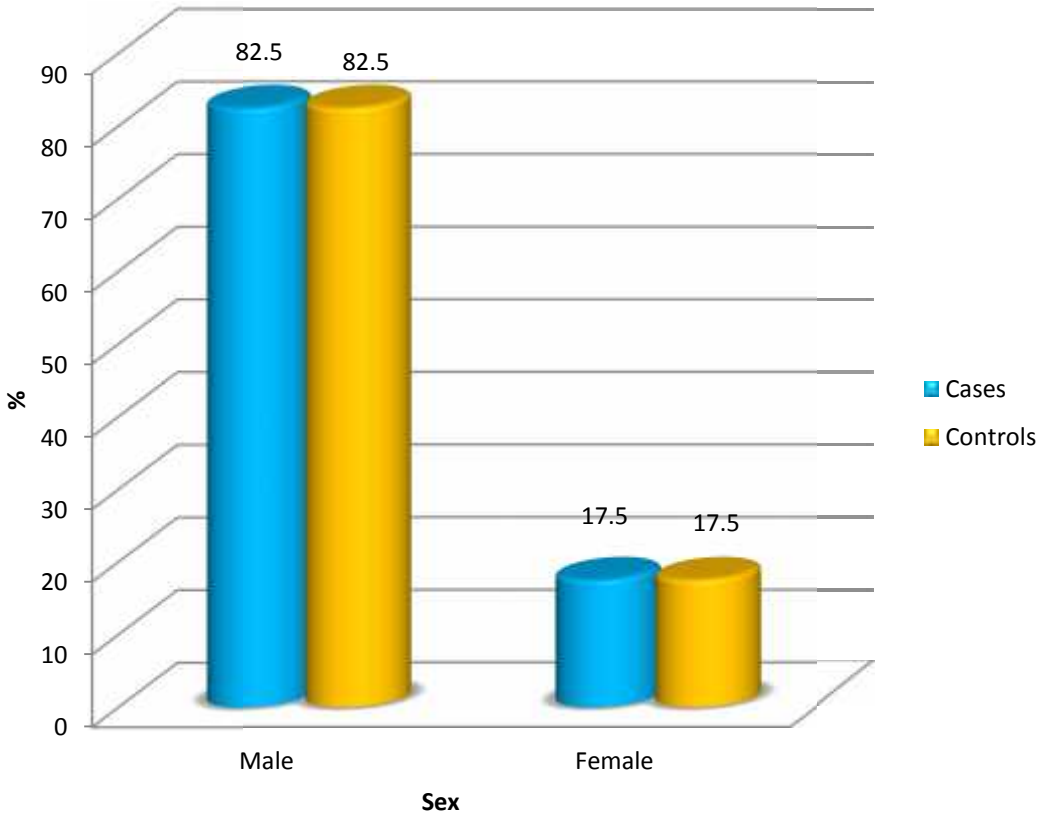


TABLE 7: BMI DISTRIBUTION OF CASES AND CONTROLS

BMI	Cases		Controls	
	No	%	No	%
< 20	2	5	1	2.5
20-25.9	24	60	33	8.25
26-30	14	35	6	15
Total	40	100	40	100

FIGURE 20:BMI DISTRIBUTION OF CASES AND CONTROLS

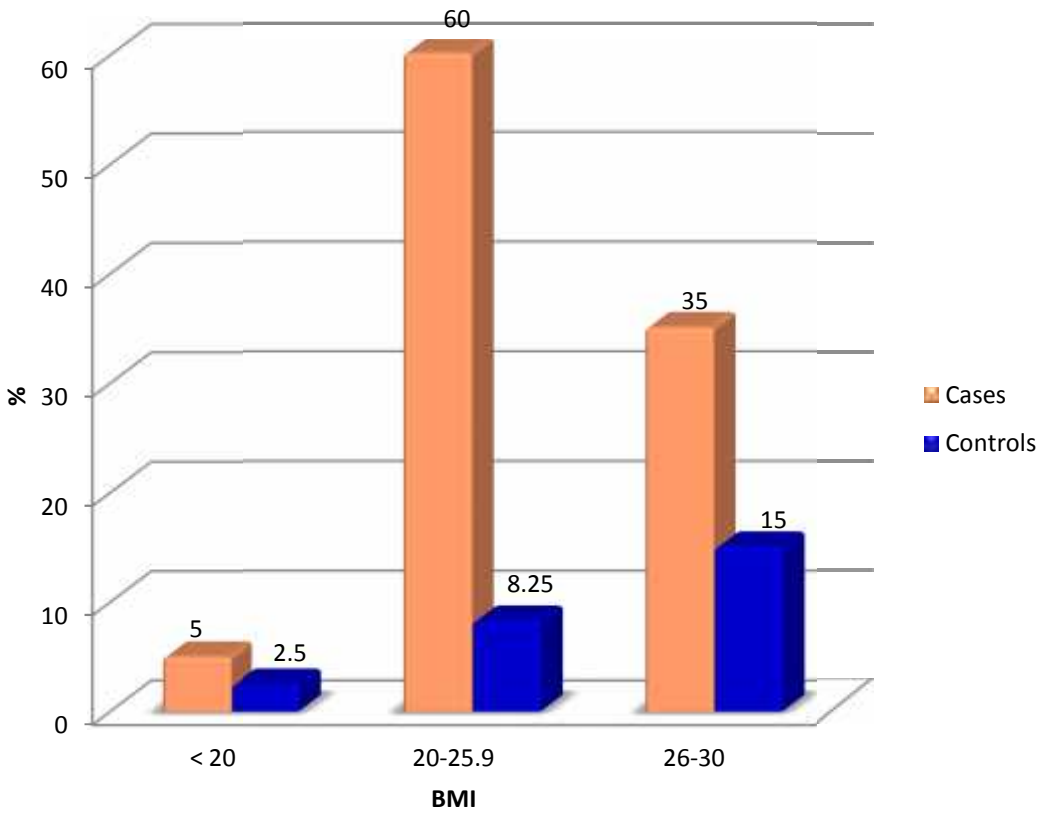


TABLE 8: DISTRIBUTION OF SERUM LIPID PARAMETERS IN CASES AND CONTROLS

Lipid parameters	Cases	Controls	t value	p value
Total cholesterol (mg/dl)	158.8±41.20	134.8±28.36	3.028	0.003
Triglycerides (mg/dl)	124.8±82.16	119.5±74.00	0.300	0.765
LDL-C (mg/dl)	94.2±36.24	73.6±32.86	2.653	0.010
HDL-C (mg/dl)	40.2±11.34	40.5±10.78	0.131	0.896
VLDL-C (mg/dl)	24.4±13.95	20.5±23.31	0.909	0.366
T.CH/HDL-C (mg/dl)	4.21±1.46	3.5±0.91	2.695	0.009
LDL-C/HDL-C (mg/dl)	2.5±1.15	1.9±1.01	2.390	0.019

Results are presented as mean ±SD

Significant figures

+ Suggestive significance $p<0.05$

TABLE 9: DISTRIBUTION OF CASES AND CONTROLS ACCORDING TO SERUM CHOLESTEROL LEVELS

Total cholesterol	Cases (n=40)	Controls (n=40)
Upto 200 (Desirable)	34 (85%)	37 (92.5%)
200-239 (Borderline)	3 (7.5%)	2 (5%)
>240 (High)	3 (7.5%)	1 (2.5%)
Inference	Percentage of patients with total cholesterol >200 is not very significant in cases as compared to controls (14% vs. 7.5%) with p= 0.479	

FIGURE 21: DISTRIBUTION OF CASES AND CONTROLS ACCORDING TO SERUM CHOLESTEROL LEVELS

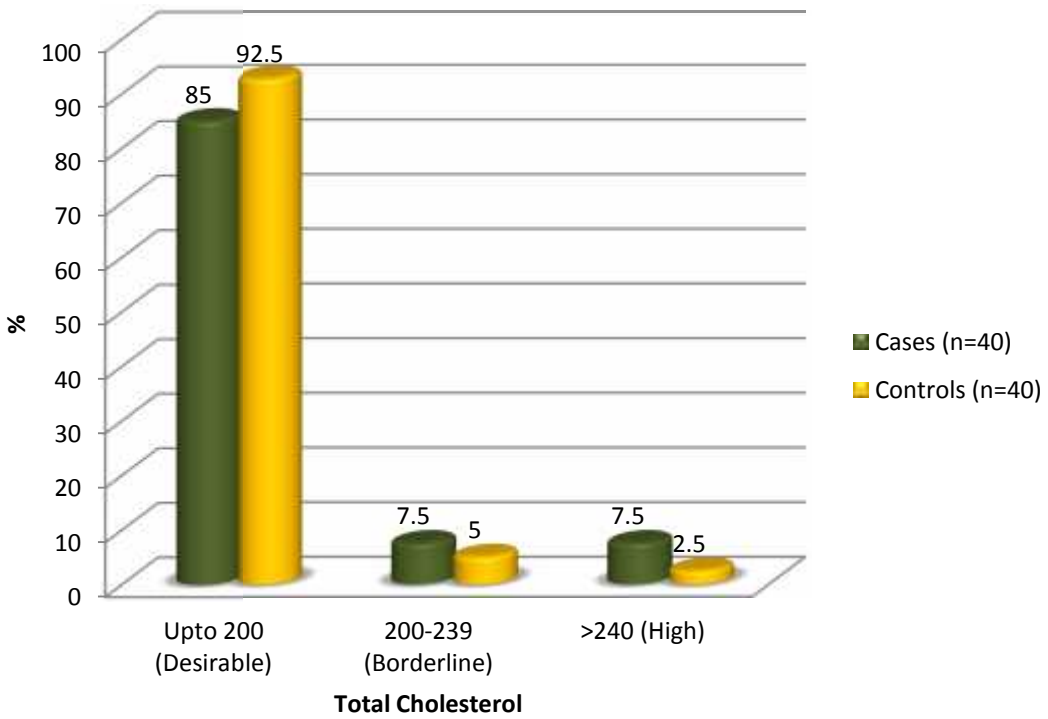


TABLE 10: DISTRIBUTION OF CASES AND CONTROLS ACCORDING TO SERUM TRIGLYCERIDE LEVELS

Triglycerides	Cases	Controls
Upto 150 (normal)	33 (90%)	32 (80%)
150 – 199 (borderline)	3 (7.5%)	3 (7.5%)
>200	4 (10%)	5 (12.5%)
Inference	Percentage of patients with triglycerides >150 is not significant in cases when compared to controls (8.5% vs. 30%) with p= 0.877	

FIGURE 22: DISTRIBUTION OF CASES AND CONTROLS ACCORDING TO SERUM TRIGLYCERIDE LEVELS

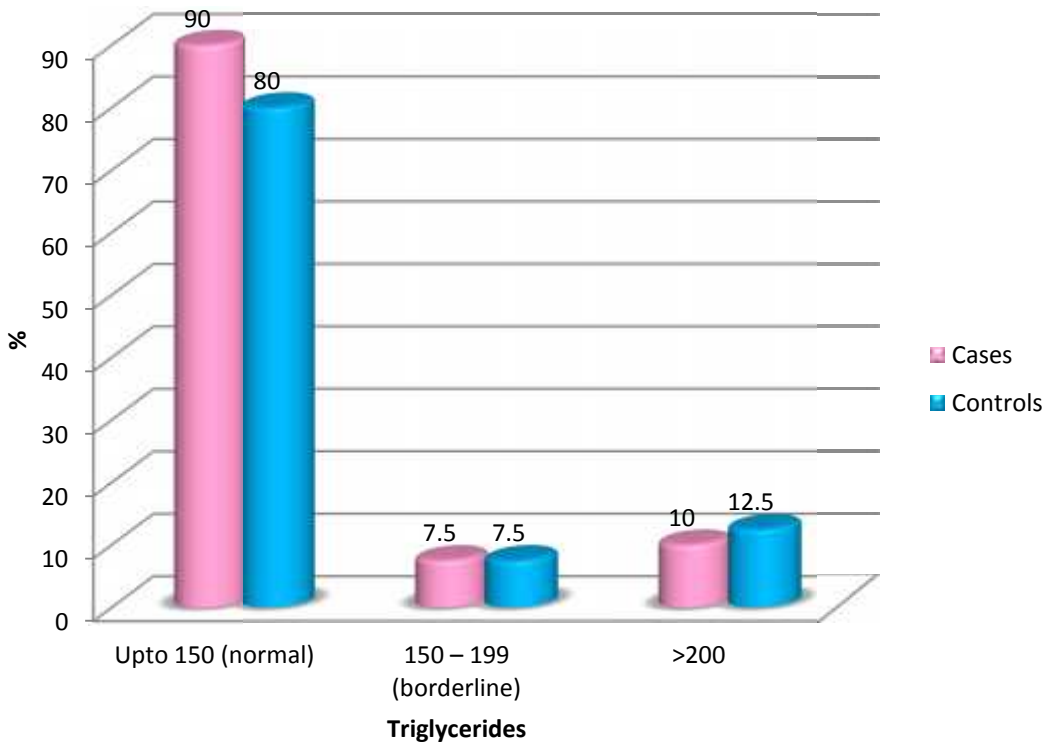


TABLE 11: DISTRIBUTION OF CASES AND CONTROLS ACCORDING TO SERUM HDL-C LEVELS

HDL-C	Cases (n=40)	Controls (n=40)
Upto 35	19 (45%)	16 (40%)
35 – 60	19 (47.5%)	22 (55%)
>60	2 (5%)	2 (5%)
Inference	Percentage of patients with HDL-C <35 is not significant in cases when compared to controls (45% vs. 40%) with p= 0.651	

FIGURE 23: DISTRIBUTION OF CASES AND CONTROLS ACCORDING TO HDL-C LEVELS

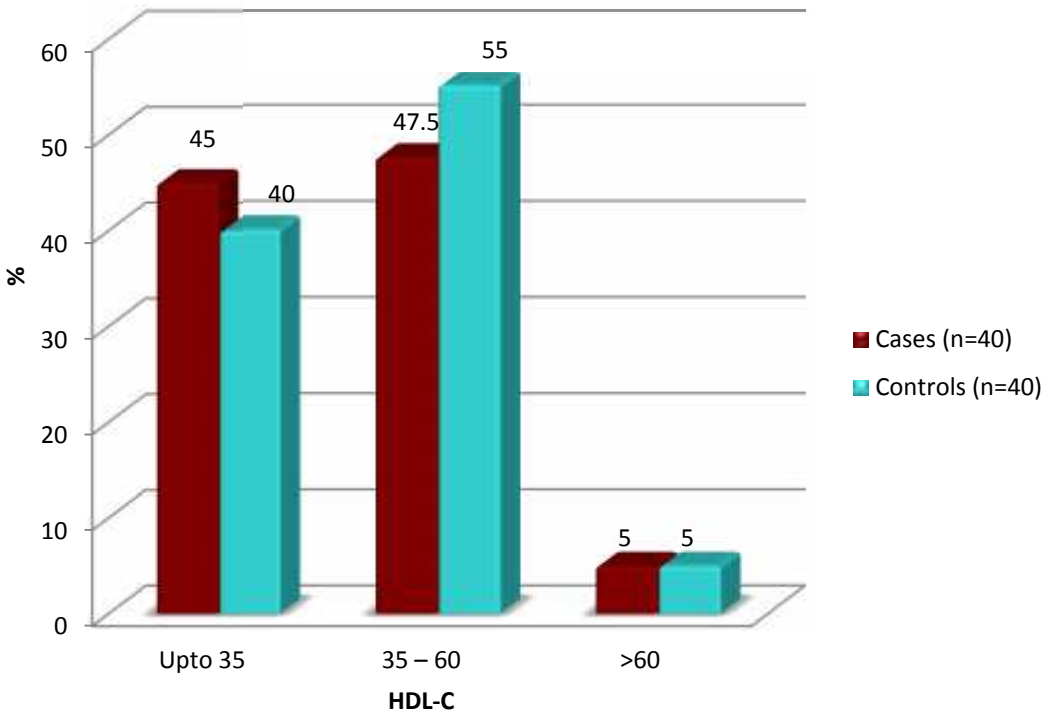


TABLE 12: DISTRIBUTION OF CASES AND CONTROLS ACCORDING TO SERUM LDL-C LEVELS

LDL-C	Cases (n=40)	Controls (n=40)
<150	38 (95%)	38 (95%)
>150	2 (5%)	2 (5%)
Inference	Percentage of patients with LDL-C >150 is equal when compared to controls (5% vs. 5%) with p= 1	

FIGURE 24: DISTRIBUTION OF CASES AND CONTROLS ACCORDING TO LDL-C LEVELS

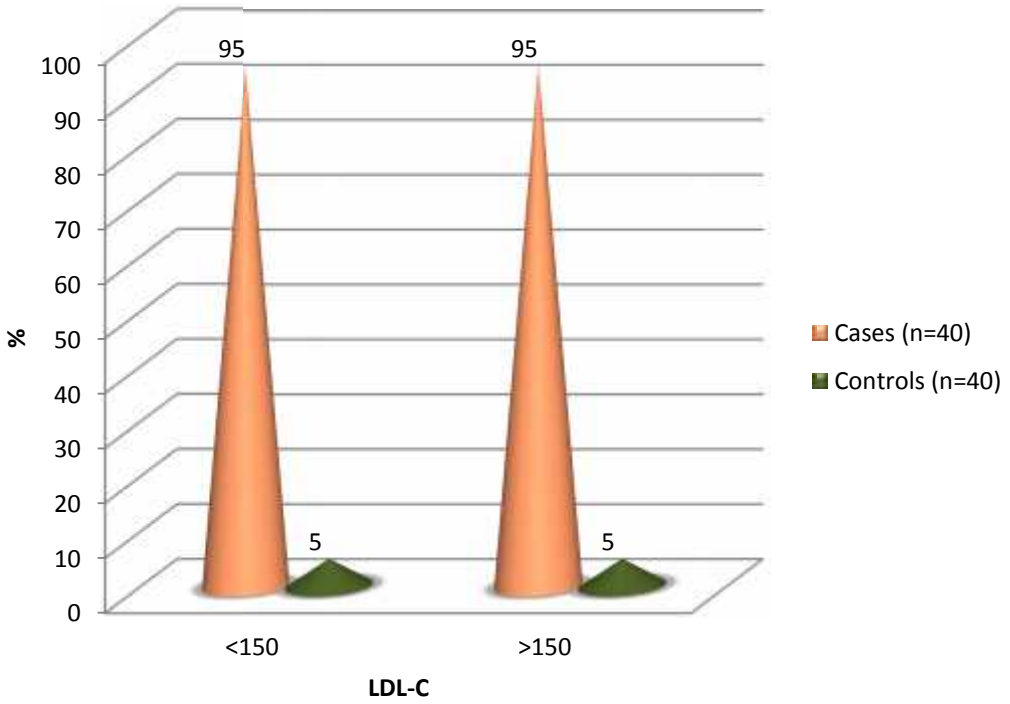


TABLE 13: DISTRIBUTION OF CASES AND CONTROLS ACCORDING TO SERUM VLDL-C LEVELS

VLDL-C	Cases (n=40)	Controls (n=40)
5 – 40	37 (92.5%)	37 (92.5%)
>40	3 (7.5%)	4 (10%)
Inference	Percentage of patients with VLDL-C levels >40 is not significant in cases when compared to controls (7.5% vs 10%) with p= 1	

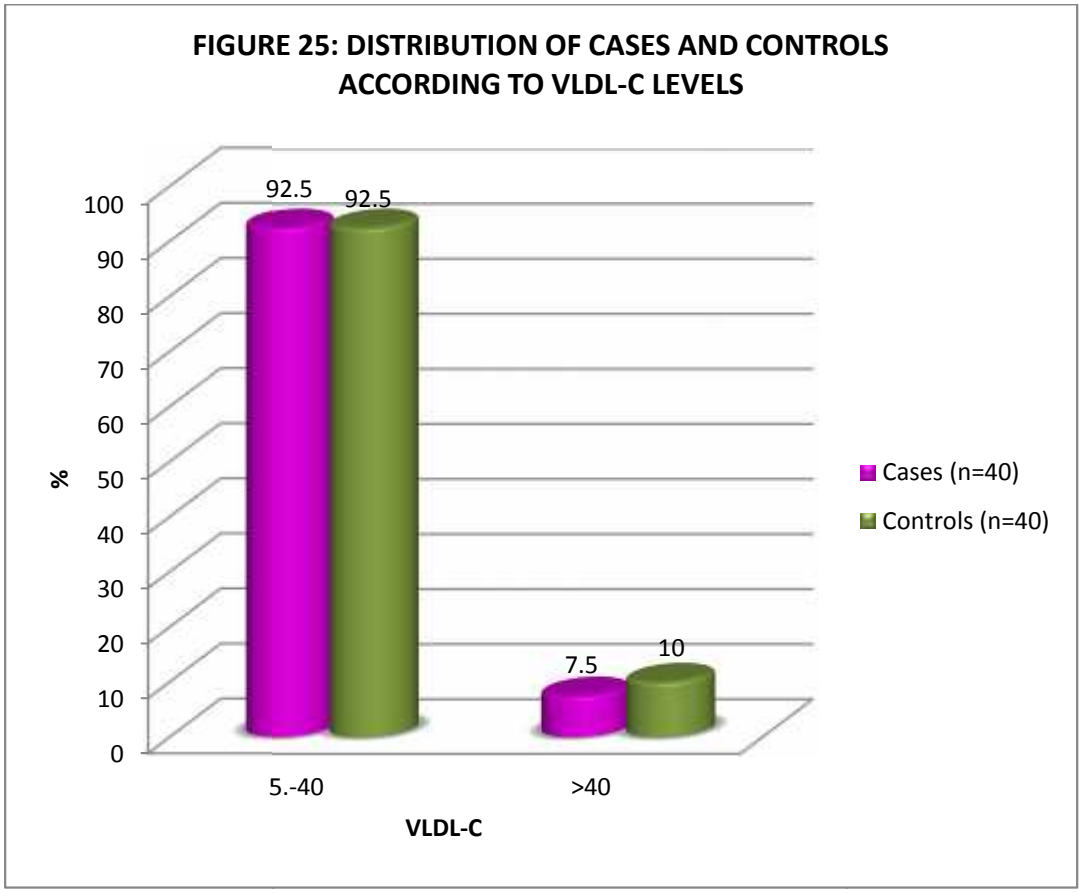


TABLE 14: DISTRIBUTION OF CASES AND CONTROLS ACCORDING TO TC/HDL-C RATIO

TC/HDL-C	Cases (n=40)	Controls (n=40)
<4.99	28 (70%)	36 (90%)
>4.99	12 (30%)	4 (10%)
Inference	Percentage of patients with TC/HDL-C ratio >4.99 is significantly more in cases when compared to controls (30% vs. 10%) with p= 0.025	

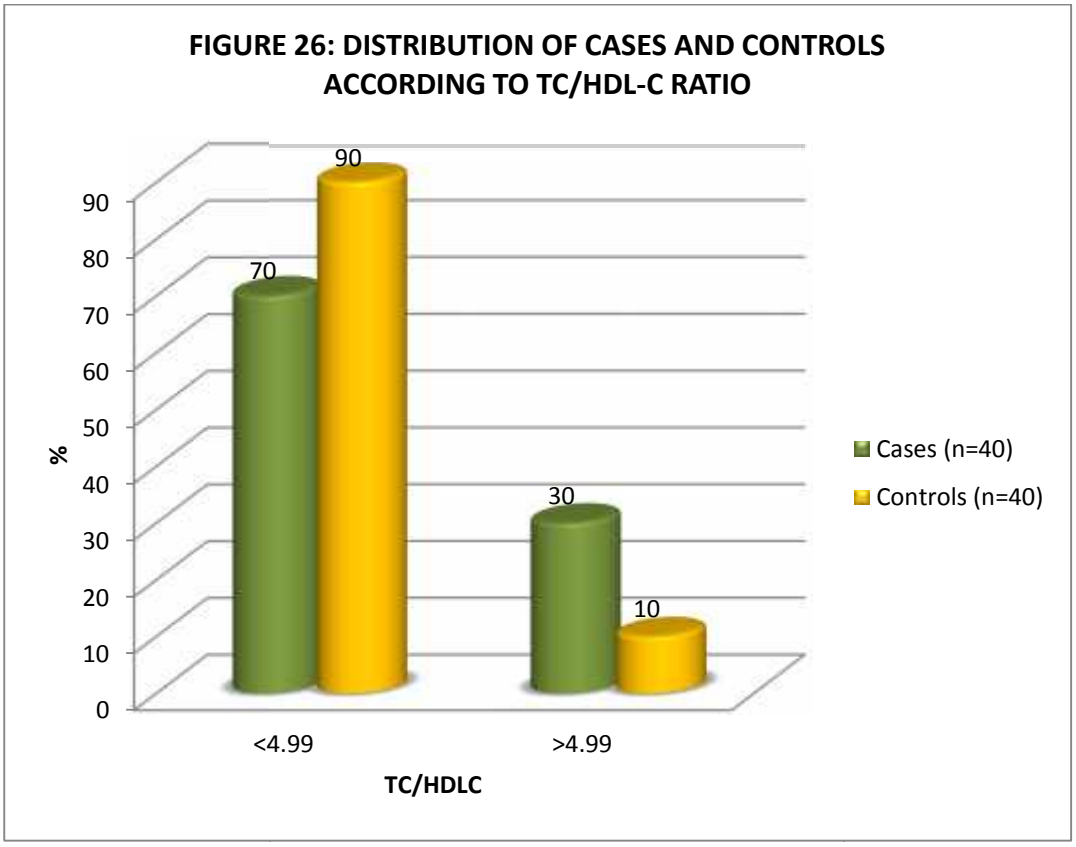


TABLE 15: DISTRIBUTION OF CASES AND CONTROLS ACCORDING TO SERUM LDL-C/HDL-C LEVELS

LDL/HDL ratio (mg/dl)	Cases (n=40)	Controls (n=40)
<3.50	30 (75%)	38 (95%)
>3.50	10 (25%)	2 (5%)
Inference	Percentage of patients with LDL-C/HDL-C ratio >3.50 is significant in cases when compared to controls (25% vs. 5%) with p= 0.012	

FIGURE 27: DISTRIBUTION OF CASES AND CONTROLS ACCORDING TO LDL-C/HDL-C RATIO

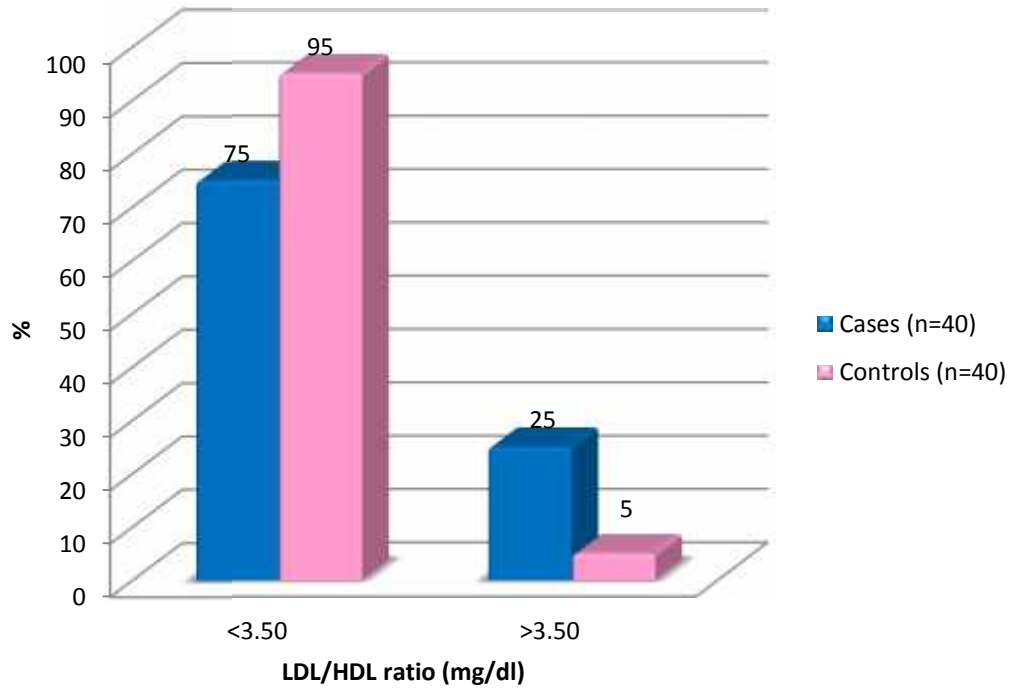


TABLE 16: COMPARISON OF HYPERLIPIDEMIA WITH THE DURATION OF ILLNESS OF PSORIASIS

Duration of illness (years)	No. of cases	Hyperlipidemia
<1	8	--
1-10	26	6
11-20	6	3
Inference	The relation between duration of illness (psoriasis) and hyperlipidemia is not significant with p=0.085	

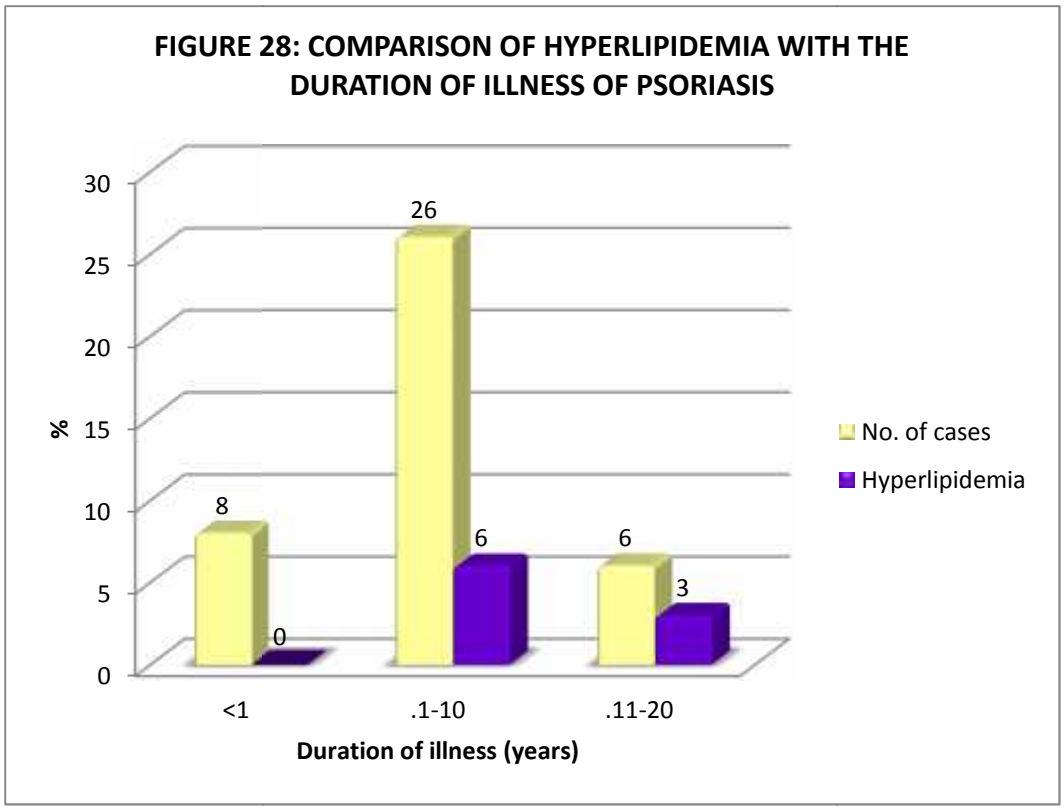


TABLE 17: COMPARISON OF PASI SCORE WITH HYPERLIPIDEMIA

PASI	No. of cases	Hyperlipidemia
0-10	33	6
11-20	5	2
21-30	2	1
Inference	The relation of PASI score with the hyperlipidemia is not statistically significant with p= 0.350	

FIGURE 29: COMPARISON OF PASI SCORE WITH HYPERLIPIDEMIA

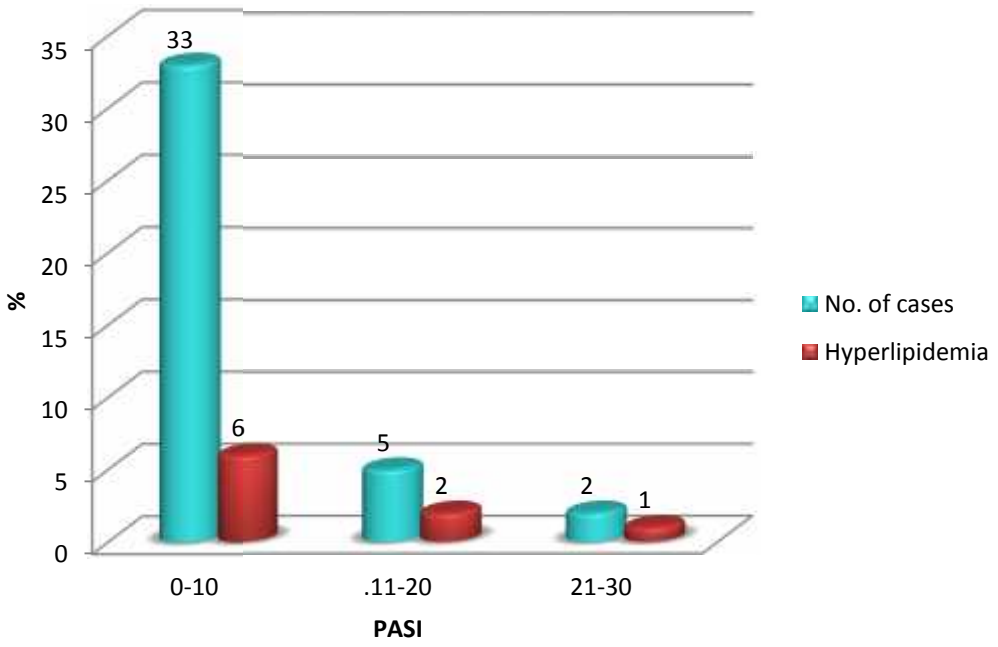


TABLE 18: COMPARISON OF NAIL CHANGES WITH HYPERLIPIDEMIA

	No. of cases	Hyperlipidemia
Nail changes	29	7
Inference	There is no statistical significance between nail changes and hyperlipidemia with p= 0.983.	

FIGURE 30: COMPARISON OF NAIL CHANGES WITH HYPERLIPIDEMIA

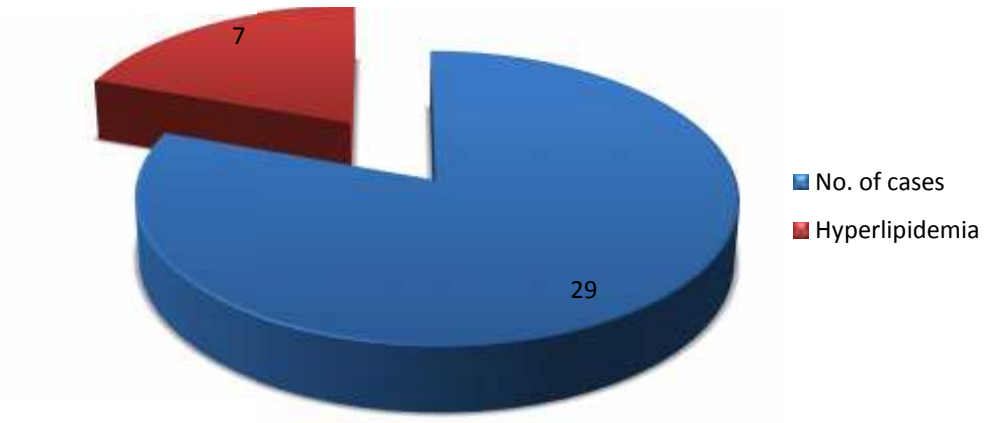


TABLE 19: TYPES OF NAIL CHANGES IN PSORIASIS WITH HYPERLIPIDEMIA

Nail changes	Normolipidemia	Hyperlipidemia
Pitting	16	7
Subungual hyperkeratosis	9	6
Onycholysis	1	1
Beau's lines	1	-
Oil drop sign	1	-

FIGURE 31: TYPES OF NAIL CHANGES IN PSORIASIS WITH HYPERLIPIDEMIA

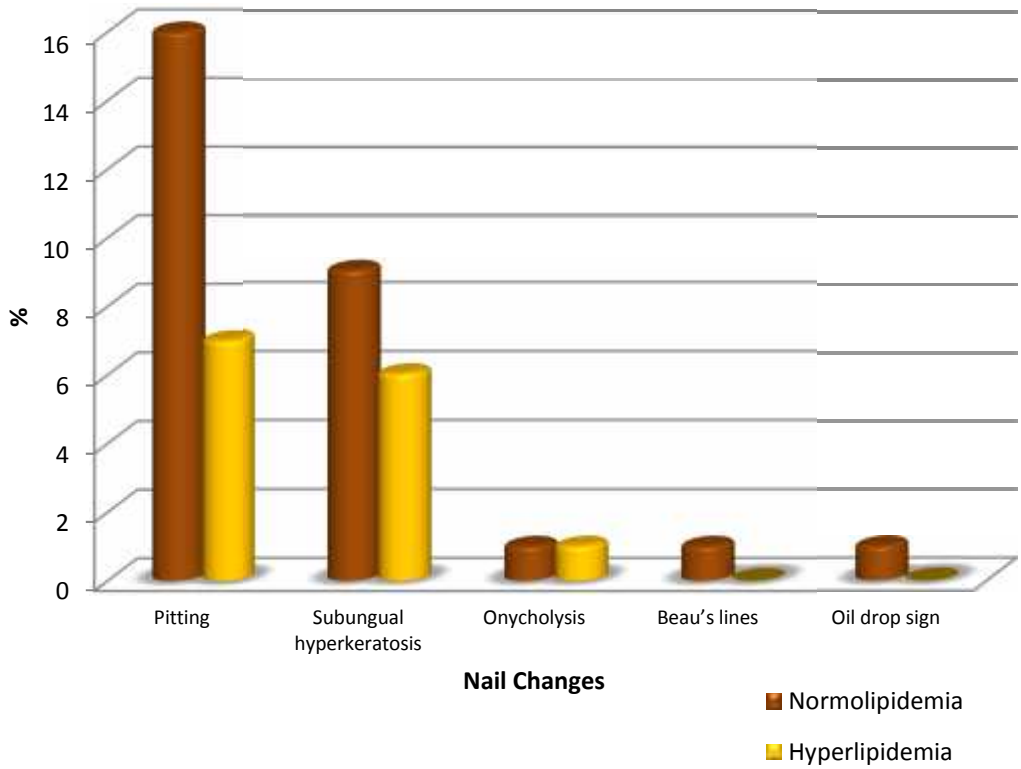


TABLE 20: COMPARISON OF JOINT INVOLVEMENT WITH HYPERLIPIDEMIA

	No. of cases	Hyperlipidemia
Joint involvement	9	6
Inference	There is no statistical significance between joint involvement and hyperlipidemia with p= 0.181	

FIGURE 32: COMPARISON OF JOINT INVOLVEMENT WITH HYPERLIPIDEMIA

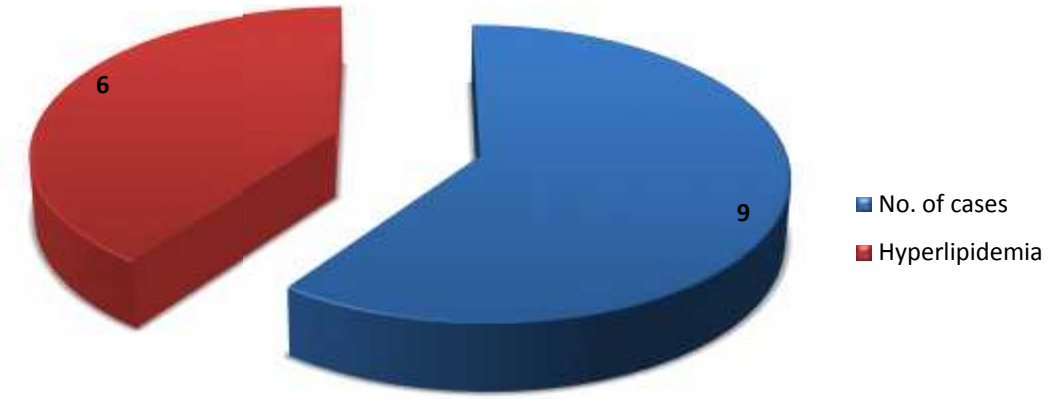


TABLE 21: TYPES OF JOINT INVOLVEMENT IN PSORIASIS WITH HYPERLIPIDEMIA

Type	Normolipidemic	Hyperlipidemic	No. of cases
Distal interphalangeal (Classical)	3	1	4
Rheumatoid arthritis like	2	2	4
Arthritis mutilans	-	1	1

FIGURE 33: TYPES OF JOINT INVOLVEMENT IN PSORIASIS WITH HYPERLIPIDEMIA

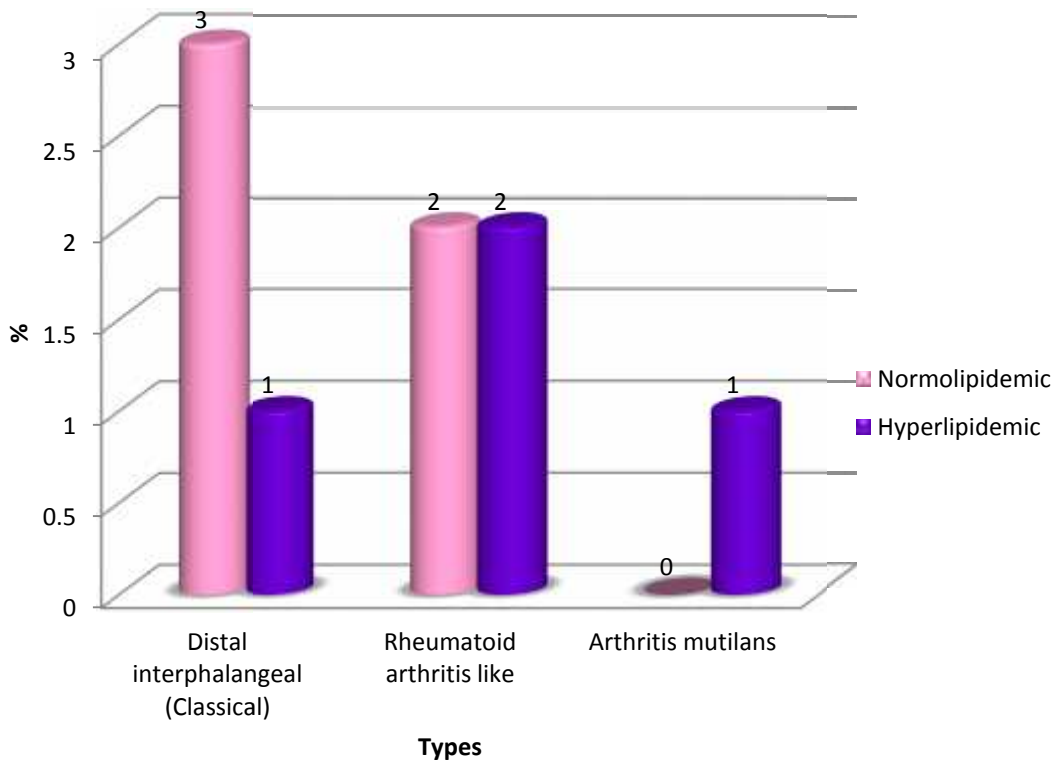


TABLE 22: TYPE OF PSORIASIS (I AND II)

Type of psoriasis	Normolipidemic	Hyperlipidemic	No. of cases
Type 1	1	1	2
Type 2	30	8	38

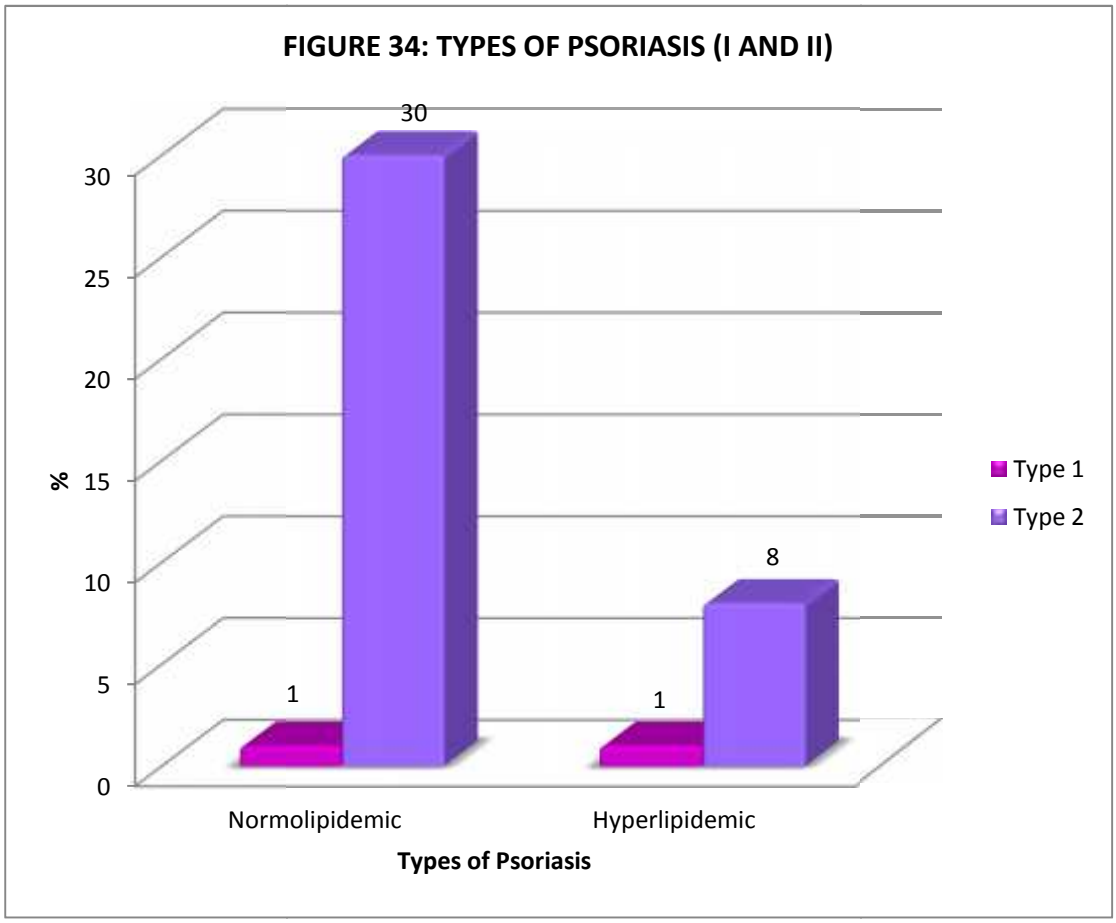
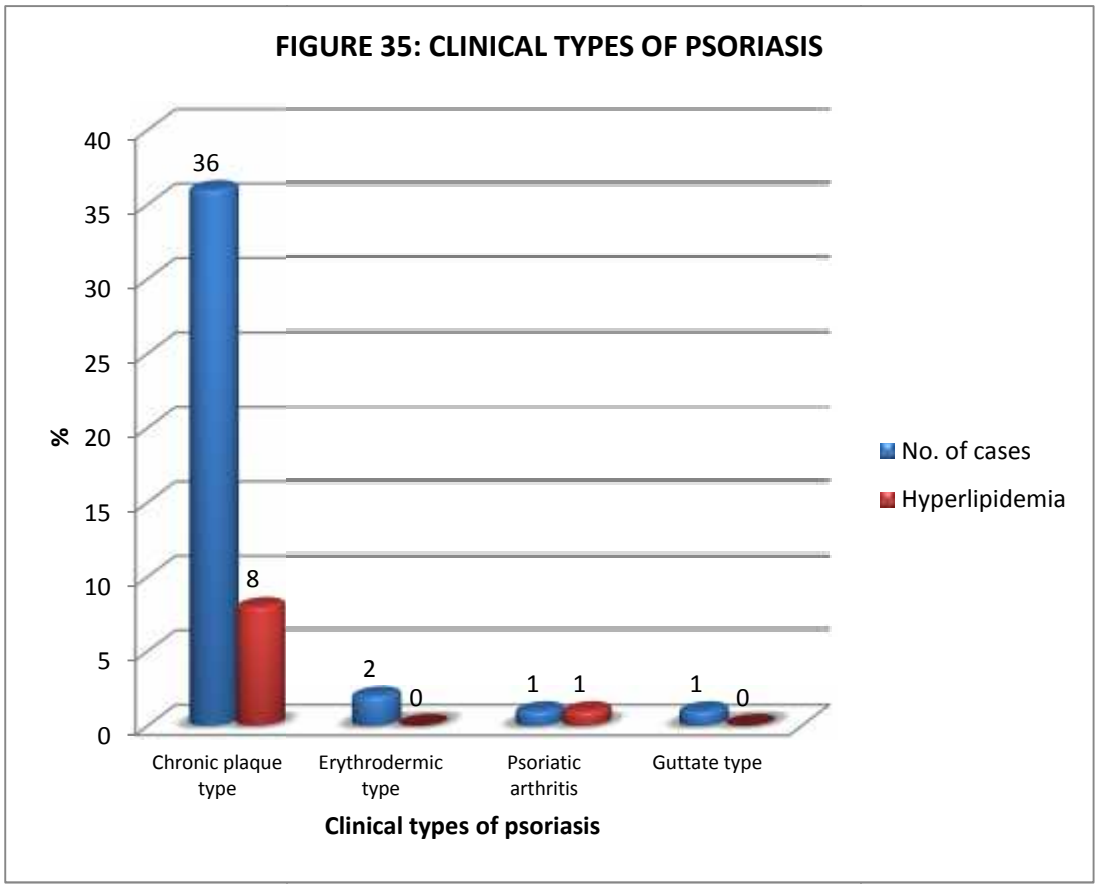


TABLE 23: CLINICAL TYPES OF PSORIASIS

Type of psoriasis	No. of cases	Hyperlipidemia
Chronic plaque type	36	8
Erythrodermic type	2	-
Psoriatic arthritis	1	1
Guttate type	1	-



STATISTICAL METHODS

Categorical outcomes were summarized by percentage. Numerical outcomes were summarized by mean and standard deviation.

To compare mean of the two groups, unpaired t test was used. To compare the rates of the two groups, Chi square test was used.

P> 0.05 was considered statistically significant.

DISCUSSION

The present study is a hospital-based study conducted over a period of 12 months from January 2011 to December 2011 in the OPD of Dermatology, Venereology and Leprosy in KLES Dr. Prabhaker Kore Hospital and MRC, Belgaum. Total number of 25800 skin patients were treated during this period, of which 40 were psoriasis cases. So the frequency of psoriasis among OPD cases was 0.15.

Psoriasis is a chronic inflammatory skin disease that is associated with an increased cardiovascular risk profile. The systemic inflammation present in psoriasis, various systemic treatments for psoriasis and an increased prevalence of unhealthy life style factors contribute to this unfavorable risk profile. The purpose of this study is to determine serum lipid disturbances in lipid profile and to study the demographic and clinical data in psoriasis.

Although there have been extensive studies of serum lipids and apolipoprotein levels in psoriasis, their importance in the etiology or in the enhancement of the disease remains controversial.[67,57,68,69] Genetic studies demonstrate that psoriasis and cardiovascular disease share common pathogenic features, for example inflammatory cytokines like TNF-α and IL-1 play an important role. The chronic inflammation in psoriasis has an unfavourable effect on the cardiovascular risk profile. Multiple cardiovascular risk factors seem to be influenced like blood pressure, oxidative stress, dyslipidemia, endothelial cell dysfunction and blood platelet adhesion.[70,71]

Systemic treatments in psoriasis reduce the cardiovascular risk by diminishing the inflammation, but most of these therapies also have adverse cardiovascular effects such as dyslipidemia, hyperhomocysteinemia and hypertension. As a consequence,

preventive measures are indicated during long-term treatments. Prospective research is warranted to accurately estimate the increased cardiovascular risk in psoriasis, to determine the underlying processes and consider preventive measures according to the absolute risk of cardiovascular disease.[70]

Lipid metabolism disorders may play a role in psoriasis pathogenesis.[72] Increase in cardiovascular diseases, myocardial infarction, cardiovascular hypertension and diabetes is proved in several studies[73] justifies high mortality and morbidity in patients with prolonged and severe disease.[74]

Mallbris et al., in a study of 200 cases of psoriasis proved that there was higher total cholesterol, VLDL-C, HDL-C, apo B and apoA1 levels compared to normal control group.[2] We found that present study was not consistent with these findings.

Piskin in his study of 100 psoriasis patients showed serum total and LDL-C levels to be significantly higher than that of control group.[72] Our present study is consistent with the above findings.

Seishma et al., observed normal levels for total cholesterol and HDL values in 38 psoriatic patients.[75] Our present study is not consistent with these findings.

Rocha-Preira reported rise in TC, TG, LDL, VLDL and reduction in HDL, a rise in lipoperoxidase products and a reduction in total antioxidant capacity and in antioxidants A and E in psoriatic patients. They also found that the worsening of psoriasis was associated with the enhancement of oxidative stress and lipid risk changes.[67]

Uyanik reported significant increase in serum triglycerides levels in 72 psoriatic patients corresponding to normal group in his study. TC, HDL, LDL in patients and control groups were similar.[5] The findings of our study are not consistent with this study.

In a study by Torkhovskaia on 192 psoriatic patients, high percentage of patients with hypo- or hypercholesterolemia, high and low plasma HDL cholesterol levels were observed, depending on disease severity. Psoriasis patients have big range not only in HDL_2 cholesterol levels but also in HDL_3 cholesterol. Data obtained suggest the existence of changes in reverse cholesterol transport system in psoriasis, which may influence skin cell proliferation.[69]

Javedi Z et al in the study of 60 psoriatic patients found significantly higher TC, TG and LDL-C values in patients compared to controls.[3] Among the many studies in serum lipid values in psoriasis, conflicting results have been reported. In studies on serum TC levels in psoriatic patients, high,[58,67,72] low[7,59] and normal,[11,60,75] values all have been reported. The findings of our study are consistent with this study.

Dreiher et al in his study on 10,669 patients and 22,996 subjects without psoriasis observed that triglycerides levels were higher in psoriasis patients and HDL-C levels were lower. This study supported previous reports of an association between psoriasis and lipid abnormalities.[76] Several studies have reported high,[7,67] low[59] and normal[11,72] serum triglyceride levels in psoriasis patients. We found that triglyceride levels in psoriasis patients were not statistically significant compared to the control group ($p=0.765$). Thus, our study is not consistent with the above study.

Tekin et al in his study of 84 patients and 40 healthy controls observed that TC, TG, LDL-C levels were significantly higher in psoriatic patients when compared to controls. Our study is consistent with the above findings.[77]

Bajaj et al in his study of 79 patients and equal number of controls showed that TC, TG and LDL-C levels were significantly higher in psoriatic patients when compared to controls.[17] The findings in our study are consistent with these findings.

Akhyani et al in his study of 50 cases 50 and controls observed that TC, TG, VLDL-C and LDL-C levels were significantly higher than those of controls. HDL-C levels did not show any significant difference between the cases and controls.[78] The findings of our study are consistent with these findings.

In several studies normal[72,75] and low[7,67,76] serum levels of HDL-C have been detected. In our study, HDL-C levels in psoriatic patients were greater than the control group (p=0.896), which is not statistically significant. As for serum LDL-C levels, high[67,72] or normal[7,11,67,72] values have also been reported in psoriasis. We found that serum LDL-C levels are higher in psoriasis patients than in control group (p=0.01).

In studies on serum VLDL-C levels in psoriatic patients, normal[72] and high[2,67] values have been reported. We found that serum VLDL-C values in psoriatic patients were statistically insignificant compared to control group (p=0.366). In our study, significantly raised TC/HDL ratio (p=0.009) and LDL/HDL ratio (p=0.019) were observed in psoriatic patients against controls.

The mean age at diagnosis of psoriasis was 40.9±13.47. 82.5% patients were between the age group of 21-50 years of age and 17.5% were between 51-70 years.

The youngest patient was 20 years old and oldest was 70 years old. Highest incidence was noted in the age group of 41-50 years. Most of the patients are in their second and fourth decade at the time of presentation. These findings are not consistent with the studies done by Dogra et al and Bedi.[16,79]

Psoriasis occurs in males and females with nearly equal frequency. In the present study of 40 psoriasis patients, 33 (82.5%) were male patients and 7 (17.5%) were female patients, the male to female sex ratio being 3.3:0.7. Studies done by Bedi, Asokan et al and Dogra et al show similar findings of male preponderance as in our present study.[16,79,80]

Indian studies report lower familial incidence of the disease. In the present study of the 40 patients, family history was positive in 5 patients (12.5%) of whom all were first degree relatives. Bedi in his study of 530 psoriasis patients reported positive family history in 14% while Kaur et al reported family history in only 2% of their patients.[81,82]

Of the 40 patients, 72.5% patients showed worsening in winter, 7.5% in summer and 12.5% did not show any seasonal variation. Majority of patients showed worsening of psoriasis in winter season. These findings are consistent with Bedi.[81,83]

In the present study, 95% were of type 2 psoriasis (late onset type). The studies done by Ferrandiz et al and Ejaz et al both showed type 1 psoriasis (early onset) as a more common type in their study. These findings are not consistent with our study.[84,85]

Of the 40 cases of psoriasis, 90% cases were chronic plaque psoriasis, followed by 5% cases of erythrodermic psoriasis and 2.5% cases each of guttate and

psoriatic arthritis. Chronic plaque psoriasis was the commonest clinical phenotype. Bedi, Ferrandiz et al and Dogra et al also showed similar findings in their study.[16,81,84]

Of the 40 psoriatic patients, 29 patients (72.5%) showed nail changes. The most frequent site of affection was the finger nails. Pitting (57.5%) was the commonest nail change, followed by subungual hyperkeratosis (37.5%). A study by Kaur et al showed pitting as the commonest nail change followed by other nail changes. Bedi in his study also showed pitting as the commonest nail change in the finger nails.[81,82]

Of the 40 psoriatic patients, 9 patients (22.5%) had joint involvement. Commonest type of joint involvement were the distal interphalangeal joint (classical type) and the rheumatoid arthritis like (10%), followed by 1 patient (2.5%) with arthritis mutilans type of joint involvement. There were no patients with asymmetrical mono arthritis type of joint involvement. Ray et al and Rajendran et al found polyarticular pattern simulating rheumatoid arthritis as the most common pattern.[86,87]

CONCLUSION

Results obtained from various studies conducted upon patients with psoriasis point altered serum lipids and its association with cardiovascular complications. In this background, an assessment of serum lipids in relation to psoriatic patients has been made.

The present study was carried out in 40 psoriasis patients and compared with age and gender matched controls. Serum lipid level was measured by enzymatic method. There was significant elevation in the TC, LDL-C, TC/HDL-C ratio and LDL-C/HDL-C ratio when compared to the control group. Serum TG, HDL-C, and VLDL-C levels were not significant when compared to the control group.

In the present study, demographic and clinical data in the patient group was also studied in relation to the hyperlipidemia. There was no significance found in their correlation.

In the present study, patients of psoriasis, irrespective of disease process and severity of illness have shown raised lipid profile. Hence, psoriasis patients should be evaluated for the further risk of cardiovascular disease.

Since lipids are involved in the immuno-inflammatory and oxidative stress process in psoriasis, the present study has explored the possible usefulness of these parameters as markers of risk factor for development of cardiovascular disease in psoriasis.

SUMMARY

The present study is a one-year observational study from January 2011 to December 2011. The source of data for the study includes all cases of psoriasis attending the dermatology OPD, at KLES Dr. Prabhakar Kore Hospital and MRC, Belgaum.

The objectives of the study were to assess lipid profile in 40 cases of psoriasis and its comparison to equal number of healthy age and gender matched controls & to study the demographic and clinical data in psoriasis based on age and gender of the patients, seasonal variation, nail involvement and joint involvement.

1. In the study, 33(82.5%) were male patients and 7(17.5%) were female patients. Of these, 24.24% male patients and 14.28% female patient were hyperlipidemic.
2. In the age distribution, there were no patients below 20 years of age group; 82.5% patients were between 20-50 years and only 17.5% were in 50-70 years. There were 42.85% cases with hyperlipidemia in 41-50 years of age group.
3. The duration of illness in relation to hyperlipidemia was calculated. There were 6 hyperlipidemic patients with the duration of illness between 1-10 years and 3 patients with duration more than 10 years with hyperlipidemia.
4. In the study, among the psoriasis patients, the highest PASI score was 25.2 and the lowest was 2.2. There was only one patient with hyperlipidemia with PASI score of 23.5.
5. Among 29 patients with nail changes, 7 (24.13%) patients had hyperlipidemia.

6. The nail changes observed in the study were pitting, subungual hyperkeratosis, onycholysis, beau's lines and oil drop sign. The commonest nail changes were pitting seen in 23 (57.5%) patients, of which 7 (9.26%) had hyperlipidemia.
7. Of the 9 patients with joint involvement, 6 (22.5%) had hyperlipidemia.
8. There were 4 (10%) patients showing distal interphalangeal and rheumatoid arthritis type of joint involvement each; 1 patient with arthritis mutilans type of joint involvement who had hyperlipidemia.
9. Of the 40 cases, 72.5% had a winter exacerbation of psoriasis.
10. Of the 40 patients, only 5 (12.5%) had positive family history.
11. 36 (90%) patients had chronic plaque type of psoriasis. 2 patients of erythrodermic type, 1 patient each of guttate and psoriatic arthritis.
12. 38 patients had type 2 psoriasis;only 2 patients had type 1 psoriasis.
13. 9 (22.5%) of the 40 patients of psoriasis show hyperlipidemia.
14. Serum TC (p=0.003), LDL-C (0.010), TC/HDL-C ratio (0.009) and LDL-C/HDL-C ratio (0.019) levels were significantly higher in psoriatic patients compared with controls.
15. Serum TG (0.765), HDL-C (0.896) and VLDL-C (0.366) levels were not statistically significant compared with controls.

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ANNEXURE – I: INFORMED CONSENT FORM

I.DO.NO. | | | |

A CROSS SECTIONAL STUDY OF LIPID PROFILE IN 40 PATIENTS OF PSORIASIS AND EQUAL NUMBER OF AGE AND GENDER MATCHED CONTROLS

The study is conducted by Dr._____ Post graduate student in M.D Dermatology under guidance of Dr. _____, Professor of Dermatology, J N Medical College, Belgaum.

Respected Sir/Madam, we invite you to participate in our study as, you are eligible for the same. During the study you will be asked some questions in detail regarding your present complaints.

Purpose of the study:

The purpose of this study is to know the lipid profile in psoriasis patient and their comparison to equal number of age and gender matched controls. You are being asked to participate in this research because you have been diagnosed to have Psoriasis. All patients attending the outpatient department, who are diagnosed to have this disease, will be requested to participate in this study during the period of one year.

Procedure and treatment:

Should you choose to participate, you will be asked to give a detailed history of your disease, undergo a physical examination, and consent to a few routine blood

and urine investigations. In addition to this, you will agree to undertake a fasting lipid profile test.

Risks and benefits:

You may undergo some amount of discomfort during the process of investigations, which may include slight pain and bleeding. However all necessary steps and precautions will be taken to ensure your safety. The result of you taking part in this research would help health care providers towards a better understanding of this disease, and thus we will be able to provide improved patient care

Alternatives:

If you decide not to participate in this study, you will still be receiving the usual standard care for your disease.

Privacy and confidentiality:

Your privacy will be respected and all information collected about you during the course of this study will be kept confidential. Your identity will remain undisclosed.

Relations with the Institutional policy:

The J N Medical College will provide, within the limitations of the laws of the State of Karnataka, facilities and medical attention to patients who suffer injuries as a result of participating in this project. In the event if you suffer any physical injury as the result of your participation in this study, you may contact Dr. _____, Telephone No. _____ or Dr. _____, Telephone No. _____.

In the event of an emergency, you should contact KLE'S Dr. Prabhakar Kore Hospital and MRC on Telephone No. 08312473777.

Financial incentives:

You shall not be receiving any payment or any financial incentives for participating in this study.

Authorization to publish results:

The results of this study may be published for scientific purpose or presented to a scientific group. Your identity, however, will be maintained confidential at all times.

Voluntary participation:

Your participation in this study is voluntary. Your decision whether or not to participate will neither affect the care of your current disease, nor your future relations with the doctor or the hospital. In case you need further information regarding your rights as a study participant, you may please contact Dr. V.D. Patil, principal and chairman of the ethical committee, J N Medical College, Belgaum on telephone No. 08312473777.

STATEMENT OF CONSENT

I.D.NO: | | | |

I Mr./Ms/Mrs.

_____

Volunteer and consent to participate in this study. I have read the consent document or it has been read to me in my vernacular language. I accept to participate in this study. All the information regarding this study is provided to me and I have understood the same. I have been given the opportunity to ask questions and obtain appropriate answers.

Participant's name:

Signature or left print of participant:

Witness name:

Signature of witness:

Signature of investigator:

Date:

If the participants are Minors (under 18), the parents sign the form, rather than participants.

ANNEXURE-II :PATIENT PROFORMA

"A CROSS SECTIONAL STUDY ON SERUM LIPID PROFILE IN 40 PATIENTS OF PSORIASIS AND EQUAL NUMBER OF AGE AND GENDER MATCHED CONTROLS"

Case no. IP.No.

Name OP.No.

Age: Date

Gender:

Occupation:

Address with phone number:

Presenting complaints and duration:

History of present illness:

1. a. Onset:
   i. Sudden ii. Gradual

   b i. Progressive ii. Stationary

H/o of erythroderma
1. Present 2. Absent

H/o of sore throat
1. Present 2. Absent

H/o of stress n strain
1. Present 2. Absent

H/o joint involvement
1. Present 2. Absent

Triggering and modifying factors:

A. Local factors:

1. Trauma
2. Operation wound
3. Vaccination
4. Insect or animal bite

B. Seasonal variation (exacerbation):

1. Winter 2. Summer

C. Pregnancy

D. Drugs

E. Sunlight

F. Alcohol and smoking

G. Obesity

Initial lesion:

1. Erythema
2. Red lesions
3. Pus filled lesion

Any associated factors:

1. Itching
2. Pain
3. Joint pain
4. Asymptomatic

Past history:

History of remissions and exacerbations:

1. Present 2. Absent

History of any other medical disorder:

1. Present 2. Absent

Family history:

History of similar history in family (first blood relatives):

1. Present 2. Absent

Treatment history:

1. Topical
2. Phototherapy
3. Systemic
4. Others

Personal history:

Diet

1. Vegetarian 2. Mixed

Appetite

1. Normal 2. Stress

Bowel/Bladder:

1. Normal 2. Altered

Sleep:

1. Normal 2. Altered

Alcohol intake:

1. Present 2. Absent

Smoking:

1. Present
2. Absent

Stress:

1. Present
2. Absent

General Physical Examination:

1. Poor
2. Moderate
3. Good

Vitals

1. Pulse bpm
2. BP (mm/Hg)
3. Temperature (F)
4. Height (Kg)
5. Weight (cm)

Pallor

Icterus

Cynosis

Clubbing

Lymphadenopathy

Edema

Mucocutaneous Examination:

Types of lesions:

Papules

1. Present
2. Absent

Plaque

1. Present
2. Absent

Pustule

1. Present 2. Absent

Erythema

1. Present 2. Absent

Distribution:

1. Symmetrical
2. Asymmetrical
3. Localized
4. Generalized

Site of lesions:

Scalp

1. Present 2. Absent

Face

1. Present 2. Absent

Neck

1. Present 2. Absent

Back

1. Present 2. Absent

Trunk

1. Present 2. Absent

Elbows

1. Present 2. Absent

Extensor aspect of extremities

1. Present 2. Absent

Flexures of upper limbs and lower limbs

1. Present 2. Absent

Palms

1. Present 2. Absent

Knees

1. Present 2. Absent

Axillae

1. Present 2. Absent

External genitalia

1. Present 2. Absent

Gluteal region

1. Present 2. Absent

Soles

1. Present 2. Absent

Size of lesion:

1. Small (0.5 to 1 cm in diameter)
2. Large (2 to 5 cm in diameter)
3. Larger(more than 10 cm in diameter)

Types of scaling:

1. Firmly adherent scales
2. Loosely adherent scales
3. Mica like scales
4. Cone or limpet like scales
5. Oyster shell like scales

Clinical pattern of presentation:

1. Plaques
2. Annular
3. Guttate or eruptive
4. Pustules
5. Erythrodermic

Nail lesion:

1. Pitting
2. Subungual hyperkeratosis
3. Onycholysis
4. Yellow discoloration
5. Beaus lines
6. Splinter hemorrhages
7. Oil drop

Joint involvement:

1. Present
2. Absent

If present which joints;

i. Distal interphalangeal

ii. Proximal interphalangeal

iii. Sacroiliac

iv. Metacarpophalangeal

v. Knee joint, elbow joint, wrist joint

Mucosal Examination:

Genital lesion:

1. Present
2. Absent

Oral lesion:

1. Present
2. Absent

Auspitz sign:

1. Positive
2. Negative

Koebner's Phenomenon:

1. Present
2. Absent

Systemic Examination:

Cardiovascular system: heart sounds

1. Normal
2. Abnormal; if abnormal specify the findings

Respiratory system: Breath sounds

1. Normal
2. Abnormal; if abnormal specify the findings

Per abdomen:

1. Normal
2. Abnormal; if abnormal specify the findings

Central nervous system:

1. Normal
2. Abnormal; if abnormal specify the findings

Investigations:

FBS: mg/dl

Lipid profile

TC: mg/dl

TG: mg/dl

HDL-C: mg/dl

LDL-C: mg/dl

VLDL-C mg/dl

TC/HDL-C RATIO:

LDL-C/HDL-C RATIO

PASI Score:

1. Scaling
2. Erythema
3. Enduration

Diagnosis:

Signature **Guide's signature**

MASTER CHART (CASES)

Sr. no	IP/OP NO.	Age (yrs)	Sex	BMI	Winter exacerbation	FBS	T.CH	TG	LDL-C	HDL-C	VLDL-C	T.CH/HDL-C	LDL-C/HDL-C	PASI	Duration of disease	Type of psoriasis
1	1457094	26	M	27	Winter	79	145	97	91	35	19	4.14	2.02	7.6	7 yrs	Type II
2	1458102	27	M	26	--------	92	138	69	60	64	14	2.15	0.93	4.0	9 mnt	Type II
3	1032851	49	M	22.3	Winter	85	148	67	57	78	13	1.89	0.73	3.5	10 yrs	Type II
4	397140	48	M	24.8	Winter	69	147	109	86	39	22	3.76	2.2	7.0	2.5 yrs	Type II
5	1465662	38	M	23	Winter	90	192	145	113	50	29	3.84	2.26	3.5	8 yrs	Type II
6	395642	48	F	27	Winter	91	168	148	106	32	30	5.25	3.31	7.5	10 yrs	Type II
7	1333359	55	M	25	--------	74	190	161	107	51	32	3.72	2.09	15	3 mnt	Type II
8	400379	27	M	24.6	Winter	90	97	85	40	40	17	2.42	1	4.0	5 yrs	Type II
9	408927	25	M	23.3	Winter	84	189	256	109	29	51	6.51	3.75	8.2	20 yrs	Type I
10	1345082	46	F	24.2	Winter	86	252	121	186.8	41	24.2	6.14	4.55	7.2	6 yrs	Type II
11	395707	28	M	21.3	Winter	79	120	63	66	41	13	2.92	1.6	7.0	4 yrs	Type II
12	399681	46	M	22.5	Winter	82	140	92	73	48	19	2.91	1.52	2.2	4 yrs	Type II
13	1509526	25	M	25	Winter	86	170	68	119	37	14	4.59	3.21	4.0	2 yrs	Type II
14	1368192	25	F	21.6	Winter	83	162	119	95	43	24	3.76	2.2	7.9	2 yrs	Type II
15	411652	40	M	19	Winter	76	197	146	131	37	29	5.32	3.54	9.5	4 yrs	Type II
16	1614995	37	M	25	Winter	82	254	194	173	42	39	6.04	4.11	12.5	10 yrs	Type II
17	416205	25	M	24	Winter	88	139	89	74	47	18	2.95	1.57	4.5	2 yrs	Type II
18	416750	45	M	25.5	-------	80	179	34	128	34	17	5.26	3.76	3.0	10 mnt	Type II
19	421969	31	M	23.4	Winter	79	141	123	85	31	25	4.54	2.74	14.4	4 yrs	Type II
20	1664495	45	M	23.3	Winter	86	245	538	125	33	87	7.42	3.78	10	10 yrs	Type II
21	1170259	66	M	23.4	Winter	88	110	61	58	40	12	2.75	1.45	---	15 yrs	Type II
22	386083	42	M	25	Winter	89	202	128	146	30	26	6.73	4.86	9.6	4 yrs	Type II
23	402961	50	M	23.5	Winter	82	118	152	58	30	30	3.93	1.93	4.5	2 yrs	Type II
24	388890	65	M	25	Winter	89	196	120	138	34	24	5.76	4.05	3.2	1yr	Type II
25	428898	35	F	25.6	-------	82	107	115	28	56	23	1.91	0.5	2.8	20 days	Type II
26	429444	45	M	26.7	Summer	77	160	69	112	34	14	4.7	3.29	25.2	3 yrs	Type II
27	429601	50	M	20.1	--------	80	111	78	45	50	16	2.22	0.9	4.6	6 mnts	Type II
28	1059874	27	M	22	--------	97	117	80	63	38	16	3.07	1.65	5.6	5 mnts	Type II
29	431752	64	M	22	Summer	78	208	205	136	31	41	6.7	4.38	7.4	3 yrs	Type II
30	431754	45	M	24.1	--------	82	153	74	104	34	15	4.5	3.05	11.9	8 mnts	Type II
31	433118	70	M	21	--------	74	109	104	57	31	21	3.51	1.83	---	6 mnt	Type II
32	1564224	48	M	26.8	Winter	77	123	233	49	27	47	4.55	1.81	4.8	12 yrs	Type II
33	436679	35	F	25.3	Winter	90	145	125	88	32	25	4.53	2.75	11.7	16 yrs	Type II
34	1088875	39	F	22	Summer	86	108	105	68	30	10	3.6	2.26	4.5	8 yrs	Type II
35	443314	21	M	20	Winter	76	169	147	112	28	31	6.03	4	5.4	2 yrs	Type II
36	447416	55	M	19	Winter	72	128	121	81	23	24	5.56	3.52	7.2	20 yrs	Type II
37	1874251	47	M	22.2	Winter	70	225	118	141	60	24	3.75	2.35	23.5	20 yrs	Type II
38	1568265	56	M	26	Winter	85	152	75	88	49	15	3.1	1.79	12.5	6 yrs	Type II
39	1883597	23	M	24.1	Winter	82	149	84	82	50	17	2.98	1.64	4.5	5 yrs	Type II
40	431728	20	F	24	Winter	78	148	74	89	49	10	3.02	1.81	10.2	4 yrs	Type I

MASTER CHART (CONTROLS)

Sr.no	IP/OP NO.	Age (yrs)	Sex	BMI	FBS	T.CH	TG	LDL-C	HDL-C	VLDL-C	T.CH/HDL-C	LDL-C/HDL-C
1	1458535	26	M	24.1	80	175	160	105	38	32	4.6	2.76
2	1462981	27	M	22.1	92	100	64	40	47	13	2.12	0.85
3	411265	49	M	25.4	76	129	134	69	33	27	3.9	2.09
4	411817	48	M	23.6	89	103	90	52	33	18	3.12	1.57
5	409956	38	M	21.6	78	70	101	28	21	21	3.33	1.33
6	411267	48	F	23.2	86	199	205	94	64	41	3.1	1.46
7	411179	55	M	21.3	93	131	167	58	40	33	3.27	1.45
8	1502245	27	M	24.7	72	200	127	135	40	25	5	3.37
9	411079	25	M	23.1	70	101	166	37	31	33	3.25	1.19
10	411267	46	F	24	86	161	107	98	28	35	5.75	3.5
11	428979	28	M	21.8	73	103	149	29	44	30	2.34	0.65
12	423536	46	M	24.5	85	159	117	102	30	27	5.3	3.4
13	411079	25	M	22.9	95	185	92	110	26	53	3.53	4.23
14	429801	25	F	25.2	75	113	50	63	40	10	2.82	1.57
15	409956	40	M	26.2	86	118	115	63	35	17	3.37	1.8
16	433497	37	M	21.1	77	118	269	33	31	54	3.8	1.06
17	457101	25	M	23.5	80	154	73	89	50	15	3.08	1.78
18	429218	45	M	20.8	98	110	120	41	45	24	2.44	0.91
19	428836	31	M	21.7	77	143	69	79	50	14	2.86	1.58
20	411817	45	M	22.9	71	145	126	75	35	35	4.14	2.14
21	411642	66	M	25.8	84	110	46	47	53	10	2.07	0.88
22	457101	42	M	20.8	83	154	73	89	50	15	3.08	1.78
23	411179	50	M	22.6	70	148	117	102	30	16	4.93	3.4
24	2118673	65	M	20.1	73	111	51	53	48	10	2.31	1.1
25	411280	35	F	22.6	92	119	110	61	36	19	3.3	1.69
26	450561	45	M	24.5	85	108	82	62	30	16	3.6	2.06
27	481025	50	M	21.1	71	130	49	72	40	18	3.25	1.8
28	463055	27	M	20.6	87	120	101	72	28	20	4.28	2.57
29	478136	64	M	22.6	76	202	210	80	60	64	3.36	1.33
30	489226	45	M	25.7	82	132	114	60	40	32	3.3	1.5
31	469011	70	M	24.5	89	136	110	70	43	23	3.16	1.62
32	461223	48	M	22	81	130	215	45	56	29	2.32	0.8
33	413880	35	F	21.9	64	120	101	72	28	20	4.28	2.57
34	466325	39	F	22.5	85	158	43	94	55	9	2.87	1.7
35	451247	21	M	26	88	120	80	70	34	16	3.52	2.05
36	426178	55	M	20.1	72	142	90	65	40	37	3.55	1.62
37	459424	47	M	19.8	95	185	449	115	38	108	4.86	0.02
38	462109	56	M	24	80	132	50	62	35	35	3.77	1.77
39	457101	23	M	20	75	154	73	89	50	15	3.08	1.78
40	462194	20	F	23.3	70	149	74	68	66	15	2.25	1.03