"ASSOCIATION OF METABOLIC SYNDROME WITH PSORIASIS: A CASE CONTROL STUDY"

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ABSTRACT

Background: Psoriasis is a chronic inflammatory disease of the skin and is associated with an increased risk of cardiovascular atherosclerosis. Metabolic syndrome, a conglomerate of various clinical and biochemical parameters is a significant predictor of atherosclerotic disease and the associated risk for cardiovascular events in such patients.

Objectives: To investigate the prevalence of metabolic syndrome in patients with psoriasis and to correlate with the type and severity of psoriasis

Methods: The study was a prospective, hospital based case-control study involving 60 adult patients with chronic plaque psoriasis and 60 healthy controls. Venous samples were taken at the enrolment visit after the subjects had fasted overnight (at least 8 h). Serum cholesterol and triglycerides were measured with enzymatic procedures. Plasma glucose was measured using a glucose oxidase method. Metabolic syndrome was diagnosed by the presence of three or more criteria of the National Cholesterol Education Programme's Adult Panel III (ATP III). Statistical analysis of the data was done using statistical processing software (SPSS-17) software.

Results: Metabolic syndrome was more common in psoriatic patients than in controls 25(41.7%) *vs* 9(15%), odds ratio (OR) = 3.368. Psoriatic patients also had a higher prevalence of hypertriglyceridaemia (48.3% vs 20%) and impaired fasting plasma glucose levels (45% vs 23%). Psoriatic patients with metabolic syndrome had mean disease duration of 9.00±6.85 years against 3.74±2.96 years in those without metabolic syndrome.

Conclusion: There is a higher prevalence of metabolic syndrome in psoriasis patients as compared to general population and so is the risk of having atherosclerotic adversity. While managing the psoriatic plaques of these patients, concerns should extend to the atherosclerotic plaques as well.

KEY WORDS:

Metabolic Syndrome, Psoriasis

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INTRODUCTION

Psoriasis is a chronic inflammatory skin disease that affects 1-3% of the population.[1,2] For most of the patients , the disease is more emotionally than physically disabling as its impact on quality of life may be significant even if relatively less body surface area is involved. The most characteristic lesions consist of red, scaly , sharply demarcated, indurated plaques, present particularly over extensor surfaces and scalp. It may occur in several distinct clinical subtypes, which can overlap: chronic plaque psoriasis (psoriasis vulgaris), guttate, pustular (generalized or localized) and erythrodermic. Psoriasis can also involve the musculoskeletal system (psoriatic arthritis) and the nail apparatus.[3,4]

The few studies that have been performed in India to determine the prevalence of psoriasis have been of patients attending clinics and hospitals. Hence, their findings 0.8%-5.6% do not reflect the true prevalence of psoriasis in the general population.[5,6]

Both genetic and environmental influences play a critical role in the etiology of psoriasis, thus psoriasis is regarded to have a multifactorial etiology, in which several genes interact with one another and with environmental stimuli. Although the precise psoriasis gene or genes have not been identified, several candidate genes have been suggested, PSORS 1-PSORS 9. The major genetic determinant is reported to be within the PSORS 1 region of the Major Histocompatibility Complex (MHC) on the chromosome 6 p21 and it accounts for 30-50% genetic susceptibility.[7,8] Most frequent Human Lymphocyte Antigen (HLA) associations of psoriasis are MHC class1 Cw6’0602 allele, HLA-B13, HLA-Bw57, HLA-DR7.[9]

Genetic, climate and physical conditions can influence the prevalence rates. Childhood psoriasis is often precipitated by an upper respiratory tract infection, notably with

streptococcus species.[10] Drugs like beta blockers, lithium, systemic steroids and anti-malarials, interferon alpha, digoxin and imiquimod can precipitate or exacerbate psoriasis.[11] Sunlight, on the other hand, will improve most patients with psoriasis while in small minority (5.5%) much of patient's psoriasis maybe provoked by strong sunlight. Patients of photosensitive psoriasis are much more likely to be fair skinned, elderly females with skin type 1 and have elevated levels of protoporphyrin IX.[12]

Psoriasis has a bimodal distribution of age of onset; the larger, early peak between 16-22 years and the later one at 57-60 years.[13] Females tend to develop psoriasis earlier than males. Severe disease is likely in patients with early onset psoriasis, who also are more likely to have an affected first degree relative.[14]

There is an overwhelming data to substantiate that psoriasis is not just a disease of skin and joints but is a systemic , inflammatory autoimmune disease that is connected with a range of co-morbidities like crohn's disease, depression, sleep apnoea etc.[15,16]

The chronic inflammatory nature of psoriasis is also thought to predispose patients to other diseases with an inflammatory component , the most notable being cardiovascular and metabolic (cardiometabolite) disorders. This concept is supported by studies showing that psoriasis is associated with cardiovascular risk factors like diabetes, obesity, hypertension, dyslipidemia, smoking and diseases including MI.[17-21] Gefland et al conducted a well designed study which showed an increased rate of death at a younger age in patients with severe psoriasis.[22]

AIMS AND OBJECTIVES

1. To study the prevalence of Metabolic Syndrome in patients with psoriasis.
2. To correlate the association of metabolic syndrome with type and severity of psoriasis.

REVIEW OF LITERATURE

The history of psoriasis is interesting and puzzling. The biblical term “lepra” was applied to various cutaneous disorders including psoriasis, vitiligo, eczema, boils and alopecia aereata.[23] The Roman sage Aurelius Cornelius is credited with the first clinical description of psoriasis. Galen was the first to use the term psoriasis and Robert Willan (1808) specifically distinguished and described it as a recognizable entity.[24] Lepra vulgaris, described by Willan, was a variety of psoriasis. In 1841, Hebra definitively distinguished the clinical features of psoriasis from those of leprosy.

The disease was initially considered to be a primary disorder of keratinocytes and early therapeutic strategies targeted the hyperplastic epidermis following the lead of oncologists to arrest keratinocyte growth using antiproliferative agents such as arsenic and later methotrexate. A direct role of T cells in the pathogenesis of psoriasis was first suggested in 1983 following the reports of clearance of psoriasis with cyclosporine A. The key role of T cells in psoriasis was conclusively demonstrated in 1996 when psoriatic lesions were induced by injecting autologous T cells into uninvolved psoriatic skin transplanted to severe combined immune – deficient mice.[25,26]

An association of rheumatic disease with psoriasis was first described in the 19th century. In 1973, the occurrence of joint disorders in psoriasis patients was classified as a specific entity with distinct patterns, including the absence of rheumatoid factor and the presence of clinical characteristics such as an equal distribution between males and females, an asymmetric involvement of small peripheral joints, dactylitis, arthritis mutilans and ankylosing spondylitis.[27]

Henseler and christophers in 1995 analyzed data from more than 40,000 patients and calculated sex and age adjusted ratios of expected and observed incidence rates of associated disorders. Their observations demonstrated that, compared with age-matched control patients without psoriasis, cutaneous immune disorders such as allergic contact dermatitis, atopic dermatitis and urticaria are under represented in patients with psoriasis while certain systemic disorders such as diabetes , heart insufficiency and obesity occur significantly more often in patients with psoriasis than in control objects. Increased resistance to cutaneous bacterial infections was also noted in patients with early onset psoriasis.[28]

AETIOPATHOGENESIS

GENETIC CONTRIBUTION TO PSORIASIS

The evidence that psoriasis may be inherited rests on population surveys, twin and other family analysis and Human Lymphocyte Antigen (HLA) studies. The most convincing evidence supporting a genetic predisposition to psoriasis is provided by high concordance rates in monozygotic twins.

When the father suffers from psoriasis, the offspring have a higher risk of developing the disease and they might do so at an early age (genetic anticipation); thereby suggesting the expression of the responsible gene(s) for psoriasis is influenced by the sex of the contributing parent (genetic imprinting).[29,30]

Linkage studies have confirmed a strong association of guttate psoriasis with the HLA-C, CDSN and HCR genes. Palmoplantar pustular psoriasis does not appear to associate with any of the three potential susceptibility loci for chronic plaque psoriasis. However,

in Japanese patients it has been reported to be associated to HLA class II DR9 and class III TNF – B*2 alleles.[31]

Henseler and Christophers in 1985 evaluated 2,147 pateints of psoriasis for the age of onset which revealed two peaks' one occurring at the age of 16 years(in females) or 22 (in males) and a second peak at the age of 60 years (in females) or 57 (in males). They also did HLA tissue typing in 112 randomly assigned patients which showed that HLA-Cw6 , known to be at the disequilibrium in psoriasis, is present in 85.3% of patients with early onset psoriasis in contrast to 14.7% patients with late onset psoriasis. Parents (father or mother) were affected in approximately half of the patients with early onset and in none belonging to group with late onset. The evaluation also revealed that the disease course was quite unstable, more severe and generalized in patients with early onset psoriasis and more than half of patients with early onset psoriasis had a first degree family member affected, where as a positive family of psoriasis was nearly absent in late onset psoriasis.[32]

ENVIRONMENTAL RISK FACTORS

1. STREPTOCOCCAL INFECTION

Telfer, Chalmers, Whale and Colman in 1992 investigated 111 patients with a sudden onset or deterioration of psoriasis for evidence of streptococcal infection. Serologic evidence of recent streptococcal infection was present in 58% of patients with acute guttate psoriasis compared with 26% of patients with guttate exacerbation of chronic psoriasis. Streptococcus pyogenes was isolated from 17% of all 111 patients, 26% with acute guttate psoriasis, 13% with guttate exacerbation of chronic psoriasis, and 14% with chronic psoriasis compared to 7% of 101 control population. This study confirmed the

strong association between streptococcus pyogenes and guttate psoriasis.[33] Ferrandiz et al in 2002 reported that guttate psoriasis, nail involvement, evidence of precipitating factors, a recurrent clinical course and a greater psychosocial impact were also more frequent in early onset group of psoriasis.[34]

Although many environmental factors have been implicated , throat infection with beta- hemolytic streptococci is the only well defined external factor that has convincingly been associated with initiation and acute exacerbation of psoriasis.

2. TRAUMA

Psoriasis at the site of an injury is well known (Koebner phenomenon; see below). A wide range of injurious local stimuli, including physical, chemical, electrical, surgical, infective and inflammatory insults, has been recognized to elicit psoriatic lesions.[35] Psoriasis is one of several conditions in which various types of trauma may elicit the disease in previously uninvolved skin. [36] The Koebner reaction usually occurs 7–14 days after injury,[37] and the reported incidence has varied between[38] and 76% of patients with psoriasis.[38] In a given patient, an all-or-none phenomenon occurs at multiple sites of injury, that is if psoriasis occurs at one site of injury it does so at all sites of injury.[39,40] Clearing of existing psoriasis following injury has been observed and termed the reverse Koebner reaction. This reaction also obeys an all-or-none rule, and the Koebner and reverse Koebner reactions are mutually exclusive. Using a standardized injury, one study found that 25% of patients gave a Koebner reaction and 67% a reverse Koebner reaction.[39]

3. DRUGS

There are many drugs reported to be responsible for the onset or exacerbation of psoriasis.[41] Chief amongst these are lithium salts, antimalarials, beta-adrenergic blocking agents, non-steroidal anti-inflammatory drugs (NSAIDs), angiotensin-converting enzyme(ACE) inhibitors and the withdrawal of corticosteroids. Their risk, however, has never been formally assessed in controlled epidemiological studies. The adverse effect of beta-blockers is based on early experiences with practolol, although data implicating those in current usage are lacking. Likewise, the risk of withdrawal of systemic or potent topical corticosteroids requires careful re-evaluation.[42]

4. SUNLIGHT

Although sunlight is generally beneficial, in a small minority of patients, psoriasis may be provoked by strong sunlight and cause summer exacerbations in exposed skin. In a questionnaire study of 2000 patients in Sweden, the prevalence of photosensitivity in psoriasis was estimated at 5.5%. [43,44] Approximately 40% of these patients gave a history of polymorphic light eruption (PLE) with psoriasis appearing as a secondary phenomenon with PLE lesions. Recent work has indicated that severely photosensitive psoriasis is predominantly female, distinct from PLE, and strongly associated with HLA-Cw6, family history and very early age of onset.[45]

5. METABOLIC FACTORS

The early onset of psoriasis in women, with a peak around puberty, changes during pregnancy and provocation of psoriasis by high dose oestrogen therapy potentially

indicates a role for hormonal factors in the disease. A questionnaire study has provided data from 65 females who had one or more pregnancies after the diagnosis was made. Psoriasis remained unaltered in approximately 40% of pregnancies, improved in 40% and worsened in 14%.[46]. In contrast, in the 3-month postpartum period, 30% remain unchanged, 10% improved and 50% deteriorated. Thus, if psoriasis changes in pregnancy, it is more likely to improve than worsen, while in the postpartum period it is more likely to deteriorate. These results have been broadly supported in other studies. [47] Although rare, generalized pustular psoriasis precipitated by pregnancy has repeatedly been reported .[48] Hypocalcaemia, for example following accidental parathyroidectomy, has been reported to occur in severe forms of psoriasis, particularly generalized pustular psoriasis and may be a predictor of poor outcome.[49,50]

PATHOGENESIS

In normal skin the ratio of proliferating to non proliferating keratinocytes, is around 60% whereas in psoriasis it is almost 100%, and the mean cycle time is reduced from 311 to 36 hours in psoriatic lesions. This keratinocytes hyperproliferation is not restricted to the basal cell compartment stem cells, but may also involve suprabasal cells.[51]

Cutaneous vasculature is characterized by prominent proliferation with large and tortuous blood vessels in the dermis. This cutaneous vascular proliferation is triggered and maintained by angiogenic cytokines and growth factors released by epidermal keratinocytes , such as interleukin – 8 (IL-8), Transforming Growth Factor - alpha (TGF-α), Tumor Necrosis Factor alpha (TNF-α), and most importantly Vascular Endothelial Growth Factor (VEGF) and its receptors are over-expressed in psoriatic epidermis and

dermal vasculature respectively. Furthermore, dermal vessels exhibit up regulation of leukocytes homing molecules such as Intercellular Adhesion Molecule 1 (ICAM-1) and E- selectin. These vascular changes occur early in the development of psoriatic lesions, suggesting that angiogenesis is an important element in this process.[52]

This deranged cutaneous homeostasis occurs as a result of a cascade of immunological events revolving around activation of T lymphocytes. Antigen Presenting Cells (APC) play an essential role in T cell activation. They comprise different types of cells including macrophages, dendritic cells and Langerhans cells. After coming into contact with an antigen in the epidermis, APC's migrate to lymph nodes where two separate signals trigger T cell proliferation. The first signal involves the specific MHC associated antigen or superantigen; the second signal requires interaction between co – stimulatory accessory molecules on APCs and T cell receptors (eg. ICAM-1/LFA-1, B7/CD28, LFA-3/CD2). These activating signals induce expression of skin homing receptors, such as Cutaneous Lymphocyte associated Antigen (CLA), on T lymphocytes, thus directing them to the skin. ICAM-1 and E- Selectin induced in psoriatic dermal vasculature facilitate the recruitment and extravasations of T cells in the dermis.[53]

Chemokines, produced by keratinocytes and inflammatory cells, are an integral part of the immune- mediated cascade in psoriasis, mainly in the recruitment, compartmentalization, and adhesion and trafficking of leucocytes and neutrophils in the disease process. The interplay between these and other cytokine growth factors generated in psoriasis lesions explains most of the clinical features of psoriasis, such as hyperproliferation of keratinocytes, increased neo-vascularization and inflammation.[54]

Precisely how T cells are activated in the genesis of psoriatic lesions is unknown. It is also unknown whether the inciting antigen is self-derived (thereby qualifying psoriasis as an autoimmune disease) or is of non-self origin. Possible events include perturbation of the barrier function of skin with release of performed or rapidly produced cytokines such as IL-1 and TNF-α; exposure of dendritic cells to bacterial products from skin flora, including superantigens; release of heat shock proteins from the epidermal keratinocytes; exposure of keratinocytes and dendritic APCs to glycolipids that bind cell surface receptors. Once T cells and dendritic APCs are fully activated, they create a "cytokine storm" composed of numerous cytokines (eg. TNF-α, IFN-γ, Interleukins 1,6,8,15,17,18,20,23); chemokines (eg. RANTES , MIP, TARC); and growth factors (eg. TGF-α, KGF, VEGF, NGF, amphiregulin). A vicious cycle is then created in which keratinocytes, endothelial cells, neutrophils, macrophages and lymphocytes in the vicinity become activated leading to the creation of a psoriatic lesion. Mast cell numbers are also increased and undergo degranulation.[55]

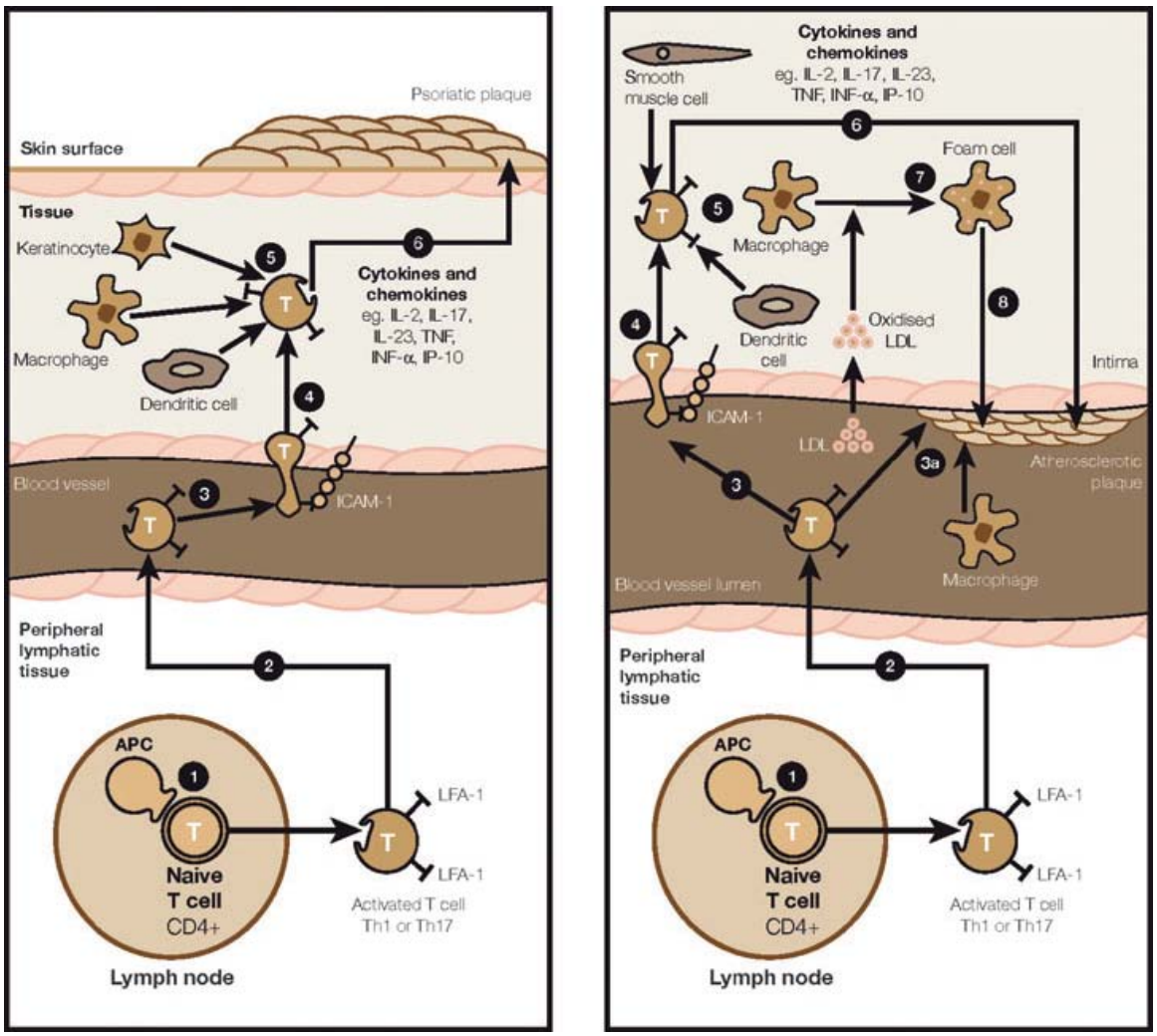
As cytokines of the TH-1 pathway like IFN-γ, TNF-α, IL-2 and IL-12, predominate in the plaques; psoriasis is classified as a TH-1 disease, which is consistent with the relative under-representation of Th-2 diseases, such as Atopic dermatitis, in patients with psoriasis. The T cell infiltrate in psoriasis consists of both CD4 positive and CD8 positive T cells with predominance of the memory effector CD45 RO + designation; these cells form clones in the epidermis and dermis. In general, activated CD4+ T cells are primarily located in the dermis and CD8+ T cells in the psoriatic epidermis, accompanied by tangled collections of dendritic APCs predominantly located in the dermis.[56]

PATHOGENETIC LINKAGE BETWEEN PSORIASIS & ATHEROSCLEROSIS

An APC identifies and processes a yet-to-be identified antigen in the skin. APC then presents, in a MHC class II-restricted fashion, processed antigen and activates naive T cells in the local lymph nodes, resulting in a clonal expansion of the Th1 arm under the influence of IL-2. The result of T cell activation is release of IFN-γ, the defining cytokine of type 1 T cells, and also TNF, which is co-produced by activated type 1 T cells. Due to effect of these cytokines there is keratinocyte proliferation, neutrophil migration, potentiation of Th-1 type response, angiogenesis, up-regulation of adhesion molecule and epidermal hyperplasia.[57,58]

During the rupture of an unstable atherosclerotic plaque, activated inflammatory cells within the plaque secrete matrix proteases leading to the degradation of the extracellular matrix proteins, weakening of the fibrous cap, leading to rupture and thrombus formation. The activation of the inflammatory process and upregulation of Th1-mediated cytokine cascades (with IFN-γ, TNF-α, IL-1 and IL-6) is a probable trigger for acute coronary syndromes as well as psoriasis, as described above.[59]

Recently cytokines IL-12 and IL-23 have also been implicated in the pathogenesis of psoriasis. IL-12 promotes growth and differentiation of naïve T cells into Th1 and cytotoxic T cells 1 where as IL-23 stimulates survival and proliferation of a unique set of T cells, termed Th17 cells.[60,61] Recent studies shows that IL-12 is thought to provide a link between inflammation and Th1 type cytokine production in coronary atherosclerosis.[62]



Immunological basis of (a) psoriatic and (b) atherosclerotic plaque formation.[63]

1. Antigen-presenting cells (APCs) activate naive T cells

within the lymph node to increase expression of leukocyte-function-associated antigen-1(LFA-1)

2. Activated T cells migrate to blood vessel

3. Activated T cells adhere to endothelium; 3a. Activated T cells and macrophages collect on endothelium

4. Extravasation occurs mediated by LFA-1 and intercellular adhesion molecule-1 (ICAM-1)

5. Activated T cell interacts with macrophages, dendritic cells and smooth muscle cells／keratinocytes

6. Re-activated T cells and macrophages secrete chemokines and cytokines that contribute to the inflammatory environment, resulting in the formation of (a) psoriatic plaque, or (b) atherosclerotic plaque

7. Macrophages are transformed into lipid-laden foam cells by uptake of oxidized LDL

8. Formation of 'fatty streaks' in the sub-endothelium and, eventually, atherosclerotic plaques.

IP = inducible protein

CO-MORBIDITIES WITH PSORIASIS

PSORIATIC ARTHRITIS

Today, PsA is classified among the spondyloarthropathies, a cluster of diseases that share common features such as absence of rheumatoid factor, axial involvement and an association with HLA-B27. An association of HLA-B27 and PsA is present in about 40-50% of patients. As this genetic marker is present in about 8% of the healthy white population, of whom 90% will never develop any form of spondyloarthropathy, routine testing for HLA-B27 might not be clinically helpful. [27] A clinical hallmark of PsA is the involvement of ligaments and tendons, known as enthesopathy and enthesitis. In the majority of cases, the onset of PsA follows skin manifestations – even so in some cases

PsA may precede skin lesions, which can complicate the diagnosis. Psoriatic nail involvement is more common in patients with PsA than in patients without PsA. The clinical course of PsA is usually independent of the course of skin symptoms, and has a high likelihood of leading to destructive changes if not treated sufficiently.

The prevalence of PsA was underestimated in the past. Although no large-scale epidemiological studies have been performed, the prevalence was thought to be in the range of 5-8% of all patients with psoriasis of the skin. Up to now, numerous studies have tried to address the prevalence of PsA leading to a wide range of prevalence rates. In a nationwide study in Germany, in which patients were first seen by a dermatologist and later referred to a rheumatologist when signs of arthritis were present, the estimated prevalence was 20.6%, which may be a better estimate of the true prevalence of PsA than the previous 5-8%. [64]

CROHN'S DISEASSE

Previous studies have provided evidence that patients suffering from at least one Immune mediated inflammatory diseases (IMID) are at a higher risk of another IMID.[65] Common immune – mediated disorders with a strong inflammatory component that are of primary interest include asthma, psoriasis, type I diabetes, rheumatoid arthritis, multiple sclerosis, systemic lupus erythematosus, vitiligo, autoimmune thyroiditis. In a recent study evaluating data from 12,601 patients with IBD, other IMID occurred at a greater frequency in IBD patients than in general population. Asthma (OR: 1.5,95%CI: 1.4-1.6), psoriasis (OR: 1.7,95%CI: 1.5-2.0), rheumatoid arthritis (OR: 1.9,95%CI: 1.5-2.3) and multiple sclerosis (OR: 2.3,95%CI: 1.6-3.3) were shown to have a higher prevalence as compared to a matched control group.[66] Studies have already shown an increased

prevalence of psoriasis and a familiar background of psoriasis in Crohn's disease as well as in Ulcerative Colitis. A possible genetic link has been described in recent years: non-MHC psoriasis susceptibility loci tend to overlap with disease regions for other inflammatory disorders such as IBD.[67] It has for example been shown that Crohn's disease associated sequence variants in the interleukin – 23 receptor (IL-23R) and IL-12B genes lead to an increased risk of psoriasis.[68-70] The IL-12 and IL-23 pathways are of importance in Crohn's disease as well as in psoriasis. IL-12 mainly induces differentiation of CD4 naïve T cells to T helper 1 cells (TH1) and activates natural killer cells, which leads to a production of type 1 cytokines such as IFN-γ, IL-2 and TNF-α. The dominant role of IL-23 may be the stimulation of a special subset of recently identified TH17 cells to produce IL-17,TNF-α and IL-6, and to develop into a Th17 phenotype.

For Crohn's disease, the main focus now is on IL-23 as it was shown that antibodies against the p19 subunit specific for IL-23 suppress chronic intestinal inflammation in an IBD model.[71] The initial evidence from clinical trials demonstrates the therapeutic efficacy of an antibody to the p40 subunit of IL-12 and IL-23 in Crohn's disease and psoriasis, highlighting the pathophysiological importance of these cytokines.[72-75]

Other genetic similarities between Crohn's disease and psoriasis are found in the HLA antigen region on chromosome 6p. Psoriasis susceptibility region 1 is located at 6p21 and the IBD susceptibility region 3 is also located at 6p. TNF-α has proven to be of major importance for both diseases as it is found in increased levels in disease lesions and TNF-α inhibitors are highly efficacious in both conditions. The TNF-α gene analyses have linked polymorphisms of TNF-α and its promoter region to Crohn's disease, psoriasis and

psoriatic arthritis,[76] although the exact positions of the single nucleotide polymorphisms found in these diseases differ. Several studies have shown functional polymorphisms in the -238 and -308 sites of the TNF-α promoter region in psoriasis and psoriatic arthritis,[76,77] whereas the -308 site could not be associated with Crohn's disease.[78] Other TNF-α promoter regions such as -1031, -863 and -857 have, at least in some studies , shown an association with Crohn's disease, although the data is still inconclusive.[78]

CARDIOVASCULAR CO-MORBIDITIES

Cardiovascular disease has been found to be an important cause of morbidity and mortality in patients with Chronic inflammatory systemic diseases (CISD)s and is associated with decreased life expectancy.[79-83] Cardiovascular disease, which is the most common cause of death in the general population, is also the most common cause of death in patients with rheumatoid arthritis.[84] Studies have suggested a link between systemic inflammation and cardiovascular events in diseases such as RA and SLE,[80,85,86] and systemic inflammation may accelerate the atherosclerotic process.[87] Psoriasis is associated with an increased cardiovascular risk profile and the chronic inflammation of this disease has an adverse effect on this risk.[88] Several cardiovascular risk factors appear to be influenced, including blood pressure, platelet adhesion, endothelial- cell dysfunction, oxidative stress, waist circumference and dyslipidaemia. In addition, cardiovascular risk factors, such as obesity and smoking, also increase the cardiovascular risk profile by stimulating psoriasis activity.[88,89]

LINKING PSORIASIS WITH CARDIOVASCULAR DISEASE AND METABOLIC SYNDROME

Recent studies have shown that psoriasis is associated with atherosclerosis. This association applies to coronary artery, cerebrovascular, and peripheral vascular diseases and results in increased mortality.[63,90-92] The presence of psoriasis is an independent risk factor for subclinical atherosclerosis. Psoriasis patients had impaired endothelial function and thicker IMT (intima media thickness) of the Common carotid artery, compared with the healthy control subjects.[93]

A spiral computer tomography study demonstrated a significantly higher prevalence and severity of coronary artery calcification as an indicator for Cardiovascular Disease (CVD) in patients with psoriasis compared to control subjects without psoriasis, supporting the notion that psoriasis is an independent risk factor for CVD.[94] Interestingly , the excessive relative risk of MI seems to persist even after adjustment for the major risk factors for CVD, suggesting that psoriasis might be considered as an independent risk factor for MI.[20] Recently a descriptive cohort study has shown that patients with psoriasis had higher risks of incident myocardial infarction, angina, atherosclerosis, peripheral vascular disease and stroke.[95] Moreover the prevalence of MI is higher in mild and severe psoriasis than in patients without psoriasis.[96,97]

METABOLIC SYNDROME

The metabolic syndrome is the constellation of known cardiovascular risk factors, including obesity, dyslipidemia, hypertension, and impaired glucose tolerance. It is believed that insulin resistance underlies the pathogenesis of the metabolic syndrome.

Excess free fatty acids from adipose tissue in these overweight individuals impair the action of insulin in skeletal muscle and the liver, leading to insulin resistance. The combination of fatty acid excess and insulin resistance leads to the over production of pro-inflammatory cytokines and prothrombotic factors in both adipose and hepatic tissue, including TNF-a, IL-6, C-reactive protein (CRP), and fibrinogen.[98]

The importance of the metabolic syndrome is the greatly increased risk it confers for a number of comorbidities, namely coronary artery disease, MI, stroke, and type 2 diabetes.[99,100,101]

There have been different classification systems for the metabolic syndrome over the years . The mostly widely used definitions include those of the World Health Organization, the US National Cholesterol Education Program and the International Diabetes Federation.[102] In all definitions , criteria for central obesity, raised triglyceride levels, reduced high-density lipoprotein cholesterol levels, insulin resistance and hypertension are involved, but do differ slightly and may influence the comparability of epidemiological studies.

There have been data published on disease concomitance in psoriasis that revealed higher prevalence rates of diseases related to metabolic syndrome. Sommer et al,[21] Gisondi et al[89] and Cohen et al[103] were the only authors to calculate odds ratios for metabolic syndrome itself. The first study compared 581 adult patients hospitalized for plaque type psoriasis with a hospital-based control group of 1.044 patients treated surgically for localized stage I melanoma. They found a higher prevalence of metabolic syndrome in psoriasis patients , with an odds ratio of 5.92.[21] Gisondi et al performed a hospital based case control study on 338 adult patients with chronic plaque type psoriasis

and 334 patients with skin diseases other than psoriasis, and described a higher prevalence of psoriasis in patients after the age of 40 years with an odds ratio of 1.65 that was directly correlated to psoriasis duration.[89] The largest study (analyzing data from 16,851 patients with psoriasis and 48,681 control subjects), by Cohen et al, used data from a national health service database. Even in this analysis involving large patient numbers, a higher prevalence of metabolic syndrome in patients with psoriasis was shown with an adds ratio of 1.3.[103]

RISK FACTORS OF METABOLIC SYNDROME

1. OBESITY

Persons with Body mass index (BMI) >25 kg/m2 and> 30kg/m2 are defined as overweight and obese respectively. The suggested BMI cut off point for Asian Indians is 23/kgm2. Young Asian Indians with a mean (SD) BMI of 23kg/m2 were found to have a higher abdominal and visceral fat mass and were significantly more insulin resistance as compare to BMI-matched Caucasian subjects.[104] Psoriasis and obesity share similar mediators of inflammation – such as TNF-a and IL-6 – and that the engines of adipocytic and psoriatic inflammation – the adipocyte and macrophage, respectively – both derive from a common mesothelial origin. Importantly, psoriasis, like obesity, is associated with high systemic and local (skin and joint) levels of TNF-a.[53,105,106] This suggests that obesity may potentiate some of the TNF-a- and IL-6-driven inflammation seen in psoriasis, additionally leading to impaired glucose regulation, dyslipidaemia, endothelial dysfunction, hypertension and a heightening of the inherent cardiovascular risk of

cutaneous psoriatic inflammation Patients with severe psoriasis have a higher BMI that is directly related to the risk of cardiovascular mortality.[107]

The combination of obesity and psoriasis is an important health care concern. Both conditions are associated with chronic inflammation, which may exacerbate the cardiovascular disease pathogenic process such as atherosclerosis.[108]

Lifestyle factors such as decreased physical activity due to social stigma or depression, presence of psoriatic arthritis and increase alcohol consumption may further exacerbate the obesity in patients with psoriasis.[109,110,111]

2. DIABETES

According to recent studies, psoriasis is related to diabetes , independent of factors such as obesity, hypertension and hyperlipidaemia. Diabetes is more prevalent in patients with severe psoriasis than in those with mild disease. TNF-alpha which plays a central role in the immunopathogenesis of psoriasis may be involved in the increased insulin resistance observed in patients with psoriasis.[19]

Cohen et al conducted a large study that included 16 851 patients with psoriasis and 74 987 subjects without psoriasis (control patients). The proportion of diabetes was significantly higher in patients above 35 years ($P < 0.05$). The age-adjusted proportion of diabetes was significantly higher in psoriasis patients as compared to the control group [odds ratio (OR), 1.38, $P < 0.05$] and was similar in men and women (OR, 1.32, 1.45, respectively). A multivariate logistic regression model showed that psoriasis was significantly associated with diabetes, independently of age and gender (OR, 1.58, $P < 0.001$).[112] Furthermore, data from large cross-sectional studies also reveal that, when compared with control subjects, the risk for diabetes mellitus rises substantially in

patients with psoriasis, with a 62% increase in risk noted in patients with severe psoriasis.[19,113] In a large observational study done by Brauchli et al the risk of incident DM was increased for patients with psoriasis as compared with a psoriasis-free comparison group. The risk increased with psoriasis duration and severity and was not driven by high BMI alone.[114]

3. DYSLIPIDEMIA

In addition to obesity, there is evidence to suggest a link between psoriasis and abnormalities in lipid metabolism. Several studies have suggested that psoriasis is associated with atherogenic dyslipidemia, including hypertriglyceridemia, high Low density lipoproteins (LDL), Very low density lipoproteins (VLDL), and lipoprotein A and low HDL, apolipoprotein B, and apolipoprotein B. [95-97,115,116] It has been proposed that lipoprotein (a) [Lp(a)] which is a genetically determined molecule whose role has been implied in cardiovascular pathology, and whose levels have been reported to be elevated in patients with psoriasis may be a factor contributing to an increased cardiovascular risk in patients with psoriasis.[117]

Several studies, although with relatively small patient populations, have demonstrated that an atherogenic dyslipidemic profile consisting of increased levels of total cholesterol, triglycerides, low-density lipoprotein cholesterol, oxidatively modified lipids, and decreased levels of HDL cholesterol is exhibited by patients with psoriasis.[118,119]

4. HYPERTENSION

The link between psoriasis and hypertension may be related to the increased levels of angiotensin-converting enzyme, endothelin -1 (ET-1) and rennin in patients with psoriasis.[120,121] Sommer et al reported that inpatients with psoriasis had a >3-fold higher

prevalence of hypertension compared with inpatients without psoriasis (OR: 3.3; 95% CI: 2.4-4.4).[10] One prospective study demonstrated an increased risk of diabetes and hypertension in women with psoriasis, even after adjustment for age, BMI, alcohol intake, and smoking status.[49]

5. CONSUMPTION OF NICOTINE AND ALCOHOL

Smoking, in particular, has been correlated with psoriasis in numerous studies , and was even associated with the clinical severity in a study evaluating 818 adult hospitalized psoriasis patients.[122] The strongest link between smoking and skin manifestations was reported for pustular form of psoriasis (i.e. plaque type psoriasis associated with pustular lesions and a generalized pustular psoriasis) with an odds ratio of 5.3 for current smokers in a study by Naldi et al.[123]

In some studies, smoking appeared to be a factor in the onset of disease. In a cross sectional study from Utah psoriasis Initiative, 78% of the patients reported that they began smoking before the onset of psoriasis.[109] Data from the literature suggest dome gender differences in smoking habits. In 550 psoriasis patients from an Italian case-control study, psoriasis was more prevalent in male ex-smokers but male current smokers had a lower prevalence of psoriasis than female current psoriasis. The effect of cigarette-years on psoriasis severity was also shown to be stronger in women. Higgins concluded that smoking is a more prominent trigger factor for psoriasis in women than in men.[124]

The available evidence on alcohol intake and psoriasis is less conclusive. Some earlier studies were not able to show an association of drinking habits and psoriasis, whereas other studies demonstrated an association both in men and women. It was proposed that the earlier studies failed to show a correlation with the disease as they did not control for

confounding factors such as tobacco use. When controlling for such factors, study results often demonstrated a significant correlation between alcohol use and psoriasis. Very recently, an association between weekly alcohol consumption and the severity of psoriasis has been observed in psoriasis patients.[125]

MATERIALS AND METHODS

This study was conducted from December 2009 to March 2011 in the Department of Dermatology, STD and Lepsrosy; Sri Devaraj Urs Medical College, Tamaka , Kolar. The study was a hospital based case control study involving a series of 60 patients and 60 controls.

INCLUSION CRITERIA

1. Age more than 18 years
2. Clinical diagnosis of psoriasis (lasting at least 6 months)

EXCLUSION CRITERIA

1. Patients receiving any systemic treatment for psoriasis or other dermatological conditions for at least 1 month before enrollment.
2. Patients having any chronic medical illness and on concomitant systemic medications.
3. Pregnant and lactating women

The controls were patients with dermatological disorders other than psoriasis attending the skin OPD. The source population for cases and controls was the same. All the cases enrolled were of classical chronic plaque type diagnosed clinically (Picture 1- 4). An informed consent was taken from all patients and patient characteristics were recorded on a standard proforma . Statistical analysis of the data was done using statistical processing software (SPSS-17).

Relevant data included age, gender, weight, height, body mass index, waist circumference, blood pressure, smoking habit, alcohol intake, age of onset and duration of psoriasis, type and severity of psoriasis.

A thorough physical examination was carried out in all patients. After clinical assessment, necessary investigations like Fasting blood sugar, Lipid profile were done in all patients along with radiographs (as per requirement).

Severity of psoriasis was assessed according to psoriasis area and severity index (PASI) and percent body surface area (%BSA) involvement. Chronic plaque psoriasis was considered to be localized or disseminated when it covered less or more than 10% of the BSA involvement. Body mass index (BMI) was calculated as weight in kilograms/height ^{2} in meters. To determine waist circumference, we located the upper hip bone and placed the measuring tape at the level of the upper most part of the hip bone around the abdomen (ensuing the tape measure was horizontal). The tape measure was snug but did not cause compression on the skin. Blood pressure was recorded as the average of two measurements after subjects have been sitting for five minutes. Metabolic syndrome was diagnosed by the presence of three or more of the five criteria of the National Cholesterol Education Programme's Adult Panel III (ATP III): waist circumference > 102 cm in men or > 88 cm in women; hypertriglyceridaemia > 1.7 mmol/l (150mg/dl); high density lipoprotein (HDL) cholesterol < 1.0mmol/l (40mg/dl) in men or < 1.3mmol/dl (50mg/dl) in women; blood pressure > 130/85 mmHg; fasting plasma glucose of > 6.1 mmol/l (100mg/dl). Venous samples were taken at the enrolment visit after the subjects had fasted overnight (at least 8 h). Serum cholesterol

and triglycerides were measured with enzymatic procedures. Plasma glucose was measured using a glucose oxidase method.

OBSERVATIONS AND RESULTS

The study included 60 cases and 60 controls

Table 1. Age and sex distribution in cases and controls

Characteristic	Cases	Controls
M/F ratio	1.40:1	1.61:1
Age range in yrs(mean)	23-70(44.73+-11.986)	20-70(43.98+-13.633)

The youngest patient in the study was 23 years old in cases and 20 years in controls while the oldest was 70 yrs in both the groups and the total mean was 44.73 years and 43.98 years respectively.

Table 2: Age Distribution in Cases and Controls

Age Distribution	Cases	Controls
18-30	8	11
31-40	13	13
41-50	22	16
51-60	10	11
>60	7	9

Table 2 shows age distribution in cases vs control with maximum no. of cases (22) as well as controls (16) in the age group of 41-50 years.

Table 3: Descriptive characteristics of cases and controls

Characteristic	Cases	Controls
Body mass index (mean± sd)	25.4307±6.89070	24.3014±2.23163
Smoker, n(%)	24(40%)	14(23.3%)
Alcohol, n(%)	22(36.7%)	17(28.3%)
Metabolic syndrome	25(41.7%)	9(15%)

Mean of Body mass index in cases and controls was comparable while the frequency of smokers and alcohol consumers were more in cases than in controls. Total number of cases diagnosed with metabolic syndrome were higher in cases (25) than in controls (9). Prevalence of metabolic syndrome was found to be higher in cases(41.7%) than in controls (15%).

Table 4 : Descriptive features of psoriatic patients with and without MS

Characteristic	With MS n=25	Without MS n=35	χ 2 or t test
Disease Duration	**9.00±6.85**	**3.74±2.96**	**.001**
Alcohol	13	9	NS
Smoker, n(%)	14	10	NS
PASI >10	6	9	NS
BSA>10	19	12	NS
Mean PASI	8.068±2.646	7.471±5.2088	NS

Mean Disease Duration in patients with metabolic syndrome was found to be much higher than In patients without it (9.00 years vs 3.74 years) and this came out to be statistically significant. Psoriasis Area and Severity Index (PASI) was more than 10 in 6 cases with Metabolic syndrome and 9 cases without Metabolic syndrome. Mean PASI in cases with MS was 8.068 and in cases without MS was 7.471 Body Surface area involvement (BSA) was more than 10 in 19 cases with metabolic syndrome and 12 cases without Metabolic syndrome.

Fig 1: Comparing the mean duration between patients with metabolic syndrome and without metabolic syndrome.

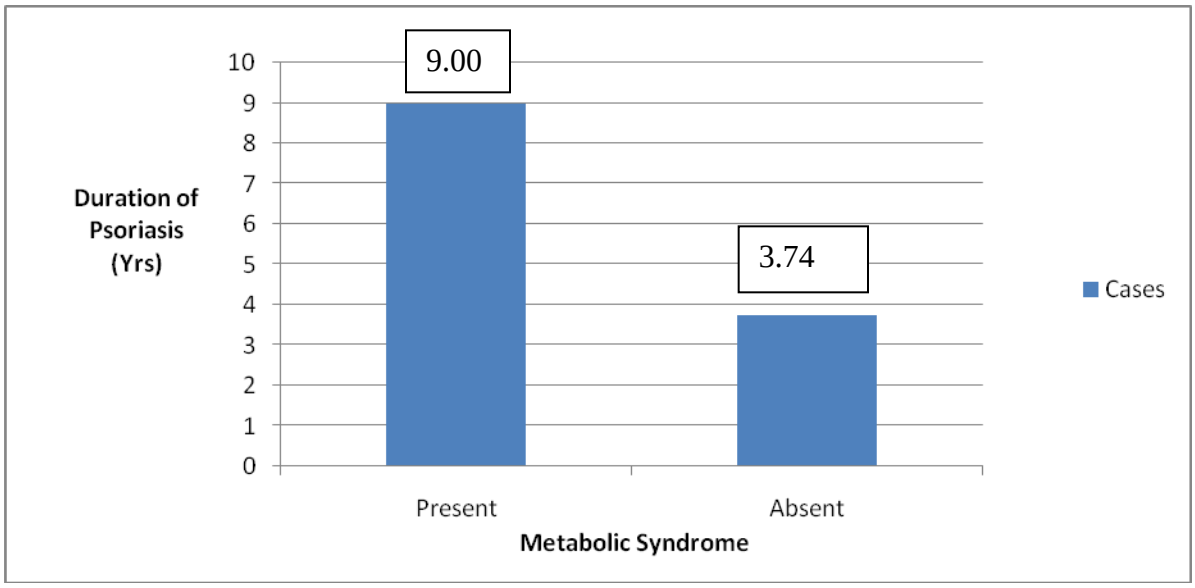
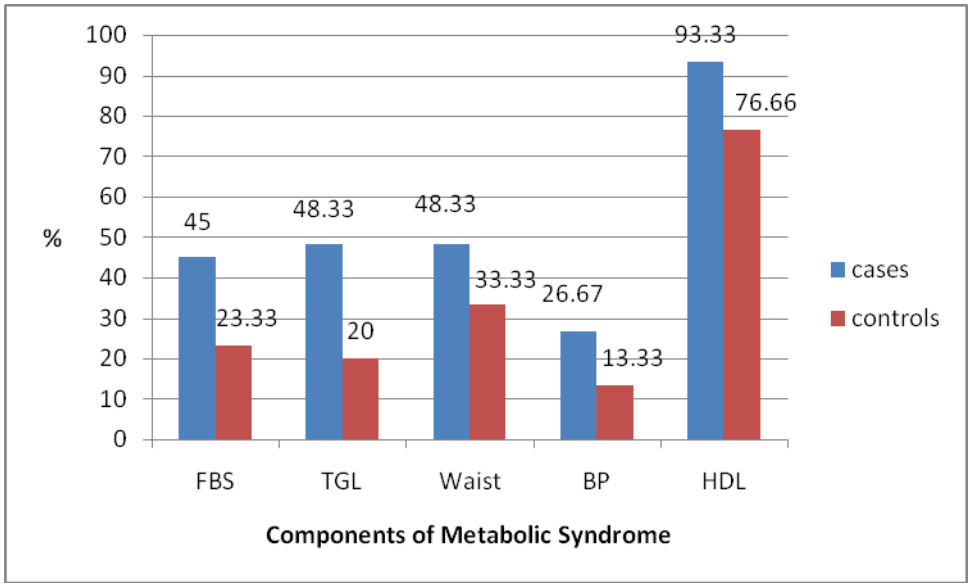


Table 5 :Distribution of clinical and laboratory findings in cases and controls

Findings	Cases n=60	Controls n=60	Odds Ratio
Triglycerides	29(48.3%)	12(20%)	2.571
HDL	54(90%)	46(76.7%)	1.750
Fasting blood sugar	27(45%)	14(23%)	1.300
Waist circumference	29(48.3%)	20(33.3%)	2.786
Blood Pressure	16(26.7%)	8(13.3%)	0.905
Metabolic syndrome	**25(41.7%)**	9(15%)	3.368

We found a higher prevalence of metabolic syndrome in cases than in controls (25/60 vs 9/60) with an Odds Ratio (OR) of 3.368. Individual components of metabolic syndrome like hyper triglyceridemia, Impaired Fasting blood sugar and hypertension were also more prevalent in cases than in controls. The prevalence of various components of metabolic syndrome in cases and controls along with odds ratio are given in Table 5

Fig 2: Depicting relative proportions of components of metabolic syndrome in cases and controls.



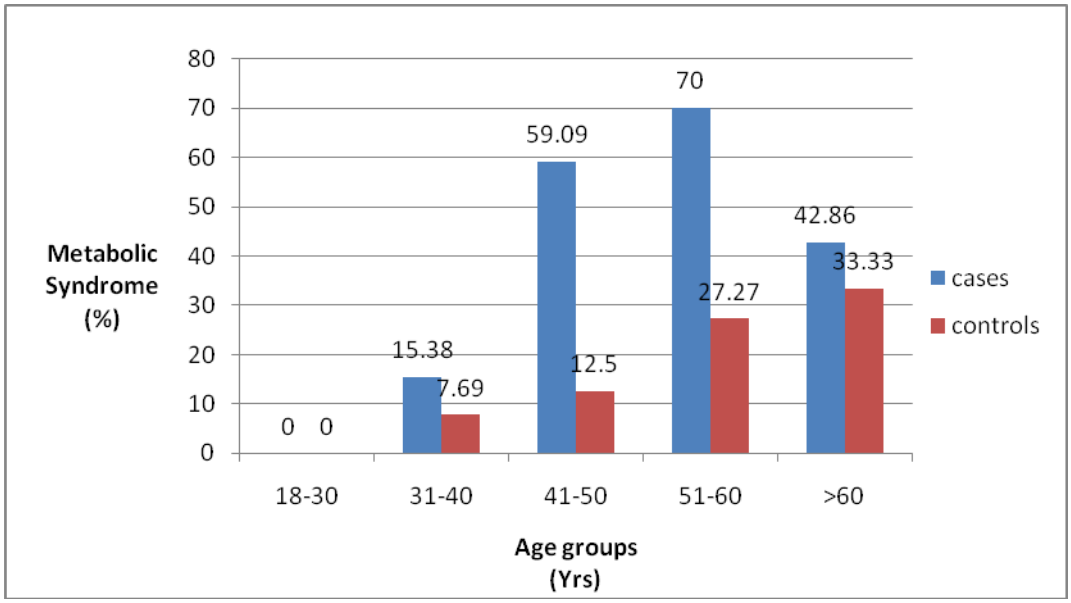
FBS= Fasting blood sugar
TGL= Triglycerides
Waist = Waist circumference
BP= Blood pressure
HDL= High density lipoproteins

Table 6: Prevalence of Metabolic Syndrome among different age groups of cases and controls

Age Distribution	MS in Cases	MS in controls
18-30	0	0
31-40	2	1
41-50	14	2
51-60	6	3
>60	3	3

Prevalence of metabolic syndrome was found to be higher in the 4^{th} and 5^{th} decades among cases.

Fig 3: Comparing age prevalence of Metabolic Syndrome among different age groups of cases and controls



Picture 1 – Classical Chronic Plaques of Psoriasis over the elbow

Picture 2 – Another erythematous, scaly , well demarcated plaque

Picture 3- Well defined plaques over the back and buttocks

Picture 4 – Psoriatic plaques involving the scalp

DISCUSSION

The hypothesis that the atherosclerotic and the psoriatic plaques are the two offshoots of same root is a focus of current research. The following few recent advances in the understanding of atherosclerosis, psoriasis and metabolic syndrome beget the consideration of exploring a common etiopathogenetic pathway for the diseases.

a. Atherosclerosis represents an ongoing low-grade systemic inflammatory state.[126]
b. Psoriasis represents a systemic inflammatory disease.[127]
c. Psoriatic patients have higher prevalence of metabolic syndrome.[89,19]
d. Psoriasis confers an independent risk for adverse cardiovascular events.[128]

Although the exact etiopathogenetic link is yet to be elucidated, certain proinflammatory cytokines and immunological mediators which are shared by the pathognetic mechanisms of the two diseases have been identified. Proinflammatory cytokines like TNF-α and IL-6, which are over expressed in psoriasis plaques, are known to contribute to features of the metabolic syndrome, such as hypertension, dyslipidaemia and insulin resistance.[107] Similar to psoriasis, the metabolic syndrome is characterized by an increase in the immunological activity of type 1 helper T cells ($T_H 1$).[129]

Many studies have been published on psoriasis vis-a-sis metabolic syndrome and the cardiovascular burden of psoriasis. (Table 7) We observed results more or less similar to those published earlier.

Diabetes Mellitus Hypertension Dyslipidemia Obesity Metabolic Syndrome

	Odds Ratio	P value	Odds Ratio	P value	Odds Ratio	P value	Odds Ratio	P value	Odds Ratio	P value
Sommer et al (21)	2.48	<0.0001	3.27	<0.0001	2.09	<0.01	2.3	<0.0001	5.29	<0.0001
Gisondi et al (89)	n.a.	n.s.	n.a.	n.s.	n.a.	<0.001	n.a.	<0.0001	1.65	0.005
Henseler and Christophers(28)	1.47	<0.005	1.9	<0.01	n.a.	n.a.	2.05	<0.05	n.a.	n.a.
Lindegard (130)	n.a.	<0.001	n.a.	<0.001	n.a.	n.a.	n.a.	0.005	n.a.	n.a.
Mallbris (131)	n.a.	n.a.	n.a.	n.a.	1.15	<0.001	n.a.	n.a.	n.a.	n.a.
Pearce et al (132)	1.03	<0.001	1.05	<0.001	1.04	<0.001	n.a.	n.a.	n.a.	n.a.
Neimann et al (19)	1.86	Sig.	1.25	Sig.	1.31	Sig.	1.84	Sig.	n.a.	n.a.
Gelfand et al (20)	n.a.	<0.001	n.a.	<0.001	n.a.	<0.001	n.a.	<0.001	n.a.	n.a.
Cohen et al (115)	1.5	<0.001	1.3	<0.01	1.2	<0.05	1.3	<0.05	n.a.	n.a.
Cohen et al (103)	1.2		1.3		n.a.	n.a.	1.7		1.3	

Table 7 :- Metabolic Syndrome and its Components

n.s. – not significant; n.a – not applicable; sig. – significant

Higher prevalence of metabolic syndrome in psoriatic patients, which can favour cardiovascular events, has been shown by P. Gisondi et al. [89] Our study also observed a higher prevalence of metabolic syndrome among psoriatic patients than the controls [41.7% *vs* 15%, odds ratio (OR) 3.368]

That cardiovascular risk factors , which are key components of the metabolic syndrome , are more strongly associated with severe psoriasis than mild psoriasis has been documented in the literature. [19] However our study showed no such correlation as PASI >10 in 6 patients with metabolic syndrome and 9 in without metabolic syndrome. Mean PASI in cases was 8.068 and in controls it came out to be 7.471.

The youngest patient in the study was 23 years old in cases and 20 years in controls while the oldest was 70 yrs in both the groups and the total mean was 44.73 years and 43.98 years respectively. (Table 1)

Mean of Body mass index in cases and controls did not show significant differences probably due to small sample size while the frequency of smokers and alcohol consumers were more in cases than in controls.(40% vs 23.3 %) and (36.7% vs 28.3%) respectively. (Table 3) Smoking, in particular, has been correlated with psoriasis in numerous studies , and was even associated with the clinical severity in a study evaluating 818 adult hospitalized psoriasis patients.[122]

Niemann et al used the General Practice Research Database and found higher rates of diabetes mellitus, hypertension, hyperlipidaemia, obesity and smoking in patients with

psoriasis than in controls. The same authors also found that patients with severe psoriasis had higher rates of obesity and diabetes mellitus than those with mild psoriasis.[19] We also observed the higher prevalence of individual components of metabolic syndrome like Triglycerides levels > 150 mg/dl (29/60 vs 12/60; OR:2.571), Fasting blood sugar > 100 mg/dl (27/60 vs 14/60; OR:1.300) and Blood pressure > 135/85 mmhg (16/60 vs 8/60; OR:0.905), HDL Cholesterol < 40 mg/dl (Males) or > 50 mg/dl (Females) (54/60 vs 46/60; OR:1.750), Central obesity >90cm (Males) or >80cm (Females) (29/60 vs 20/60; OR:2.786) in patients of psoriasis than controls. (Table 5 and Fig 2)

These findings once again support the scientific notion that psoriatic patients should be evaluated and appropriately treated for these metabolic derangements so that practicing physician is saved from missing the forest for the tree. While analyzing the prevalence of metabolic syndrome in different age groups, the fact that metabolic syndrome becomes more prevalent among psoriatic patients in higher decades of their life reveals itself.

We had maximum no. of cases (22) as well as controls (16) in the age group of 41-50 years. Minimum no. of cases were 7 and controls 9 in the age group of more than 60 years. (Table 2)

Age wise distribution of metabolic syndrome in cases was higher than controls after the age of 30 in P. Gisondi's Study.[89] Our study also showed similar results, and the prevalence was more higher in cases than in controls especially in the 4^{th} and 5^{th} decades. (Table 6 and Fig 3)

We also observed longer mean disease duration in psoriatic patients with metabolic syndrome than those without metabolic syndrome (9.00 ± 6.85 vs 3.74±2.96 yrs) with P-value=0.001.(Table 4 and Fig 1)

SUMMARY

1. This case control study was conducted from December 2009 to March 2011 with total number of 60 patients in each group
2. Age distribution was maximum in the age group of 41-50 in both cases and controls while Male:Female ratio was 1.40:1 in cases and 1.61:1 in controls
3. All the cases were of chronic plaque type of Psoriasis.
4. Mean PASI score in cases was 8.068 while in controls it was 7.471.
5. Prevalence of metabolic syndrome was found to be higher in cases than in controls (41.7% vs 15%)
6. Individual components of metabolic syndrome i.e. triglycerides(48.3% vs 20%), fasting blood sugar (45% vs 23%) were also more prevalent in cases than in controls.
7. Risk factors for metabolic syndrome as well were higher in frequency in cases than the control group, Smoking (40% vs 23.3%) and Alcohol (36.7% vs 28.3%)
8. Cases with metabolic syndrome had longer mean duration of psoriasis than in controls (9.00 years vs 3.74 years) and this came out to be statistically significant
9. We did not find any association of metabolic syndrome with the severity of psoriasis
10. We could not correlate the association of metabolic syndrome with the type of psoriasis as all the cases enrolled in the study were of chronic plaque type.

CONCLUSION

In this study we found that there is higher prevalence of metabolic syndrome in psoriatic patients and though many studies have shown it is associated with the severity of psoriasis, we found longer mean duration of psoriasis in patients with metabolic syndrome

It is possible that depression, eating habits, psychosocial inactivity, stress and inflammatory mediators associated with psoriasis favor metabolic syndrome. Such an association also suggests that psoriatic patients without metabolic syndrome need to be counseled properly so that behavioral modification in association with appropriate management of their psoriasis may make the emergence of cardiovascular risk factors less likely.

Due to a small sample size we could not get statistically significant findings Future studies are needed to better understand the nature of this relationship and the implications this could have for management and treatment of patients with psoriasis .

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PROFORMA

Name: Age:

Name of Father/Husband: Sex:

Name of Mother/Wife: Occupation:

Address: Hospital no.:

Ph:

Presenting Complaints:

Duration:

History of presenting illness:

Age of onset:

Onset - Insidious/Sudden

Progression - Rapid/insidious/stationary

Initial Site -

Exacerbating Factors - Infection/Trauma

Dietary Factors -

Environmental Factors-

Occupation factors -

Joint changes -

Any other associated diseases-

Past History:

History of similar lesions in the past- Present/Absent

History of Diabetes:
Hypertension:

Family history:

History of Diabetes Mellitus:
Hypertension:
Psoriasis:

Personal history:

Smoking Alcohol

Treatment History:

Corticosteroids:

Hypoglycemics:

Antihypertensives:

General Examination

Built:

Nourishment:

Clubbing:

Oedema:

Lymph nodes:

Pallor:

Icterus:

Cyanosis:

Pulse Rate:

Blood Pressure: At first :
After 5 min :
Avg of the two:

Measurements:-

Waist Circumference:

Weight:

Height:

BMI(kg/cm2):

Local Examination

Site:

Shape:

Type of lesion: Macule/Papule/Pustule/Plaque

Border: Well defined/ill defined

Surface:

Scaling: Present/Absent

Type of Scaling: Colour
Loosely Adherent/Tightly Adherent

Surrounding Skin:

Koebner's Phenomenon:

Nail Changes:

Pitting

Onycholysis:

Subungual Hyperkeratosis

Transverse Groove

Thickening

Destruction

Splinter Hemorrhage

Mucous membrane:

Joint Changes:

Psoriatic Arthritis

Assymetric oligoarthritis: Polyarthritis:

Distal Phalangeal Joint only: Spondylitis:

Arthritis mutilans:

Eyes:

Type of psoriasis: Plaques with scalp lesions/Plaques only/Scalp only/
Sebopsoriasis/Palmoplantar/Guttate/Erythrodermic

Signs of Hyperlipidemia: Xanthoma/Xanthelasma/Acrus Senilis

Associated skin lesions:

PASI

Head(h)- Erythema Upper limb(u)-Erythema

Induration -Induration

Desquamation Desquamation

Trunk(t)- Erythema Lower Limb(l)-Erythema

Induration Induration

Desquamation Desquamation

0=nil, 1=mild, 2=moderate, 3=severe, 4=very severe

Area Wise Percentage involvement of the involved sites

Head(Ah)	Upper limb(Au)
Trunk(At)	Lower limb(Al)

1 = <10% area; 2 = 10-29%; 3 = 30-49%; 4 = 50-69%; 5 = 70-89%; 6= >90%

PASI = 0.1 (Eh + Ih + Dh) Ah + 0.2 (Eu + Iu + Du) Au + 0.3 (Et + It+ Dt) At + 0.4 (El + Il + Dl) Al

=

Systemic Examination

CVS:

RS:

ABD:

CNS:

Investigations

Blood: Hb: ESR:

TC: FBS:

DC:

LFT

Serum total bilirubin:	Total protein:
Direct bilirubin:	Gamma GT:
SGOT:	Albumin:
SGPT:	Globulin:
Alkaline Phosphatase	A/G ratio

Urine: Albumin:

Sugar:

Microscopy:

Lipid Profile

Cholesterol: HDL:

Triglycerides: LDL:

ECG X-RAY

Metabolic Syndrome will be diagnosed based on the National Cholesterol Education Program's Adult Treatment Panel III (NCEP ATP III).

-Elevated waist circumference	
Men	Equal to or greater than 40 inches(102cm)
Women	Equal to or greater than 35 inches(88cm)
-Elevated Triglycerides	Equal to or greater than 150mg/dl
-Reduced HDL Cholesterol	
Men	Less than 40mg/dl
Women	Less than 50 mg/dl
-Elevated blood pressure	Equal to or greater than 130/85 mm Hg
-Elevated fasting glucose	Equal to or greater than 110 mg/dl or use of medication for hyperglycemia

Does the patient has metabolic syndrome?

YES NO