

# Psoriasis and Cardiovascular Risk Profile: A Comprehensive Review.

## Abstract:

Psoriasis is an inflammatory immune-mediated, chronic skin disease with many co-morbidities involving complex pathogenic interactions between the innate and adaptive immune systems. In people living with psoriasis, there is an increased probability of having other health conditions such as cardiovascular illnesses. A growing number of studies show that classic risk factors which lead to cardiovascular diseases and metabolic syndromes are common in psoriasis patients, leading to a more significant cardiovascular burden. The present article aims to synthesize what is known in the literature concerning the epidemiological and clinical data relating to cardiovascular risk factors and psoriasis. The many pathophysiological mechanisms which justify this association for stratification of the risk profile in psoriatic patients are also reviewed, along with the implementation of different cardiovascular prevention strategies. The benefits and drawbacks of the numerous therapies frequently used to prevent cardiovascular diseases and analyze specific psoriasis medications that impact risk factors of cardiovascular illnesses or the significant arterial events in psoriasis patients. The detailed assessment of the various cardiovascular risk profiles in psoriasis patients has been discussed profoundly. Also, the several mechanisms involving the inflammatory cytokines released from the cells during inflammation, especially in dyslipidemia, atherogenic process resulting in plaque formation, hypertension, diabetes, obesity, and even the efficacy of statins, have been reviewed from the sources of different articles published in different parts of the world.

**Keywords:** Psoriasis; immune-mediated; chronic skin disease; cerebral vascular events; cardiovascular diseases; cardiovascular risk ; inflammation; hypertension

## Introduction :

Psoriasis is an inflammatory immune-mediated and chronic skin disease with several co-morbidities that includes the complex interactivities between both types of immune systems, which are innate and adaptive immune systems of the body and affect about 2% of the population(1).

Psoriasis is a multisystemic inflammatory disease frequently associated with various co-morbidities, particularly severe events such as cerebrovascular diseases, namely stroke and cardiovascular diseases(2,3). Evidence-based studies that have been published in various parts of the world have shown that the frequency of risk factors involved in the development of cardiovascular events in the physical body, namely, smoking, hypertension, obesity, physical inactivity, hyperlipidemia, diabetes mellitus, and subclinical atherosclerosis are elevated in psoriasis patients (3,4). The pivotal role of inflammation in the body, and metabolic diseases, has been shown to produce an increased risk of cardiac illnesses by their collaborative action in

these patients(5). Also, several, epidemiologic studies such as McDonald and et al. showed that the hazards linked with all vascular events were 2.2 fold increased in the hospitalized psoriasis patients when comparison was made with the controls with other dermatological conditions (6).

The present review synthesizes the literature about epidemiological and clinical-based corroboration, which connects the various factors causing cardiovascular events and diseases to psoriasis. Also, the application of different cardiovascular prevention strategies such as aspirin, antihypertensive therapy, lipid-lowering drugs, and hypoglycaemic agents is discussed to evaluate specific psoriasis medications' response to severe cardiovascular risk factors and diseases.

A detailed assessment of cardiovascular risk profiles in psoriasis patients :

- **Hypertension**

Many studies have concluded significant associations between the prevalence of hypertension and psoriasis disease(7,8,9,10). Hypertension was found to be more common in those with mild psoriasis, with an odds ratio of 1.30 and, similarly, a ratio of 1.49 for severe psoriasis, according to a meta-analysis(11). Hypertensive patients have been shown to have elevated chances of developing psoriasis in a health study involving 77,728 nurses of hospitals (12). A recently conducted case-control study suggested that those patients who have both psoriasis and hypertension were five-fold more on monotherapy anti-hypertensive regimen, 9.5 times increased chance of being on dual hypertensives and 16.5 times on triple antihypertensive treatment than patients within psoriasis (8).

- **Diabetes mellitus**

Various studies have shown that the frequency of diabetics is more significant in people living with psoriasis (7,8,9,10). In 108,132 patients who have psoriasis, the menace ratios for the incidence of diabetes mellitus type 2 were 1.11 in mild psoriasis and 1.46 in the severe psoriasis group(13). Another recently published article, including studies of eight cohorts, has reported a relative risk of 1.50 for incidence of diabetes in psoriasis patients(14). Several factors such as increased obesity, decreased physical activity; unhealthy lifestyles are linked to insulin resistance associated with inflammatory mechanisms. Many genetic pathways, including the incretin effect and genes such as CDKAL1, PTPN 22, ST6GAL1, JAZF1, are also related to diabetic patients (type 2 )and psoriasis (15,16).

- **Dyslipidemia**

According to many studies, a higher frequency of dyslipidemia was suggested in psoriasis patients (7,8). Increased probability of cholesterol levels linked with patients of psoriasis(1). Psoriasis is associated with atherosclerosis, and other lipid abnormalities were discovered five years before the onset of psoriasis [17]. Also, a recently published article showed that the average oxidized LDL concentration in patients with psoriasis was discovered to be greater than those of study controls [18].

Atherosclerosis is initiated by accumulating small LDL particles in tunica intima and by oxidation, product oxidized LDL (oxLDL), which transforms into foam cells upon entering macrophages, leading to atherosclerotic plaques formation. (19)The vascular wall cells are injured by all the products of oxidized LDL. After that, the inflammatory cytokines and mediators promote low-grade inflammatory processes leading to further disease progression

(19). HDL acts as a chemical shuttle for cholesterol transfer from peripheral tissues to the liver and suppresses various atherogenic mechanisms(19). In some studies, psoriasis patients were found to have significantly higher mean ox LDL. Mehta et al. also enlightened the fact that the effluent capacity of high-density lipoproteins, which is mainly involved in the inhibition of atherogenic mechanisms by altering the cholesterol transport and monocytic infiltration, was significantly diminished beyond the factors which help in the increased chances of developing cardiovascular diseases in psoriasis patients(20). The formation of atherosclerosis, including a higher hazard of cardiovascular illnesses, is closely linked with the levels of apolipoprotein B, the main apoprotein component of LDL cholesterol. Lipoprotein (a) is another form of LDL which has apolipoprotein B bridged by a disulfide bond to apolipoprotein-a and has both roles in atherogenicity and thrombus formation. Lipoprotein a is also very much susceptible to lipid peroxidation. A recently released meta-analysis has conveyed the theory that apolipoprotein B and lipoprotein levels were discovered to be more common in psoriasis patients when compared to the controls of the study(21).

- **Obesity**

Several studies have published that psoriasis is coupled with the increased prevalence of obesity, particularly central obesity(7,18,19). An Argentinian prototype study (1286 psoriasis patients and 2547 controls) has obtained that the frequency of overweight ( $p < 0.01$  and 43% vs. 40%) and obesity ( $p < 0.01$ , 30% vs. 24%) were significantly more in those who has psoriasis in comparison with the controls [22]. A study conducted in Denmark found that many adolescents with mild psoriasis were facing obesity (8.6% vs. 1.7%,  $p = 0.008$ ). The body measurements of abdominal obesity were also higher than the study controls (23).

- **Metabolic syndrome**

Metabolic syndrome consists of hyperglycemia, central obesity, hypertension, and dyslipidemia. It has been elicited that Metabolic abnormalities are linked with a twofold increment in having the consequences of cardiovascular events or diseases and a 1.5 times increment in death [24]. A recently published meta-analysis article that included 63 studies encompassing 15,939 patients with psoriasis and 103,984 study controls have observed that 30.3% of psoriasis patients were obtained with Metabolic syndrome compared with 21.7% subjects in the control group. Meta-synthesis has revealed the linkage between so metabolic and metabolic, ic syndrome, elevated in South America [26]. Thus, we conclude that the Interleukin -23 and Th17 cells can be associated with cutaneous and metabolic features in psoriasis patients [27].

- **Addictions of cigarette smoking and alcohol use**

Addictive habits, such as smoking cigarettes, bidis, and alcohol consumption, are already well-known risk factors that play a role in the increased incidence of cardiovascular diseases. Various studies enlightened the incremental frequency of alcohol use and cigarette smoking habits in people with psoriasis (28,29,30). A published meta-synthesis showed the notability and substantial linkage between cigarette smoking and the graveness of psoriasis illness. The role of nicotine in the production of elevated levels of cytokine secretions, namely, IL -12,2 (interleukin), in the pathogenesis of psoriasis has been found. Cigarette smoking produces free radical ions and interferes with MAPK pathways (mitogen-activated protein kinase), JAK-STAT pathways, and NF-kB(nuclear kappa B) pathways relevant to psoriasis. A crucial role played by nicotine in the origin of psoriasis by elevating the secretion of cytokines, namely, tumor necrosis factor (TNF), IL-12, and G-CSF (31). This facilitates keratinocytes' adhesive

quality and migration in the skin and interferes with immune cell signaling, causing an immunomodulatory effect(32).

- **Physical activity**

A meta-analysis that included a combined data of 13 studies with 149,499 participants reported that not much difference was obtained in the exercise done by the psoriasis patients and those without psoriasis when the total effect was analyzed thoroughly(33). However, another meta-analysis showed that people living with psoriasis did vigorous exercise significantly less when compared to the study groups with a relative risk of 0.76 and p less than 0.00001. Lower intensity exercises were more linked to psoriasis patients with more psoriatic lesions and self-awareness. A study conducted in America in which the connection of physical activity and psoriasis was evaluated also showed that less hazard of psoriasis was independently associated with vigorous physical exercise(34). Physical activity can affect the risk of psoriasis through the role of systemic inflammatory mediators.

- **Cardiovascular prevention strategies**

**Statins** are the keystone in the management of cardiovascular risk. According to a recently published study, the appropriate candidates for statin therapy were analyzed by assessing two strategies of cardiovascular prevention in psoriasis patients(35). A study encompassing atorvastatin with diabetes patients and secondary cardiovascular prevention statin trials was included in a post hoc analysis(36). It reported that total cholesterol, LDL cholesterol, similar apolipoprotein B were reduced in patients who had psoriasis and those not having psoriasis when given statins therapy. Many societies involved in atherosclerosis and Rheumatism in Europe and ESC also recommended using a multiplying factor such as 1.5 for adjusting the calculated risk and following the statin therapy of the mass population, while the other think of psoriasis as a chronic disease that increases the elevated chance of developing cardiovascular diseases, thus favoring the statins use in people who have intermediate risk (37,38). The results show that only some should be given a statin regimen. High-intensity statins decrease LDL cholesterol levels by more than 50%. A comprehensive randomized clinical study showed that severe psoriasis disease might have improvement by statin therapy (39).

**Aspirin**

NSAIDs are linked with increased exacerbations in psoriasis patients, but another study has provided that there may be no link between the probability of having psoriasis or patients with joint problems manifesting as arthritis and the use of aspirin (40).

- **Antihypertensive therapy**

Beta-blockers are associated with exacerbations of psoriasis. (41,42,43). Beta-adrenergic receptors in the skin are inhibited by beta-blockers, leading to less intracellular levels of CAMP(cyclic adenosine monophosphate), which has a crucial role in differentiating and preventing cell proliferation. In T cells, the phosphorylation mechanisms are elevated by them, and it causes cellular hyperproliferation and psoriasiform change by surplus release of enzymes from neutrophils and macrophages and lymphocytes as well(44,45). Also, the increased hazard of having unchecked blood pressure was associated with severe psoriasis (46).

- **Hypoglycaemic agents**

Various evidence suggested that biguanides such as metformin therapy lower the chances of having psoriasis in diabetics(47,48). Several hypoglycaemic drugs are used in the therapy of diabetes mellitus (type2 mainly), such as glucagon-like peptide -1 receptor agonists, dipeptidyl peptidases-4 inhibitors, thiazolidinediones, and biguanides, has beneficial effects on psoriasis(49). The most frequently used anti-diabetic drug is Metformin which has been reported to lower the probability of psoriasis in diabetics(47,48). Also, a randomized controlled trial elicited the

patients of psoriasis with Metformin therapy having improved health compared with the placebo drugs (50).

### **Imaging Techniques for Assessment:**

For assessing subclinical atherosclerosis and early atherosclerosis, indicators such as pulse wave velocity, carotid mid-intimal thickness, endothelial function, and coronary calcium score given by computed tomography are used in psoriasis patients, particularly autoimmune illnesses generally (51,52,53,54,55). Carotid atherosclerotic plaques have been found in psoriasis patients and psoriasis patients with arthritis frequently(56,57). A frequent observation in severe psoriasis patients has shown a coronary calcium score of >400 even upon adjusting the risk estimates given by the Framingham score(58). A recent meta-study elicited that the people living with psoriasis had a higher probability of Coro calcium score being more significant than 0 and greater than 100 compared with the study controls(59).

Approximation of the risk of developing increased cardiovascular diseases using a traditional scoring system has many, while these predictions instruments were not explicitly developed in psoriasis patients. However, the performance of these scores is suboptimal as the traditional cardiovascular risk factors do not fully explain the increased cardiovascular risk in patients with psoriasis, and current risk functions do not represent other contributing factors. Cardiovascular risk is often underestimated due to the above factors(19). Another meta-analysis has shown that the Framingham scoring system has certain disadvantages when correctly stratifying psoriasis patients(60). Following a carotid ultrasonography examination, most patients in the intermediate-risk group and nearly half of those in the low-risk group were reclassified in a higher-risk group. The underestimation of risk was showing increments in people who had psoriatic arthritis. A released article that has assessed the scores of risk factors gave a classification of the majority of psoriasis patients as “low risk” [61].

According to a study by Gisondi et al. also, the score of risk factors given by Framingham was very much increased in psoriasis patients than in comparison with the study controls at five years (mean  $\pm$  SD  $5.3 \pm 4.4$  vs.  $3.4 \pm 3.3$ ,  $p < 0.001$ ) and at ten years ( $11.2 \pm 8.1$  vs.  $7.3 \pm 6.3$ ,  $p < 0.001$ ) [62]. Also, a study proved that reclassification should be done after adding psoriasis as a factor in the scoring system. The intermediate and high-risk psoriasis should be given for the substantial percentage of patients having intermediate low cardiovascular risk as given by the Framingham score (63). Few studies on various treatment modalities for psoriasis were reported(64-67).

### **Conclusions :**

Several studies have shown that psoriasis is a multisystemic inflammatory autoimmune disease that impacts not only skin and joints but also may be linked with cardiovascular co-morbidities .Higher frequency of risk factors which contributes notably in developing cardiovascular events or diseases such as hypertension, diabetes ,smoking ,obesity, dyslipidemia ,obesity ,metabolic syndrome has been shown to be associated with psoriasis patients.The use of different cardiovascular prevention strategies and pharmacotherapy are being studied for better application of knowledge on psoriasis.Several article published in different parts of the world have shown that psoriasis is a multisystemic autoimmune disease with inflammation mechanisms which has its impacts on not only on bones, skin but also may be linked with cardiovascular co-morbidities .Higher frequency of risk factors which contributes notably in developing cardiovascular events or diseases such as hypertension, diabetes ,smoking ,obesity, dyslipidemia ,obesity ,metabolic syndrome has been shown to be

associated with psoriasis patients. The use of different cardiovascular prevention strategies and pharmacotherapy are being studied for better application of knowledge on psoriasis. A growing number of studies show that classic risk factors which leads to cardiovascular diseases and metabolic syndromes are common in psoriasis patients, leading to greater cardiovascular burden. The present article aims to synthesize what is known in the literature concerning the epidemiological and clinical data relating cardiovascular risk factors and psoriasis. The many pathophysiological mechanisms which justify this associations for stratification of the risk profile in psoriatic patients are also reviewed along with the implementation of different cardiovascular prevention strategies. The benefits and drawbacks of the numerous therapies which is frequent used in the prevention of cardiovascular diseases and analysis of specific psoriasis medications which have impact on risk factors of cardiovascular illnesses or the significant arterial events in the psoriasis patients. The detailed assessment of the various cardiovascular risk profiles in those patients who are suffering from psoriasis has been discussed profoundly. Also the several mechanisms involving the inflammatory cytokines released from the cells during inflammation specially in the dyslipidemia, atherogenic process resulting in plaque formation, hypertension, diabetes, obesity and even the efficacy of statins has been reviewed from the sources of different articles published in different parts of the world.

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