



## RESEARCH ARTICLE

### FREQUENCIES OF PSORIASIS AND ITS COMPLICATIONS AMONG TYPE - II DIABETES CASES: A META-ANALYSIS OF SHORT CRITICAL CORRELATIONAL REVIEWS FROM 2010 THROUGH 2016

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#### ABSTRACT

**Background:** Psoriasis affects approximately 120–180 million people worldwide. Over recent years, a series of findings have shown an increased frequency of Metabolic Syndrome and its components amongst subjects with Psoriasis, the reported prevalence of Psoriasis across countries ranges between 0.09% and 11.4%, making Psoriasis a serious global problem. Although the degree of complications may differ across different strata, some problems related to safety of therapies and costs are relevant to all. The increasing volume of studies on psoriasis indicates that it has been considered a challenging disease from several points of view such as the patient, health care providers and health insurance companies. However, the burgeoning reports regarding the magnitude and its complications remain to be systematically summarized and documented. It is this limited meta-analysis and critical review made on the burden of psoriasis and its complications among the current particular study population (type II diabetes mellitus cases that provide the rationale of this review. **Objective:** The main aims of this review was assessing the magnitude and present the discrepancies of psoriasis and its complications among Type 2 Diabetes Mellitus through reviewing of the global literature made available in academic search engines from 2010 to 2016. **Methods:** Available Published Electronic articles and full-length researches were accessed in different journals searching widely in Pubmed, Biomed, Google scholar, Grey literature, Pop line, Hinari and others. All accessed literatures which have relevance to prevalence and complications of psoriasis among type 2 diabetes mellitus from 2010 to 2016 were included for the review process. **Result:** The prevalence of Psoriasis across countries varies between 0.09% and 11.4. An increase in the income of the country (modern life), obesity, tobacco addiction, physical inactivity, depression, poor food habits and psychological stress are components factors amongst subjects with Psoriasis that increases risk of diabetes mellitus. **Conclusion:** Psoriasis is one amongst these notorious auto-immune disorder having deep psychological and social impacts. Psoriasis is a non- contagious skin disease affecting both sexes equally and confers a higher risk (up to 2.48) of Diabetes. Disease outcome in T2DM patients with comorbid Psoriasis was clearly worse.

**Key words:** Psoriasis, Type - II diabetes, Auto immune disorder, Co, Morbidity, Non – Continuous, Skin Disease

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#### INTRODUCTION

The desire to have beautiful and healthy looking skin has been a centuries-old quest for humans. Skin with brighter complexion and smoother surface tends to be perceived as being healthier and more attractive. Beyond its obvious roles of keeping our insides in and the outside out, skin has many less conspicuous duties: its sweat glands help regulate temperature; its nerves provide the sense of touch; its deeper cells produce vitamin D; and its appearance advertises our age and health. For those who can read skin's language, a close examination reveals clues about the whole body's health.

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For instance, changes in the skin color may indicate homeostatic imbalances in the body (Ng, 2015). Skin disease is one of the most common human illnesses which pervades all cultures, occurs at all ages, and affects between 30% and 70% of individuals. Its detrimental effects on health range from physical incapacity to death. The International Classification of human disease lists more than 1,000 skin or skin-related illnesses, a pattern dominated by a few conditions accounting for most of the skin disease burden. Skin remains the 18<sup>th</sup> leading cause of health burden worldwide (Hay, 2010). Patients of skin disease tend to experience physical, emotional and socio-economic embarrassment in the society. Psoriasis is one amongst these notorious auto-immune disorders that have deep psychological and social impacts. Pathologically, Psoriasis is a non- contagious skin disease affecting both sexes equally, and can occur at any age, although it most commonly appears for

the first time between the ages of 15 and 25 years. Psoriasis is characterized by accelerated self-renewal of cells due to their excessive growth and reproduction<sup>1</sup> which leave them to live 4-10 days. As a result, migration outside has no time to differentiate and they are not quite functional. Many Psoriatic tolerate constant pain from cracking and bleeding lesions, and bear the humiliation and discomfort of continually flaking skin. Itching and pain can interfere with basic functions, such as self-care and sleep<sup>2</sup>. It is a genetic multifactorial disease of the skin, which affects approximately 2% of the population. The cause of the disease remains unknown. It has been suggested that it is probably caused by some kind of autoimmune mechanism, though the triggering antigen has yet to be identified (Al-Shobaili, 2013). Over recent years, a series of publications has appeared showing an increased frequency of Metabolic Syndrome and its components amongst subjects with Psoriasis, leading in turn to an increased risk of cardiovascular disease and death. Amongst these patients, a higher level of prevalence of a series of factors has also been described, which could account for the more extensive presence of Metabolic Syndrome and heightened cardiovascular risk. Such factors include tobacco addiction, obesity, physical inactivity, depression, poor food habits and psychological stress (Reich, 2008). Psoriasis is a complex autoimmune inflammatory disease that occurs in genetically susceptible individuals and presents with the development of inflammatory plaques on the skin. Although early concepts of the pathogenesis of Psoriasis focuses primarily on keratinocyte hyper-proliferation, dysregulation of the immune system is now recognized as a critical event in this disease. Its etiology remains unclear, although there is evidence for genetic predisposition. Although there is a suggestion that Psoriasis could be an autoimmune disease, no autoantigen that could be responsible has been defined yet. Psoriasis can also be provoked by external and internal triggers, including mild trauma, sunburn, infections, systemic drugs and stress (Chandran, 2010).

Psoriasis involves the skin and nails, and is associated with a number of comorbidities. Skin lesions are localized or generalized, mostly symmetrical, sharply demarcated, red papules and plaques, and usually covered with white or silvery scales. Lesions cause itching, stinging and pain. Between 1.3% and 34.7% of individuals with Psoriasis develop chronic, inflammatory arthritis (PsA) that leads to joint deformations and disability. Between 4.2% and 69% of all patients suffering from Psoriasis develop nail changes. Individuals with Psoriasis are reported to be at increased risk of developing other serious clinical conditions such as cardiovascular and other non-communicable diseases (International Diabetes Federation, 2014). Psoriasis causes great physical, emotional and social burden. Quality of life (QoL), in general, is often significantly impaired. Disfiguration, disability and marked loss of productivity are common challenges for people with Psoriasis. There is also a significant cost to mental well-being, such as higher rates of depression, leading to negative impact for individuals and society. Social exclusion, discrimination and stigma are psychologically devastating for individuals suffering

from Psoriasis and their families. It is not Psoriasis causing the exclusion – it is largely society's reaction to it and this can change (International Diabetes Federation, 2014).

### Statement of the Problem

Worldwide Psoriasis is affecting, as presumed, approximately 120–180 million people. The population prevalence of Psoriasis has been reported to range from 2% to 3%. Around 150,000 new cases of Psoriasis are reported annually. Studies in developed countries have reported higher prevalence rates of on average about 4.6%. Information on the prevalence of Psoriasis in Ethiopia is extremely limited (Gimbel, 2013). This indicates that (1) Psoriasis is a worldwide problem; and (2) understanding its prevalence and impact in Ethiopia is of utmost importance. Over and above Psoriasis being an irritating skin condition, it can also corroborate other metabolism related problems. Specifically, chronic inflammation in Psoriasis leads to increased insulin-like growth factor-II (IGF-II) in the skin and blood of Psoriasis patients. IGF-II promotes epidermal proliferation and is also implicated in promoting atherosclerosis, in modulating body fat mass and lipid metabolism in mice, and is linked to diabetes and hyperlipidemia in animal and human models (Rapp, 1999). Psoriasis has been considered a challenging disease from several points of view such as the patient, health care providers and health insurance companies. Although issues may differ between these groups, some problems related to safety of therapies and costs are relevant to all. Psoriasis can have a major impact on the patient's health related quality of life (HRQOL) causing higher levels of anxiety, depression, worry and even suicidal thoughts. The reduced physical and mental functioning associated with Psoriasis is even comparable to that observed in patients with Cancer, Arthritis, Heart disease, Diabetes and Depression. However, the impact on the HRQOL is not directly related with the severity of the skin symptoms: patients with mild disease from a clinical perspective may report substantial HRQOL impairment. Interestingly, Psoriasis related HRQOL impairment does not change significantly in time suggesting that its impact is stable and that it remains a difficult disease to cope with (Augustin, 2010). Anti-Psoriatic treatments may provide temporary relief, but a survey among Psoriasis patients found that none of the prior mentioned traditional systemic therapies were highly satisfactory. Clinical trials suggest that the degree of clinical response to a therapy has a linear relationship to the patients' HRQOL improvement. It is suggested that in order to have a substantial impact on HRQOL the improvement in skin clearance needs to be substantial (i.e.  $\geq$ PASI 75) and the strongest HRQOL improvements were measured in those subjects with a PASI response of 90% or more. Ideally, the ultimate treatment goal in patients with Psoriasis would be complete clearance, but achieving a positive risk: benefit ratio from a physician's and patient's perspective is more realistic (Schäfer, 2011).

### Justification of the study

Over recent years, a series of findings have appeared showing an increased frequency of Metabolic Syndrome and its components amongst subjects with Psoriasis, The reported prevalence of Psoriasis in countries ranges between 0.09% and 11.4%, making Psoriasis a serious global problem. Information on the prevalence of Psoriasis in Ethiopia is extremely limited so the significance of our review is:-

<sup>1</sup>In the course of providing their protective function, skin cells get damaged so that they must be replaced. Therefore, our body produces new skin cells deep in the dermal matrix. These cells migrate upward towards the surface as they mature. Some mature skin cells undergo a process called keratinization. It eventually leads to cell death leaving a layer of drier, harder organic material (cell bodies). In a normal healthy adult, the normal skin turnover occurs once in every 30-40 days (5, 6).

<sup>2</sup>Approximately 60% of Psoriasis patients missed an average of 26 days of work a year due to their illness.

As Psoriasis have a major impact on the patient's health related quality of life (HRQOL) causing higher levels of anxiety, depression, worry and even suicidal thoughts. Psoriasis has a complex relationship with metabolic diseases such as obesity. Studies have shown that, compared with the general population, patients with psoriasis are more frequently overweight ( $25 \leq \text{BMI} < 30$ ) or obese ( $\text{BMI} > 30$ ). T2DM patients with comorbid Psoriasis were significantly higher compared to Type 2 Diabetes patients without Psoriasis. Insulin therapy was significantly more frequent in patients with Psoriasis. To create awareness amongst clinicians and the public at large, as Psoriasis is increasing in magnitude with co-morbidities of Diabetes mellitus disease in an alarming rate nationally and globally, as a result, the clinician will design better treatment modalities and improve the quality of life of the patient based on the current generated knowledge and to be a base line data for further researcher who are interested to investigate this issue.

### Objective

The main aim of this review was to assess the magnitude of psoriasis and its complication among Type 2 Diabetes Mellitus by proper focuses on reviewing of the global literature from 2010 to 2016.

### Literature Review

The term Psoriasis is originated from the Greek word *psorian*, meaning to have itch and was first described by Celsus (25 B.C. -45 A.D.) in his work *De Re Medica*. Many early Psoriatics were misdiagnosed as suffering from Leprosy, Impetigo, Scabies or Pyoderma. In 1809, Robert Willan was the first to partially differentiate psoriasis from other skin diseases (Alan Menter, 2013) and in 1841, Ferdinand Von Hebra (Viennese dermatologist ascribed the name Psoriasis in the English dictionary (<http://psoriasis.bafree.net/history-of-psoriasis.php>). Psoriasis is a complex autoimmune inflammatory disease that occurs in genetically susceptible individuals and presents with the development of inflammatory plaques on the skin. Although early concepts of the pathogenesis of Psoriasis focused primarily on keratinocyte hyperproliferation, dysregulation of the immune system is now recognized as a critical event in this disease. The evolving knowledge of the role of the immune system in Psoriasis has had a significant impact on treatment development. It can occur at any age, and is most common in the age group 50–69. The reported prevalence of Psoriasis in countries ranges between 0.09% and 11.4%, making Psoriasis a serious global problem (Danielsen, 2013 and Boehncke, 2015). Its etiology remains unclear, although there is evidence for genetic predisposition. Although there is a suggestion that Psoriasis could be an autoimmune disease, no autoantigen that could be responsible has been defined yet. Psoriasis can also be provoked by external and internal triggers, including mild trauma, sunburn, infections, systemic drugs and stress (Chandran, 2010). Psoriasis involves the skin and nails, and is associated with a number of comorbidities. Skin lesions are localized or generalized, mostly symmetrical, sharply demarcated, red papules and plaques, and usually covered with white or silvery scales. Lesions cause itching, stinging and pain. Between 1.3% and 34.7% of individuals with Psoriasis develop chronic, inflammatory arthritis (PsA) that leads to joint deformations and disability. Between 4.2% and 69% of all patients suffering from Psoriasis develop nail changes. Individuals with Psoriasis are reported to

be at increased risk of developing other serious clinical conditions such as cardiovascular and other non-communicable diseases (International Diabetes Federation, 2014).

### Clinical and Histological Features of Psoriasis

Psoriasis is a prototypical Th-1 inflammatory disease characterized by expansion and activation of Th-1 T cells, antigen presenting cells, and Th-1 cytokines. Similarly, chronic Th-1 inflammation is an important to the pathophysiology of obesity, Metabolic Syndrome, Diabetes, Atherosclerosis, and Myocardial Infarction. For example, circulating levels of Th-1 cytokines, adhesion molecules such as ICAM-1 and E-selectin, and angiogenic factors, such as vascular endothelial growth factor (VEGF) are elevated in Psoriasis, obesity, and coronary artery disease. The inflammatory mediators of these conditions have pleiotropic effects on diverse processes such as angiogenesis, insulin signaling, adipogenesis, lipid metabolism, immune cell trafficking, and epidermal proliferation (Yoo, 2007). Therefore, the metabolic aspects of chronic Th-1 inflammation, angiogenesis, and epidermal hyper-proliferation in Psoriasis have the potential to impact other conditions such as Diabetes, Atherosclerosis, and Thrombosis. Conversely, inflammatory molecules and hormones produced in conditions such as obesity, Diabetes and Atherosclerosis may influence the pathogenesis of Psoriasis by promoting susceptibility to the development of Psoriasis or through increasing the severity of established Psoriasis. Additionally, underlying the immune abnormalities shared by these disorders is a complex role for genetics in promoting their development. Here, we will briefly review abnormalities in inflammation, angiogenesis, metabolism, and genetics which are common to these phenotypically distinct disorders (Sabat, 2007). Chronic inflammation can lead to dysfunction in a variety of organ systems. Th-1 inflammatory cytokines such as TNF- $\alpha$  are elevated in the skin and blood of patients with Psoriasis and are critical to recruiting T cells to the skin and joints, promoting angiogenesis, and epidermal hyper-proliferation. Similarly, TNF- $\alpha$  is secreted in adipose tissue and is an important feature of the chronic low level inflammation seen in obesity. Insulin resistance, which is common to Psoriasis and the metabolic syndrome, may be mediated in part through inflammatory cytokines such as TNF. For example, TNF may lead to insulin resistance through a variety of pathways such as impairing insulin signaling by inhibiting the tyrosine kinase activity of the insulin receptor; by activating peroxisome proliferator-activated receptor (PPAR) $\delta$  which promotes epidermal proliferation and modulates adipogenesis and glucose metabolism; and by suppressing adiponectin secretion from adipocytes, which is an important anti-inflammatory molecule that also functions in regulating insulin sensitivity (Sabat, 2009 and Icen, 2009).

Furthermore, chronic inflammation in Psoriasis leads to increased insulin-like growth factor-II (IGF-II) in the skin and blood of Psoriasis patients. IGF-II promotes epidermal proliferation and is also implicated in promoting atherosclerosis, in modulating body fat mass and lipid metabolism in mice, and is linked to diabetes and hyperlipidemia in animal and human models (Rapp, 1999). Although inflammatory cytokines such as TNF have been extensively studied, emerging data have recently demonstrated the central role of IL-20 and IL-17 in the pathogenesis of Psoriasis. IL-17 is secreted by a new subclass of CD4<sup>+</sup> cells, the Th17 cell, and plays an important role in the pathogenesis

of Psoriasis and broadly activates inflammation in a variety of organ systems. For example, IL-17 is also elevated in the sera of patients with unstable coronary artery disease and is also preferentially expressed in animal models of aged coronary arteries that are susceptible to ischemia (Icen, 2009). Critical to sustaining chronic inflammation and epidermal hyperproliferation in psoriasis is angiogenesis. Immunocytes and keratinocytes in psoriatic skin produce angiogenic factors, such as VEG-F, that promote angiogenesis and endothelial cell activation. VEG-F levels are increased in plaques of psoriasis and serum concentration of VEG-F correlates with clinical severity of disease. VEG-F is also increased in hyperinsulinemic states like metabolic syndrome in which adipocytes are its primary source. Therefore, it is possible that hyperinsulinemic states such as obesity and metabolic syndrome may promote susceptibility to Psoriasis or exacerbate existing Psoriasis not only through their aforementioned role in promoting inflammation, but also through increased and sustained levels of circulating. Finally, genetics play a critical role in susceptibility to Psoriasis and metabolic disorders (18, 19). Over 20 genetic loci containing varying numbers of genes, many of which have no known function, have been associated with Psoriasis susceptibility. Of these, several are also associated with susceptibility to metabolic diseases. For instance, the Psoriasis susceptibility loci PSORS2, PSORS3, and PSORS4 are also associated with loci of susceptibility for Metabolic Syndrome, Type 2 Diabetes, familial hyperlipidemia and cardiovascular disease. Furthermore, individual genes associated with Psoriasis such as CDKAL1, which have no known function, are also associated with Type-2 Diabetes. Finally, genes with known function in cardiovascular risk, such as the ApoE4 isoform of ApoE are significantly more prevalent in patients with chronic plaque and guttate Psoriasis than in controls (Yoo, 2007).

### Co-Morbidities of Psoriasis

The multi-aspect nature of Psoriasis as a systemic disease associated with numerous multi-organ abnormalities and complications has been recognized in many epidemiologic studies. Psoriasis and its comorbidities share a common etiological linkage, it is hypothesized that proinflammatory cytokines contribute to dyslipidemias, atherogenesis, peripheral insulin resistance, T2DM, Hypertension etc.

Although Psoriasis is classically associated with the development of inflammatory plaques on the skin, increasing evidence supports the recognition of Psoriasis as a multisystem chronic inflammatory disorder with multiple associated comorbidities. Examples of extracutaneous disorders that have been linked to Psoriasis include: Psoriatic arthritis, Obesity, Metabolic syndrome, Cardiovascular, cerebrovascular, and peripheral vascular disease, Malignancy, Autoimmune disease, Nonalcoholic fatty liver disease, Chronic Obstructive Pulmonary disease, Obstructive sleep apnea, Psychiatric disorder and Alcohol abuse (Brown, 2009).

### Psoriasis as a Problem

Psoriasis has been considered a challenging disease from several points of view such as the patient, health care providers and health insurance companies. Although issues may differ between these groups, some problems related to safety of therapies and costs are relevant to all. Psoriasis can have a major impact on the patient's health related quality of life

(HRQOL) causing higher levels of anxiety, depression, worry and even suicidal thoughts. The reduced physical and mental functioning associated with Psoriasis is even comparable to that observed in patients with Cancer, Arthritis, Heart disease, Diabetes and Depression. However, the impact on the HRQOL is not directly related with the severity of the skin symptoms: patients with mild disease from a clinical perspective may report substantial HRQOL impairment. Interestingly, Psoriasis related HRQOL impairment does not change significantly in time suggesting that its impact is stable and that it remains a difficult disease to cope with (22). Anti-Psoriatic treatments may provide temporary relief, but a survey among Psoriasis patients found that none of the prior mentioned traditional systemic therapies were highly satisfactory. Clinical trials suggest that the degree of clinical response to a therapy has a linear relationship to the patients' HRQOL improvement. It is suggested that in order to have a substantial impact on HRQOL the improvement in skin clearance needs to be substantial (i.e.  $\geq$ PASI 75) and the strongest HRQOL improvements were measured in those subjects with a PASI response of 90% or more. Ideally, the ultimate treatment goal in patients with Psoriasis would be complete clearance, but achieving a positive risk: benefit ratio from a physician's and patient's perspective is more realistic (24).

### Association of Psoriasis and T2 Diabetes Mellitus

Psoriasis has a complex relationship with metabolic diseases such as obesity. Studies have shown that, compared with the general population, patients with psoriasis are more frequently overweight ( $25 \leq \text{BMI} < 30$ ) or obese ( $\text{BMI} > 30$ ). Adipose tissue, including adipocytes and resident macrophages, may serve as a significant source of TNF- $\alpha$ . Risk for Psoriasis has been shown to increase with increasing BMI ( $P=0.001$ ). This pro-inflammatory state in obesity may explain the association between Psoriasis and obesity and these pro-inflammatory cytokines might also influence the course and presentation of Psoriasis. In a study performed by with increase of the severity of the disease, these cytokines are significantly elevated in severe Psoriasis patients than in mild to moderate one which is attributed to the role of these cytokines in the pathogenesis and progress of Psoriasis and their elevation is responsible for the development, maintenance and resolution of Psoriatic lesions. When patients with Psoriasis are more likely to be obese, that implies they will also have the comorbid conditions of those with obesity. The risks of Diabetes, hypertension and dyslipidemia start to rise from a BMI of about 21.0 kg/m<sup>2</sup> there by deteriorating the cardiovascular risk profile. Inflammation plays a role in the pathogenesis of some glucose disorders in adults. Obesity has genetic as well as environmental causes (22). Obesity is more than just a risk factor; it has a causal effect in the development of type 2 DM against a genetic background. The evolution from obesity to type DM results from a succession of pathophysiological events: (a) Augmentation of the adipose tissue mass, leading to increased lipid oxidation; (b) Insulin resistance noted early in obesity, revealed by euglycemic clamp, as a resistance to insulin mediated glucose storage and oxidation. Blocking the function of the glycogen cycle; (c) Despite maintained insulin secretion, unused glycogen prevents further glucose storage leading to type 2 DM; (d) complete  $\beta$ -cell exhaustion appears later (25). Studies have also reported a high prevalence of Diabetes among patients with Psoriasis. Inflammation is strongly related to insulin resistance, although the question of whether treatment directed at the inflammatory process could lead to

benefits, such as decreasing the development of Diabetes, has yet to be answered. In a study of 200 patients with Psoriasis at an Italian clinic reported that 41.5% had Diabetes compared with 24.3 % of controls (n=280; P< 0.001) (Brown, 2009).

### **The Burden of Psoriasis on T2 DM**

HbA1c values of T2DM patients with comorbid Psoriasis were significantly higher compared to Type 2 Diabetes patients without Psoriasis. Insulin therapy was significantly more frequent in patients with Psoriasis. In Type 2 Diabetes patients with comorbid Psoriasis were more often depressed. Additional adjustment for use of steroids did not alter this finding. Severe hypoglycemia was significantly more common in T2DM with Psoriasis. Additional adjustment for insulin did not change the significantly higher event rate of severe hypoglycemia in Psoriasis patients (WHO, 2016). Hypertension was more frequent in patients with Psoriasis and the use of antihypertensive drugs was more common. A significant difference in autoimmune thyroid disease was observed, with a higher prevalence in T2DM patients with comorbid Psoriasis. Psoriasis with T2DM patients used steroids significantly more often. 50% of T2DM patients with comorbid Psoriasis were treated with topical steroids and 50% with systemic steroids. The frequency of smokers was higher in T2DM patients with Psoriasis. Metabolic control was worse in T2DM patients with comorbid Psoriasis. This may be probably due to reduced insulin sensitivity in Psoriasis patients (<https://www.psoriasis.org/advance/type-2-diabetes-drug-helps-psoriasis-too> and International Diabetes Federation, 2014). Depression occurred three times more frequently in T2DM patients with comorbid Psoriasis compared to patients without Psoriasis. It is well known that Psoriasis patients experience psychosocial difficulties such as depression, anxiety, and avoidance of social activities due to living with a chronic, disfiguring condition and fear from rejections by other persons, especially due to their visible Psoriatic lesions (Gerkowicz, 2012).

It was reported that an individual's emotional state might influence the development of Psoriasis. Furthermore, a meta-analysis concluded that there is a bidirectional relationship between Depression and T2DM. It was reported that there is a strong association between Depression and the incidence of T2DM (29). However, in T2DM patients there was a modest increased risk of Depression. Moreover, it was reported that antidepressant medication was increased in Diabetes patients with Psoriasis compared to the reference population without Psoriasis. The rate of severe Hypoglycemia was significantly higher in Psoriasis patients. Contrary to other studies, the difference could not be explained by insulin therapy. However, a previous study reported that Depression is a positive predictor of Hypoglycemia in T2DM patients (Coto-Segura, 2013).

### **The Burden of Psoriasis**

Psoriasis occurs worldwide. It affects men and women of all ages, regardless of ethnic origin, in all countries. Published data on the prevalence of Psoriasis in countries vary between 0.09% and 11.4%. In most developed countries, prevalence is between 1.5 and 5%. There is also evidence to suggest that the prevalence of Psoriasis may be increasing. Many studies have demonstrated that Psoriasis can impact substantially on Quality of life, even when a relatively limited body surface area is affected (IDF, 2014).

### **Incidence and Prevalence Psoriasis**

There are very few studies on the incidence of Psoriasis. Registration of Psoriasis cases is not compulsory, meaning reliable data are difficult to find. A review of published literature revealed only a handful of credible studies on the incidence of Psoriasis. One study showed that the overall sex- and age-adjusted incidence rate of Psoriasis in Minnesota in the U.S.A., between 1980 and 1983, was estimated at 0.60 per 1000 person-years. A study of 511 532 individuals in Italy between 2001 and 2005 reported an incidence of Psoriasis (adults receiving a first-ever diagnosis of Psoriasis) of 2.30–3.21 cases per 1000 person-years. In 2012, a 2-week Psoriasis screening study via medical consultation was performed in three countries simultaneously—Algeria, Tunisia and Morocco, where incidence of Psoriasis was estimated at 10.36, 13.26 and 15.04 per 1000, respectively. Relatively more studies have focused on the prevalence of Psoriasis. Depending on the region, the prevalence studies varied from 0.09% in the United Republic of Tanzania to 11.4% in Norway. A very weak correlation between geographic latitude and Psoriasis prevalence was found. Psoriasis appears to occur most commonly in populations of northern Europe and least in populations of eastern Asia. Some studies investigated the ethnic differences in the prevalence of Psoriasis. According to a 2001 study in the United States, people with Caucasian or Black ancestry and others had a prevalence of 2.5%, 1.3% and 1.0%, respectively. In another United States study from 2009–2010, these differences were higher, with the prevalence for Caucasians, Blacks, Hispanics and others at 3.6%, 1.9%, 1.6% and 1.4%, respectively (Danielsen, 2013 and IDF, 2014).

### **Risk Factors**

There are several risk factors that may provide the environmental stimulus for T-cell proliferation leading to the development of Psoriasis. They include psychological stress, certain medication such as antimalarial drugs, beta blockers, lithium and non steroidal, anti-inflammatory drugs, a history of skin infection, obesity, smoking and alcohol consumption (IHME, 2012).

### **Psychological Stress**

The recognition of psychological needs in patients with Psoriasis is critical for managing the condition. Psoriatics can have a substantial psychological and emotional impact on an individual, which is not always related to the extent of skin disease. There are elevated rates of various psychopathologies among patients with Psoriasis including poor self-esteem, sexual dysfunction, anxiety, depression, and suicidal ideation. In different studies (most of them are retrospective) from about one third to about three fourth of Psoriatics believed that there was a stress worsening of their Psoriasis. The results of another study do not indicate a major significance of stress for plaque Psoriasis patients (Coto-Segura, 2013).

### **Diabetes**

The actual prevalence of Diabetes Mellitus in Ethiopia could be as high as 8% as suggested by some institution-based studies, aside from what is projected by IDF in 2012 as 3.32% in 2012. Although strong nationwide surveillances have not been conducted, the DM expansion rate is growing in alarming rate, and so are associated morbidity and mortality rates (Alan

Menter, 2013). The distribution of T1DM, and T2DM in Ethiopia, shows regional variations, T1DM is more dominant in rural parts, whereas TYPE 2 DIABETES is more common in small and big cities of the country. Moreover, the occurrence of TYPE 2 DIABETES in the country looks to progress so fast and going to become the leading cause of morbidity and mortality among non-communicable diseases. This is largely associated with an increase in the income of the country, and gradual life style shift of the people into "modern" life (Romanowska, 2008 and Davidovici, 2010). Diabetes is one of the rapidly increasing noncommunicable diseases and an important, severe and growing public health problem worldwide. The number of subjects diagnosed with T2DM is increasing (Alan Menter, 2013). The cause of T2DM is multifactorial (genes and epigenetics, insulin resistance, overweight, and physical inactivity). Previous studies indicated an association between T2DM and Psoriasis. Recent estimates from the 2013 International Diabetes Federation [IDF] suggest that the number of adults living with Diabetes in the world will rise from 382 million in 2013 to 592 million in less than 25 years (Khalid, 2013). Sub-Saharan Africa, like the rest of the world, is experiencing an increasing prevalence of Diabetes alongside other non-communicable diseases. Ethiopia, which is one of the developing nations, is at a risk of increased Diabetes incidence. The number of deaths attributed to Diabetes reached over 21,000 in 2007. This estimate has increased to about 25,000 in 2011 (Armstrong, 2013). Type-2 Diabetes constitutes about 85 to 95% of all Diabetes in high-income countries and accounts for an even higher percentage in low and middle-income countries. The term "Diabetes Mellitus" encompasses a heterogeneous group of disorders characterized by insulin hypo secretion and/or insensitivity (WHO, 2016). Type 1 DM is a chronic autoimmune disease associated with selective destruction of insulin producing pancreatic  $\beta$ -cells. A variety of gene loci have been studied to determine their association with type 1 DM. The nature of autoantigen(s) responsible for the induction of type 1 DM is unknown. The identification of autoantigens in type 1 DM is essential both for diagnostic purposes and for potential immunotherapeutic intervention in the disease process. Type 2 DM has a greater genetic association than type 1 DM. Perturbations in glucose metabolism due to insulin resistance are further exacerbated when insulin production is compromised. Insulin resistance is a characteristic feature of most patients with T2D Mellitus (WHO, 2016). Several cross-sectional studies in non-diabetic subjects on the general population or in individuals with impaired glucose tolerance (IGT) / impaired fasting glucose (IFG) have confirmed that acute-phase reactants such as CRP (and sometimes the cytokines IL-6 and TNF- $\alpha$  are positively correlated with measures of insulin resistance/plasma insulin concentration, BMI/waist circumference, and circulating triglyceride and negatively correlated with HDL cholesterol concentration. In general, increasing components of the metabolic syndrome in individuals are associated with higher levels of inflammatory markers. In subjects with IGT or IFG, IL-6 but not TNF- $\alpha$  appears to be elevated compared to individuals with normal glucose tolerance and in one study, inflammatory markers were related to insulin resistance but not to insulin secretion (Augustin, 2010; Baeta, 2014 and Davidovici, 2010).

### Shared Pathogenesis

Psoriasis and Diabetes have a certain common underlying pathogenic mechanisms. Both have inflammatory nature and

both are associated with T-lymphocyte-mediated adaptive immune events and mechanisms, involving innate immunity. Specifically, both Psoriasis and Diabetes are associated with T-helper.Th-1 inflammatory cytokines such as TNF- $\alpha$  are elevated in the skin and blood of patients with Psoriasis and Diabetes. Similarly, TNF- $\alpha$  is secreted in adipose tissue and is an important feature of the chronic low level inflammation seen in obesity and Insulin resistance, which is common to Psoriasis and the Metabolic Syndrome, may be mediated in part through inflammatory cytokines such as TNF. The adipocyte is another important component of inflammation. Adipose tissue secretes inflammatory cytokines such as TNF- $\alpha$  and IL-6, and CRP levels increase with increasing weight (Huerta, 2007 and 37. <https://www.psoriasis.org/advance/type-2-diabetes-drug-helps-psoriasis-too>). A new concept is that obesity leads to macrophage infiltration of adipose tissues, perhaps because of the action of factors produced by adipocytes themselves, with macrophages rather than adipocytes producing some of the typically measured inflammatory cytokines. In this view, macrophages may produce factors such as TNF- $\alpha$ , causing insulin resistance, while both macrophages and adipocytes produce factors that increase hepatic CRP synthesis, such as IL-6. A major problem limiting our understanding of the genetic basis of T2DM is that many environmental and genetically based factors influence insulin sensitivity and insulin secretion: these include age, gender, ethnicity, physical fitness, diet, smoking obesity, and fat distribution. The prevalence of obesity, diabetes, and Metabolic Syndrome has been shown to be increased in Psoriasis patients in the general population. As early as 1950's, there was epidemiological evidence suggesting a correlation between inflammation and insulin resistant states such as obesity, but the mechanistic links were unknown. In the last decade, however, it has become increasingly evident that obesity and the concomitant development of inflammation are major components of insulin resistance. Studies in human obesity and insulin resistance have revealed a clear association between the chronic activation of pro-inflammatory signaling pathways and decreased insulin sensitivity. For example, elevated levels of tumor necrosis factor- $\alpha$  (TNF  $\alpha$ ), interleukin-6 (IL-6) and interleukin-8 (IL-8) have all been reported in various Diabetic and insulin-resistant states. It was noticed that a non significant difference in the glycemia values of the Psoriasis group vs non-Psoriasis group. However it has to be pointed out that this study has not taken into consideration other factors like for instance obesity, fat level, HTA which play an important role in insulin resistance (<http://psoriasis.bafree.net/history-of-psoriasis.php>).

## METHODS AND MATERIALS

### Study Area and Period

The study was conducted on a literature of articles and full-length researches in pub med, Google scholars, Archive dermatology and other search engines of 2010 to 2016 from July to August, 2016. Published Electronic journals based cross-sectional study design was employed. All literature from pub med, Google scholars, Archive dermatology of 2010 to 2016. Literature from pub med, Google scholars, Archive dermatology of 2010 to 2016 that related to Psoriasis and T2 DM. Literature review of electronic journals that are relevant to Psoriasis prevalence and its complication among T2 DM from 2010 to 2016 were included. Literatures those are not relevant to Psoriasis prevalence and its complications among T2 DM from 2010 to 2016 and published before 2010.

## Data Collection Techniques

Electronically published journals were collected from pub med, Google scholars, Archive dermatology and other search engines of 2010 to 2016

### Data collection tools

The computer, internet access is required for reviewing of journals published in English.

### Data quality assurance, management and analysis

All reviewed literature of electronic journals from pub med, Google scholars, Archive dermatology of 2010 to 2016 was checked for its relevance and completeness after searched by group members. After reviewed literatures of electronic journals summarized, key conclusion of Psoriasis magnitude and its complication among T2DM was made.

### Findings of the review

The authors accessed around 88 reviewed literature materials, out of which 43 were found to be relevant to address the objective of this review. These materials are henceforth articles for the current critical review among T2DM from 2010 to 2016.

### Prevalence of psoriasis

Psoriasis is one amongst these notorious auto-immune disorders having deep psychological and social impacts. Psoriasis is a non-contagious skin disease affecting both sexes equally, and can occur at any age, although it most commonly appears for the first time between the ages of 15 and 25 years. The evolving knowledge of the role of the immune system in Psoriasis has had a significant impact on treatment development. It can occur at any age, and is most common in the age group 50–69. Worldwide Psoriasis is affecting, as presumed, approximately 120–180 million people. The reported prevalence of Psoriasis in countries ranges between 0.09% and 11.4%, making Psoriasis a serious global problem. Around 150,000 new cases of Psoriasis are reported annually. Studies in developed countries have reported higher prevalence rates of on average about 4.6%. The population prevalence of Psoriasis in Ethiopia has been reported to range from 2% to 3%.

### Complications of Psoriasis

Over recent years, a series of publications has appeared showing an increased frequency of Metabolic Syndrome and its components amongst subjects with Psoriasis, leading in turn to an increased risk of cardiovascular disease and death. Amongst these patients, a higher level of prevalence of a series of factors has also been described, which could account for the more extensive presence of Metabolic Syndrome and heightened cardiovascular risk. Such factors include tobacco addiction, obesity, physical inactivity, depression, poor food habits and psychological stress. Psoriasis causes great physical, emotional and social burden. Quality of life (QoL), in general, is often significantly impaired. Disfigurement, disability and marked loss of productivity are common challenges for people with Psoriasis. There is also a significant cost to mental well-being, such as higher rates of depression, leading to negative impact

for individuals and society. Social exclusion, discrimination and stigma are psychologically devastating for individuals suffering from Psoriasis and their families. It is not Psoriasis causing the exclusion – it is largely society's reaction to it.

### Association between psoriasis and Type 2 diabetes mellitus

Clear differences between T2DM patients with and without comorbid Psoriasis could be demonstrated by this review. Disease outcome in T2DM patients with comorbid Psoriasis was clearly worse. Moreover, differences in Diabetes therapy were observed. Psoriasis patients required a more intensive Diabetes therapy. Therefore, clinicians should focus on comorbid diseases such as Psoriasis in T2DM patients. Since an earlier intervention may improve the Psoriasis outcome, a more intensive screening is important. T2DM patients with comorbid Psoriasis should be further encouraged to improve their metabolic status in order to lower the risk for complications. Lifestyle changes such as physical activity showed a positive influence on metabolic control, Diabetes treatment, BMI, and cardiovascular risk profile in T2DM patients. Psoriasis is associated with a significantly increased risk of co-morbidities, especially for those patients with moderate to severe disease. These health associations should be taken into consideration when evaluating the burdens of Psoriasis and designing effective treatment plans. Psoriasis is a prototypical Th-1 inflammatory disease characterized by expansion and activation of Th-1 T cells, antigen presenting cells, and Th-1 cytokines. Similarly, chronic Th-1 inflammation is an important to the pathophysiology of obesity, Metabolic Syndrome, Diabetes, Atherosclerosis, and Myocardial Infarction. Therefore, the metabolic aspects of chronic Th-1 inflammation, angiogenesis, and epidermal hyperproliferation in Psoriasis have the potential to impact other conditions such as Diabetes, Atherosclerosis, and Thrombosis. Conversely, inflammatory molecules and hormones produced in conditions such as obesity, Diabetes and Atherosclerosis may influence the pathogenesis of Psoriasis by promoting susceptibility to the development of Psoriasis or through increasing the severity of established Psoriasis. Additionally, underlying the immune abnormalities shared by these disorders is a complex role for genetics in promoting their development. The association between Psoriasis and T2DM is even stronger. Numerous cross-sectional studies have shown that Psoriasis, especially severe disease, confers a higher risk (up to 2.48) of Diabetes. The increased prevalence of Diabetes in patients with Psoriasis appears to be independent of traditional Diabetes risk factors such as obesity and dyslipidemia. The shared genetic background may also contribute to the susceptibility to both Psoriasis and Diabetes. In the light of the co-morbidities associated with Psoriasis, managing these patients should not be limited to their skin symptoms, but should also include a holistic approach.

## DISCUSSION

Based on different review of psoriasis magnitude and its compilation among T2DM, different international publications indicate that the multi-aspect nature of Psoriasis as a systemic disease associated with numerous multi-organ abnormalities and complications has been recognized. Many epidemiologic studies with various designs link Psoriasis to systemic metabolic comorbidities. Psoriasis and its comorbidities share a common etiological linkage, it is hypothesized that pro-inflammatory cytokines contribute to dyslipidemias, athero-

genesis, peripheral insulin resistance, T2DM, Hypertension etc. The relationship between Psoriasis and other diseases has drawn increasing interest in recent years. Psoriasis is associated with several co-morbidities, including Psoriatic Arthritis, cardiovascular disease, obesity, Diabetes, hypertension, Dyslipidemia, Metabolic Syndrome, Nonalcoholic Fatty liver disease (NAFLd), Cancer (Ca), Anxiety and Depression. Psoriasis can have a major impact on the patient's health related quality of life (HRQOL) causing higher levels of anxiety, depression, worry and even suicidal thoughts. The reduced physical and mental functioning associated with Psoriasis is even comparable to that observed in patients with Cancer, Arthritis, Heart disease, Diabetes and Depression. However, the impact on the HRQOL is not directly related with the severity of the skin symptoms: patients with mild disease from a clinical perspective may report substantial HRQOL impairment. Interestingly, Psoriasis related HRQOL impairment does not change significantly in time suggesting that its impact is stable and that it remains a difficult disease to cope with. Numerous cross-sectional studies have shown that Psoriasis, especially severe disease, confers a higher risk (up to 2.48) of Diabetes. The actual prevalence of Diabetes Mellitus in Ethiopia could be as high as 8% as suggested by some institution-based studies, aside from what is projected by IDF in 2012 as 3.32%, although strong nationwide surveillances have not been conducted, the DM expansion rate is growing in alarming rate, and so are associated morbidity and mortality rates. The distribution of T1DM, and T2DM in Ethiopia, shows regional variations, T1DM is more dominant in rural parts, whereas T2 DM is more common in small and big cities of the country. Moreover, the occurrence of T2 DM in the country looks to progress so fast and going to become the leading cause of morbidity and mortality among non-communicable diseases. This is largely associated with an increased in the income of the country, and gradual life style shift of the people into "modern" life. Previous studies indicated an association between T2DM and Psoriasis. Recent estimates from the 2013 International Diabetes Federation [IDF] suggest that the number of adults living with Diabetes in the world will rise from 382 million in 2013 to 592 million in less than 25 years. Psoriasis has a complex relationship with metabolic diseases such as obesity. Studies have shown that, compared with the general population, patients with psoriasis are more frequently overweight ( $25 \leq \text{BMI} < 30$ ) or obese ( $\text{BMI} > 30$ ). The prevalence of Psoriasis in countries vary between 0.09% and 11.4%. In most developed countries, prevalence is between 1.5 and 5%. There is also evidence to suggest that the prevalence of Psoriasis may be increasing. Many studies have demonstrated that Psoriasis can impact substantially on Quality of life, even when a relatively limited body surface area is affected.

## Conclusion and recommendation

### Conclusion

- Psoriasis is a non- contagious skin disease affecting both sexes equally, and can occur at any age, although it most commonly appears for the first time between the ages of 15 and 25 years.
- The prevalence of Psoriasis across countries varies between 0.09% and 11.4%.
- In most developed countries, prevalence of Psoriasis is between 1.5 and 5%.
- Psoriasis is one amongst these notorious auto-immune disorder having deep psychological and social

impacts. Psoriasis causes great physical, emotional and social burden, quality of life (QoL), in general, is often significantly impaired.

- Numerous cross-sectional studies have shown that Psoriasis, especially severe disease, confers a higher risk (up to 2.48) of DM.
- Psoriasis has a complex relationship with metabolic diseases such as obesity. Studies have shown that, compared with the general population, patients with psoriasis are more frequently overweight ( $25 \leq \text{BMI} < 30$ ) or obese ( $\text{BMI} > 30$ ).
- An increase in the income of the country and gradual life style shift of the people into "modern" life increases risk of Diabetes Mellitus.
- Disease outcome in T2DM patients with comorbid Psoriasis was clearly worse. Psoriasis patients required a more intensive Diabetes therapy. Therefore, clinicians should focus on comorbid diseases such as Psoriasis in T2DM patients.

### Recommendation

- Given the potentially high prevalence of Psoriasis, we recommend Federal Ministry of health to increase knowledge or awareness of health professionals and clinicians in particular as psoriasis patients require a more intensive Diabetes therapy. Therefore, clinicians should focus on co-morbid diseases such as Psoriasis in T2DM patients.
- Further studies are needed on magnitude and complication of Psoriasis among Diabetes Mellitus at clinical setup to render conclusive evidence.
- Since information on the prevalence of Psoriasis in Ethiopia is extremely limited, we therefore, recommend the government to continue and strengthen information accessibility by creating awareness.

### Strength and limitations of the study

- Through all shortages of finance and time the target objective was achieved.
- The study suffers from the usual limitation of the use of secondary data for review -as it poses "chicken - egg" dilemma.
- As the study is a descriptive correlational study analyzed at group level across different studies, thus it is unlikely to make an inference at the individual level.
- Coverage may be limited as, all relevant reports on psoriasis may have not been accessed as the study largely relied on open access papers.

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CDKL 1	CyclinDependent kinase –like
COPD	Chronic Obstructive Pulmonary Disease
CRP	C-Reactive Protein
HDL	High Density Lipoprotein
HLA	Human Leukocytic Antigen
HTA	Human T Antigen
IDF	International Diabetic Federation
IL	Interlukin
IGF	Impaired Glucose Fasting
IGT	Impaired Glucose Tolerance
MS	Metabolic syndrome
NCD	Non-communicable disease
PASI	Psoriasis Activity and Severity Index
PPAR- $\delta$	Peroxisome Proliferator- activated receptors- sigma
PsA	Psoriatic Arthritis
PSORS	Psoriasis Susceptibility Loci
QoL	Quality of Life
ROS	Reactive Oxygen Species
Th cells	T-helper cell
TNF- $\alpha$	Tumor Necrosis Factor- alfa
VEGF	Vascular Endothelial Growth Factor
VLDL	Very low – density lipoprotein
WHO	World Health Organization

## Annex

### ACRONYMS

ApoE Apolioprotein- E

BMI Body Mass Index  
 CD4 cells Cluster of Differentiation cells

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