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Comorbidities in Psoriasis: A Narrative Literature Review

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ABSTRACT
Comorbidities in Psoriasis: A Narrative Literature Review. Psoriasis is a chronic inflammatory disease with multisystemic morbidities. The most common comorbidities of psoriasis include psoriatic arthritis, cardiovascular disease, metabolic syndrome, overweight/obesity, inflammatory bowel disease, and mental disturbance in terms of depression. Evidence shows an association of psoriasis with comorbid diseases and have been proposed as related to the chronic inflammatory status of psoriasis. The presence of such comorbidities affects the therapeutic choices for clinicians in comprehensive way. The understanding of these pathogenesis relation and regular screening for early diagnosis of the comorbid diseases will certainly lead to better management of the disease. This is because the management paradigm of psoriasis does not only target repair of skin lesions but also works together with other scientific disciplines to prevent and treat comorbid diseases holistically. Patient often visit the clinician regularly and it is important to recognize and address early signs of psoriatic comorbidities to prevent further deterioration and improve quality of life. The purpose of this review is to summarized pathogenesis and screening recommendation of comorbidity associated with psoriasis, which may be essential for future clinician guideline in order to achieve holistic therapy of psoriasis and quality of life improvement.

1. Introduction

Psoriasis is a chronic autoimmune disease that causes multisystemic inflammation characterized by skin inflammation, epidermal hyperplasia, and an increased risk of various other morbidities.[1,2] Psoriasis co-morbidities are thought to have an association with the chronic inflammatory condition of psoriasis. Research on the relationship between psoriasis and systemic comorbidities has expanded rapidly in the last few decades.[3,4]

Some of the most frequent comorbidities are psoriatic arthritis, cardiovascular disease, metabolic syndrome, obesity, inflammatory bowel disease, and mental disorders such as depression.[2] Psoriasis patients are reported to be around 30% will experience psoriatic arthritis (PsA).[5] In addition, patients with severe or moderate psoriasis have a higher risk of cardiovascular comorbidities and metabolic syndrome.[6] Severe psoriasis implicates those with over 30% lesions of body surface area (BSA) and moderate psoriasis implicates those with 10-30% lesions of BSA.[1] This severity level along with the duration of psoriasis would interfere the inflammation cascade that relate to the pathogenesis of the comorbidities.[3] The prevalence of the metabolic syndrome in patients with psoriasis ranges from 14.3% to 50%, and psoriatic patients are at least double the risk of developing metabolic syndrome compared to non-psoriatic individuals. The risk of psychological disorders related to psoriasis, namely anxiety disorders is also quite high and is reported to be 1 in 123 psoriasis patients per year and the risk of

suicide attempts is 1 in 2500 psoriasis patients per year.[6–8]

Psoriasis co-morbidities are reported to have not received proper management and will also affect the patient's quality of life significantly.6,9 Meanwhile, various studies have reported on the pathogenesis and screening recommendations for the comprehensive management of psoriasis comorbidities. However, the current psoriasis management paradigm does not only focus on the successful skin improvement, but also preventing and treating comorbid diseases holistically by the collaboration with other disciplines. This literature review aims to summarize the various pathogenesis and screening recommendations for psoriasis comorbidities so that it can be a guide for clinicians in order to achieve holistic management to improve the quality of life of psoriasis patients.

Vascular Comorbidity

Psoriasis has been reported to be associated with increased morbidity and mortality from cardiovascular events based on research, especially in severe and long-lasting psoriatic skin disease. Severe psoriasis has been reported to increase the risk of cardiovascular disease (CVD); acute myocardial infarction, abdominal aortic aneurysm, stroke, aortic valve stenosis, atrial fibrillation, and coronary artery disease. The relationship between psoriasis and cardiovascular disease has been studied by analyzing the molecular mechanisms responsible. These include general genetic factors and inflammatory pathways, adipokine secretion, insulin resistance, lipoproteins, angiogenesis, oxidative stress, and hypercoagulability.[9–11]

The pathogenesis of psoriasis and cardiovascular disease is reported to have similarities, they have similar main mediators, namely Th1 and Th17. Crowly et al. reported that psoriasis and atherosclerosis have a mechanism linking the two (Figure 1). Th1 and Th17 cells and their respective cytokines are the main mediators involved in the pathogenesis of these two diseases. Cytokines common to both diseases include IL-1, IL-6, IL-10, leptin, and adiponectin. Inflammation is the main thing that underlies the theory that combines psoriasis and CVD.[4]

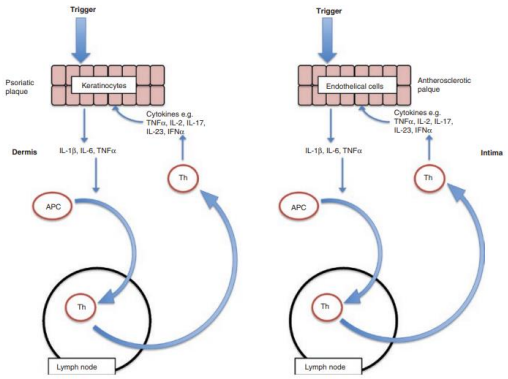

Figure 1. Overlapping pathogenesis of psoriasis and cardiovascular disease. Th CD4 lymphocyte (Th1 and Th17), APC antigen presenting cell[4]

Chronic inflammation in psoriatic skin lesions will affect systemic and vascular inflammation, atherosclerosis, and thrombosis.[11] Inflammation plays an important role in the development of vascular disease and has implications for endothelial dysfunction and the development of atheroma which begins with T-cell activation and endothelial infiltration by macrophages. This is followed by

atherosclerotic plaque formation and thrombus development. Plaque activation and thrombus development have implications for subsequent ischemic events. Plaque formation and plaque destabilization are strongly influenced by inflammatory cytokines, T cells, and macrophages.[4]

Furthermore, a psoriatic march model has been proposed to explain the pathogenic relationship between psoriasis and CVD (Figure 2). According to the psoriatic march model, the systemic inflammation present in psoriasis causes insulin resistance and induces endothelial dysfunction. It is known that chronic inflammation in psoriasis and atherosclerosis can induce the production of adipokines and proinflammatory cytokines, leading to insulin resistance and further endothelial dysfunction which can increase the risk of CVD. Subtypes of inner adipose tissue can also produce large amounts of adipokines and chemokines, such as monocyte chemotactic protein (MCP)-1 and IL-8, which are known to stimulate atherosclerosis. Elevated leptin and resistin expression levels can activate the expression of pro-inflammatory cytokines such as MCP-1, IL-6, IL-2, and tumor necrosis factor-α (TNF-α), all of which act as atherogenesis-promoting molecules and can promote inflammation. through monocyte migration and macrophage activation. Furthermore, adipokines can alter the effective function of insulin in blood vessels by affecting capillary mobilization. These causative factors can lead to metabolic syndrome or atherosclerosis, which can lead to myocardial infarction or stroke in psoriasis patients.[12]

Psoriasis patients also have an increased prevalence of CVD risk factors, including metabolic syndrome. Metabolic syndrome is a number of conditions related to lifestyle such as obesity, hypertension, glucose intolerance, and dyslipidemia. The metabolic syndrome can be associated with moderate to severe psoriasis with a high prevalence (~50%). Psoriasis patients (more women than men) have at least twice the risk of developing the metabolic syndrome or one part of the metabolic syndrome than healthy individuals. The link between psoriasis and metabolic syndrome is not just a coincidence. Factors that explain the link between the two diseases are a combination of genetic components, common immune-inflammatory pathways, environmental factors, smoking, alcohol consumption, psychological stress and low physical activity.[2,4] Smoking and alcohol consumption are known cardiovascular risk factors and have an increased prevalence in patients with psoriasis. An increase in the number of Th17 lymphocytes in the peripheral blood in smokers may explain the increased risk of psoriasis in cigarette users.[11,12]

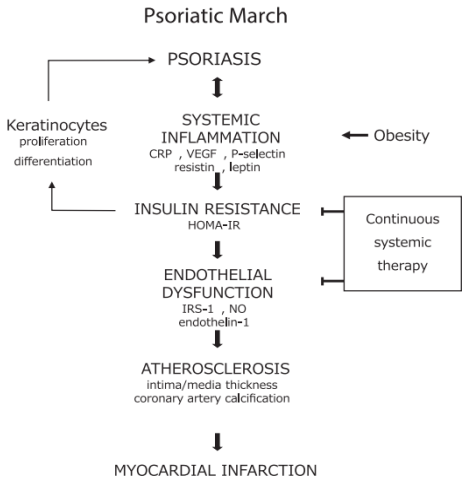

Figure 2. Psoriatic march concept[12]

Overweight and obesity, which contribute to the metabolic syndrome, also have a dose-response relationship with psoriasis. The greater the body mass index (BMI), the more likely psoriasis will occur. Obesity is a morbidity associated with mild chronic inflammation associated with increased levels of c reactive protein (CRP), TNFα, IL-6, IL-17 and other cytokines. The relationship between psoriasis and obesity is complex and likely to be multifactorial including immune, genetic and behavioral mediation. Adipocyte and activated inflammatory macrophages may contribute to psoriasis and overweight/obesity. Adipose tissue produces hormones, adipokines, and proinflammatory cytokines that are responsible for psoriasis, namely IL-1, IL-6, and TNF-alpha.[2,4]

A number of studies have shown that patients with psoriasis show reduced levels of high-density lipoprotein (HDL) and/or increased levels of low-density lipoprotein (LDL), very-low-density lipoprotein (VLDL), and triglyceride levels. High-density lipoprotein has the functions of reverse cholesterol transport, anti-oxidative capacity, and anti-inflammatory properties by regulating dendritic cell differentiation, and reducing T cell activation and IL-12 production. This function is reduced during chronic inflammation such as psoriasis. On the other hand, LDL accumulates in the blood vessels to produce active oxygen and impair the function of vascular endothelial cells, but it has been shown to increase with increasing TNF-α in patients with severe psoriasis.[4,12]

Hypertension is associated with an increased risk of CVD morbidity and mortality. Several studies have reported a positive relationship between psoriasis and hypertension. The role of inflammation was reported in several previous studies on psoriasis patients as a potential mechanism linking psoriasis with hypertension. Elevated serum renin concentrations, known to increase blood pressure, have been reported in psoriasis patients. In addition, serum levels of endothelin-1, a potent vasoconstrictor, appear to be increased in psoriasis patients.[4]

Epidemiological studies show that the relationship between psoriasis and type 2 diabetes is related to the severity of psoriasis. Knowledge regarding the mechanistic relationship between psoriasis and diabetes is still limited. Th1 lymphocytes and their cytokines have been reported to be involved in both diseases. Tumor necrosis factor-α induces insulin resistance and is a key cytokine in the pathogenesis of psoriasis. At the same time, diabetic patients with psoriasis have a higher incidence of diabetic micro- and macrovascular complications. In addition, a genetic link may increase susceptibility to type 2 diabetes in patients with psoriasis and there is emerging evidence of a shared susceptibility locus including the CDKAL1 gene.[4]

The risk of CVD in psoriasis patients is also reported to be influenced by adequate treatment of the patient. Crowley et al. reported that psoriasis patients who received adequate treatment were also reported to experience a reduced risk of CVD events. Several studies have specifically assessed several CVD markers in psoriasis patients including blood vessel dilatation, carotid vessel intima thickness and PET scanning. Several studies have reported the theory that adequate therapy can suppress inflammation in psoriasis and improve markers of CVD morbidity and mortality.[4] Thus, by understanding the relationship between CVD and psoriasis comorbidities, clinicians can be more careful and immediately provide adequate psoriasis therapy. can reduce the incidence of CVD comorbidities in psoriasis patients.

Psoriasis Arthritis

Psoriasis arthritis (PsA) is a common comorbidity in psoriasis patients and it is reported that one-third of psoriasis patients experience PsA during their lifetime. Furthermore, approximately 85% of PsA patients are reported to have a previous history of

skin psoriasis or coexistence of skin psoriasis. Arthritic psoriasis is an inflammatory musculoskeletal disease associated with skin psoriasis. This condition affects men and women about the same between the ages of 40 and 50. The diversity of organ systems involved includes peripheral and axial joints, entheses, skin, and nails. Psoriasis arthritis is characterized by joint stiffness, pain, and swelling and can progress to debilitating joint damage. Arthritic psoriasis is also reported to be associated with nail psoriasis and onycholysis which is present in approximately 80% to 90% of PsA patients.[6]

Arthritic psoriasis has periods of relapse and remission but can lead to persistent inflammation if left untreated. The onset of arthritis may precede, coincide with, or follow the presence of psoriasis skin lesions. Psoriatic skin lesions usually precede arthritis in 75% of cases, and coexist with PsA in 10%. Some reported cases of PsA precede skin psoriasis in 15% of cases. Correlation between the type or severity of skin lesions and the presence, type, or extent of joint damage is not common. Risk factors for a more severe course of arthritis include early presentation at an early age, female gender, polyarticular involvement, genetic predisposition, and early radiographic signs of disease.[13]

Several clinical manifestations of certain psoriasis skin lesions were reported to experience more PsA including psoriasis of the scalp and intergluteal. The degree of skin lesion severity was also reported to be associated with a higher risk of PsA. Clinical symptoms on nails with a prevalence of 40% in psoriasis patients is a risk factor for PsA. Nail psoriasis causes damage to the nail plate and matrix and pitting nails are the most common. Clinical symptoms of severe psoriasis, psoriasis of the nails, scalp and intergluteal are signs for clinicians to pay attention to the possibility of PsA when treating psoriasis patients.[13]

The classification that is commonly used today is the CASPAR criteria (The Classification Criteria for PsA). The involvement of rheumatologists in the early clinical symptoms of PsA is important because the clinical symptoms of PsA are very heterogeneous even though they meet the CASPAR criteria. Some of the clinical symptoms of psoriasis mentioned above, namely severe psoriasis, scalp, nail, and intergluteal psoriasis are important indicators in diagnosing PsA. Laboratory tests in the form of rheumatoid factor (RF) and anticyclic citrullinated peptides (anti-CCP) are important markers to exclude rheumatoid arthritis. Rheumatoid arthritis patients will have positive values on RF and anti-CCP examinations while those on PsA will have negative results. Examination of genotyping for HLA-B27 has high clinical and prognostic value because HLA-B27 is higher in patients with early PsA, axial PsA, severe enthesitis, and uveitis. Radiographic examination is recommended for PsA patients to evaluate the characteristics of PsA joint damage including erosion of the juxta-articular bone and formation of new bone. This examination may also show enthesophytes at the site of previous entheseal trauma or inflammation. Doppler musculoskeletal ultrasonography and MRI can be used to assess disease activity as needed to differentiate tissue edema and vascularity. The results of the PsA doppler examination in the form of enthesitis and MRI showing enthesitis, entesophytes, and bone marrow edema support the diagnosis.[13]

Furthermore, there is a diagnostic algorithm in establishing psoriasis arthritis as shown in Figure 3. Patients with symptoms of musculoskeletal inflammation in the form of pain, stiffness, or joint swelling, pain or swelling in the tendons (i.e, heels, plantar fascia), inflammatory back pain, signs "Sausage" on the fingers or toes is one of the early markers of a PsA. The next step is that psoriasis criteria can be fulfilled if there is an active sign of psoriasis plus one of the boxes below it marked*. In addition, there is also a simple PsA screening method

that can be used, namely PEST (the Psoriasis Epidemiology Screening Tool).

Other Immune-mediated inflammatory diseases

Psoriasis has been reported to be associated with other immune-mediated inflammatory diseases (IMID), including inflammatory bowel disease (IBD), especially Crohn's disease and ulcerative colitis, rheumatoid arthritis, systemic lupus erythematosus, Sjogren's syndrome, and systemic sclerosis. The exact pathophysiological mechanism for this association is not known. Several factors, including genetics and environment, are thought to play a role in the mechanism of the occurrence of other IMIDs. Certain stressors, such as smoking and microbial agents, may also act as common triggers. A higher prevalence of psoriasis and multiple IMIDs has also been observed in some geographic areas, especially areas with higher latitudes; however, the exact environmental factors that could explain this association are unknown.[7,9,14]

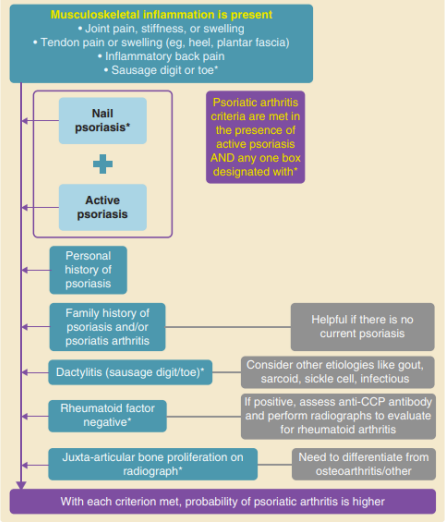

Figure 3. Psoriatic arthritis diagnostic algorithm[13]

Although the exact mechanisms underlying autoimmune comorbidities are not fully understood, damage to basement membranes, melanocytes and hair by chronic psoriatic inflammation can initiate and precipitate autoimmune skin-related diseases. The association of Crohn's disease and collagen disease, systemic lupus erythematosus (SLE), rheumatoid arthritis, Sjögren's syndrome, and systemic sclerosis, has been demonstrated in psoriasis patients. Some psoriatic patients develop collagen disease after treatment with biologic drugs.[15]

Similar to psoriasis, the IFNs complex, LL-37/DNA and plasmacytoid dendritic cells (DCs) play important roles in triggering and developing SLE. Interferon accelerates the formation of the DNA-LL37 complex which activates plasmacytoid DCs to produce high levels of IFN and IL-23, then IL-23 induces the production of IL-17 which promotes autoimmunity. Crohn's disease is also strongly associated with TNF-α/IL-23 signaling because both anti-TNF-α and anti-IL-23 biologics are very effective for this disease.[4,15] Daugaard et al. reported that administration of a TNF inhibitor accompanied by the biologic agent ustekinumab proved effective in the treatment of IBD and psoriasis so that it could be a good therapeutic option.[9]

Mental Disorder

Mental disorders have been known as psoriasis comorbidities, especially depression and anxiety.

Until now, the prevalence of mental disorders in psoriasis patients is difficult to ascertain but is estimated to be 10-60% of the total psoriasis patients. The highly visible clinical symptoms of psoriasis result in a variety of significant social stigma causing maladaptive coping mechanisms and increased stress. Several studies have reported an increased prevalence of depression and mood disorders associated with psoriasis.[4,9]

Psoriasis is a chronic inflammatory disease mediated by T lymphocytes, with a Th1 and Th17 profile, and dendritic cells, which are activated and increased in skin lesions. These cells migrate to the skin and release inflammatory cytokines. High levels of proinflammatory cytokines have been reported in major depressive disorder and have been shown to be associated with disease severity. These findings, however, do not clearly indicate whether depression causes inflammation or vice versa, and whether there is a biological possibility in other cases.[16]

Depression is thought to be mediated by dysfunctions in the regulation of neurotransmitters including serotonin, norepinephrine, dopamine, gamma-aminobutyric acid (GABA), and glutamate. The common pathogenic pathway for psoriasis and depression may involve IL-12 which is elevated in depression and is also a key cytokine defined in the pathogenesis of psoriasis. Interleukin 2 and interferon α (IFN-α) directly increase the enzymatic activity of indolamine-2,3-dioxygenase, which increases the conversion of tryptophan to quinurenin and, therefore, reduces the synthesis of tryptophan to serotonin. Decreased serotonin levels and increased kynurenine produce depressive symptoms.[4,16]

Depression is primarily related to changes in the secretion of melatonin, the hormone that controls circadian rhythms. Melatonin is involved in the sleep cycle and modulates the immune response by reducing levels of inflammatory cytokines. Dysregulation of melatonin has been observed in psoriasis patients, with reduced nocturnal hormone levels. Decreased melatonin causes disinhibition of the release of melanocyte stimulating hormone (MSH), which then contributes to depressive symptoms.[16]

IL-1β, and IL6. Most patients with psoriasis report episodes of stress at the onset or exacerbation of the disease. This suggests that mood variations can modulate disease outcome. In turn, psoriasis exacerbations can increase comorbid depression and anxiety. Early screening is very important for this comorbidity. Measuring screening for comorbid mental disorders, especially depression and anxiety in psoriasis, can use the Goldberg Anxiety and Depression Scale (GADS). This measuring instrument consists of 18 questions consisting of 9 questions about symptoms of anxiety and 9 questions about symptoms of depression. Patients were asked to answer questions according to how they felt in the last month.[16]

Other Comorbidities

Other comorbidities present in psoriasis include fatigue conditions, ocular comorbidities, and several types of malignancy. Fatigue is a subjective experience, and has been defined as an excessive and persistent feeling of weakness that reduces a person's ability to carry out daily activities including working effectively and contributing to general family and social conditions. Fatigue is generally characterized by a feeling of weakness and lack of motivation which can greatly interfere with the patient's daily life. Fatigue is an often overlooked and under-studied phenomenon in psoriasis. Previous studies have reported that approximately 50% of psoriasis patients suffer from clinically important fatigue. Assessment of the degree of patient fatigue was assessed using three different general fatigue instruments including the fatigue Visual Analog Scale (fVAS), the Fatigue Severity Scale (FSS), and the Short Form 36 (SF-36) vitality scale. Cut-off values were defined as ≥50 for

fVAS, ≥4 for FSS, and ≤35 for the SF-36 vitality scale. Assessment for fVAS is done by subjective assessment of the patient based on a scale of 0 for the mildest to 10 for the most severe. There are a total of 18 questions on the fVAS, including assessing tiredness, sleepiness, anxiety, energy, feeling active, feeling strong, feeling efficient, etc. The degree of fatigue was associated with pain and depression, but not with psoriasis severity. Thus, it is necessary to assess fatigue in psoriasis patients.[17,18]

Ocular comorbidities, such as uveitis, have been found in a number of psoriasis patients. Ocular comorbidities are important for diagnosis and treatment, and can easily be overlooked. The risk increases especially in patients with concomitant PsA as studies have shown that patients with PsA and severe psoriasis have a 2.4-fold higher risk of developing non-infectious uveitis than the general population. Physicians can screen patients by assessing ocular manifestations in the psoriasis screening questionnaire. Doctors can also identify clinical characteristics of uveitis, including: red eyes, eye pain, light sensitivity, blurred vision, floaters and reduced vision or using the OcMaPS (Ocular Manifestations in Psoriasis Screening) questionnaire. Patients who have any of the ocular symptoms or with a history of ocular manifestations are referred to an ophthalmologist for a complete examination.[19]

Screening Recommendation

Treatment and care of psoriasis patients by dermatologists nowadays need to pay more attention not only to skin diseases but also to their comorbidities. Doctors in this case have an important role to play in screening and following up on comorbidities in daily clinical practice. Daugard et al. has made a summary of the guidelines which are summarized in (Table 1). It is hoped that this guide will help physicians improve holistic care not only for psoriasis of the skin but also for various co-occurring morbidities in patients.[9]

In general, the first step in recommending management and screening for comorbidities is to explain to all psoriasis patients that there is an increased risk of developing some of these diseases and comorbid conditions. Screening for cardiovascular disease should be done routinely every year, or twice per year, especially in patients with moderate to severe psoriasis. Evaluation of cardiometabolic risk factors (including hypertension, diabetes, BMI ≥25, hypercholesterolemia and hyperlipidemia) using national guidelines.[6,9]

Consider earlier and more frequent screening for cardiovascular risk factors in patients with more severe disease. Patients with CVD risk factors are considered to have a 1.5 times greater risk of experiencing CVD and these risk factors need to be treated. Refer to primary care physician for further evaluation if there is evidence of hypertension, hyperlipidemia or hypercholesterolemia, and/or prediabetes or new diabetes. Encourage patients with obesity to maintain a healthy lifestyle and schedule regular follow-ups with their doctors; consider bariatric surgery if body mass index is >40 and other weight loss measures are not working.[6,9]

Screening for PsA is also carried out routinely at every visit, paying attention to symptoms of swelling, redness and pain in the joints. Note complaints of nocturnal axial pain or pain in the Achilles tendon or plantar fascia. Screen and evaluate for peripheral inflammatory arthritis, dactylitis, enthesitis, and axial involvement (screening questionnaire can use the Psoriasis Epidemiology Screening Tool) or CASPAR. Refer to a rheumatology specialist in patients with suspected PsA or a positive assessment on screening.[6]

Screening for IMID, especially IBD (Crohn's disease, ulcerative colitis), pay attention to patients with symptoms of abdominal pain/cramps after eating, weight loss, recurrent diarrhea, bloody or mucous stools, rectal pain or bleeding, tenesmus or urgency of the lower digestive tract. Refer the patient

with any of these symptoms to a gastroenterologist for further evaluation. Initiate psoriasis treatment for patients with inflammatory bowel disease who develop psoriasis from lesions while prescribing anti-TNF-α medications. Consider discontinuing anti-TNF-α if psoriasiform lesions persist. Avoid anti-IL-17 drugs in patients with IBD.[6,9]

Screening for mental disorders in the form of depression, anxiety, and other psychological challenges related to stress due to illness is needed, especially in psoriasis patients who have not received adequate management for a long time. Evaluation of anxiety and depression (a screening questionnaire such as the Goldberg Anxiety and Depression Scale may be considered). Refer to an appropriate specialist for further evaluation if there is evidence of anxiety, depression or suicidal ideation. Use psoriasis treatments as a means to improve associated anxiety and depression.[6,8,9]

Table 1. Management and screening recommendations based on psoriasis co-morbidities

Psoriasis comorbidities	Recommendation
All psoriasis patients	Inform the Patient of the Increased Risk
Psoriatic arthritis	Be aware of joint symptoms including swelling, redness and soreness Be aware of night - time axial pain, or pain in the Achilles tendon or plantar fascia Screen with PEST does not detect axial arthritis or CASPAR Refer to a rheumatologist when PsA is suspected or positive scores on screening tools are obtained
Cardiovascular disease	Screen patients with moderate-to-severe psoriasis, annually or biennially, for cardiovascular risk factors with a validated screening tool Consider multiplying the score of the cardiovascular risk factor by up to 1.5 and treating them thereafter Cardiovascular risk factors: In addition to pharmaceutical intervention and CVD prophylaxis, it is recommended to guide psoriasis patients to dietary intervention, physical training, weight loss to achieve a BMI Attention toward obesity, diabetes type 2, hypertension and dyslipidemia
Other immune modulated diseases	Regarding IBD: Awareness of postprandial stomach pain/cramps, weight loss, frequent diarrhea, blood or mucus in stool, rectal pain or bleeding, rectal tenesmus or bowel urgency ⇒ Referral to gastroenterologists if any of these symptoms are present Awareness towards screening patients with psoriasis with severe skin disease since they bear the highest IBD risk
Mental disorder	Be aware that longstanding undertreated psoriasis may increase the risk of depression, anxiety and other psychological challenges and illness - related stress Screening tool Anxiety and Depression Scale Referral to psychiatrist if affirmative to ≥4 questions Goldberg A&D scale, or affirmative to ≥2 questions on Goldberg A&D subscale
Other Comorbidities	Be aware of fatigue and screen with fVAS or FSS Be aware of ocular comorbidities such as eye redness, eye pain, light sensitivity, blurred vision, floaters and decreased vision or use OcMaPS tools and refer to ophthalmologist if at least one ocular symptom as well as patients with a history of ocular manifestations Address reduced health-related quality of life and assist the patient in building knowledge and obtaining guidance as per local possibilities

Screening for other co-morbidities, namely watching for signs of fatigue in the form of lethargy, depression, loss of thirst and hunger. Patients can be screened with the Fatigue Severity Scale (FSS). Pay

attention to ocular comorbidities in the form of red eyes, eye pain, light sensitivity, blurred vision, floaters and decreased vision or use the OcMaPS questionnaire and then refer to an ophthalmologist if there is one of the ocular symptoms or a history of ocular manifestations. Pay attention to the decrease in the patient's quality of life and direct the patient to increase knowledge and obtain guidance according to ability at the local health place or facility.[9,19]

5. Conclusion

Psoriasis is a chronic systemic inflammatory disease that can cause various comorbidities. Various reports have explained various theories or hypotheses related to the relationship between psoriasis and its comorbidities. The severity of psoriasis is related to the possibility of comorbidities. Patients with severe psoriasis are at increased risk of having one or more psoriasis comorbidities. Patient education and routine screening of psoriasis comorbidities in psoriasis skin control patients into clinical practice is important. Psoriasis management and screening guidelines are expected to help clinicians to optimize holistic psoriasis treatment in order to improve the quality of life of psoriasis patients.

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