

## COMORBIDITIES PROFILE OF PSORIASIS PATIENTS AT PROF. I.G.N.G. NGOERAH GENERAL HOSPITAL, DENPASAR

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### ABSTRACT

**Introduction:** Psoriasis, an immune-mediated inflammatory disease, is known to be associated with a range of comorbidities, including arthritis, cardiovascular disease, and psychosocial disorders. Our research focused on understanding the prevalence of comorbidities in psoriasis patients and their implications for treatment and long-term outcomes. **Material and methods:** This is a cross-sectional–retrospective study conducted at Prof. I.G.N.G. Ngoerah General Hospital from 2018 until 2022. **Results:** This study included 124 psoriasis patients, ranging in age from 2 to 77 years. The sex distribution was 57.25% males and 42.71% females. Almost all the patients had no comorbidities (71.77%), followed by the patients with one comorbidity (14.51%) and more than one comorbidity (13.70%). The comorbidities of psoriasis patients were dyslipidemia (31.45%), obesity (28.22%), hypertension (16.93%), type 2 diabetes mellitus (12.90%), metabolic syndrome (12.09%), coronary artery disease (4.03%), psychiatric disorder (4.03%), renal disorder (3.22%), and thyroid disease (0.80%). **Discussion:** This study showed that 28.25% of psoriasis patients have comorbidities, including cardiovascular and metabolic disorders (metabolic syndrome, type 2 diabetes mellitus, dyslipidemia), joint (arthritis psoriasis), and psychiatric disorders. **Conclusion:** Our findings highlight the necessity of understanding and managing the comorbidities associated with psoriasis, which provides crucial insights for the medical community and patients. Effective comorbid conditions management can enhance psoriasis outcomes and decrease complications.

**Keywords:** comorbidities, dyslipidemia, hypertension, obesity, psoriasis.

### INTRODUCTION

Psoriasis is an immune-mediated inflammatory disease characterized by skin inflammation, epidermal hyperplasia, increased risk of arthritis, cardiovascular disease, and psychosocial disorder.<sup>1</sup> The hallmark of psoriasis is a well-defined erythematous plaque with scales covering it. Genetics, immunology, and the environment contribute to psoriasis's complex and multifaceted pathogenesis.<sup>2</sup> A study by Daglioglu et al. found that the severity of psoriasis can negatively impact a person's quality of life (QoL), as QoL decreases with increasing disease severity.<sup>3</sup> Stress is also reported to affect the quality of life of psoriasis patients. A study by Suryawati et al. supports this, showing that stress is a risk factor for higher Dermatology Life Quality Index (DLQI) scores in patients with psoriasis (PR 6.80, CI 95% 0.96-48.33;  $p < 0.05$ ). Moreover, a positive correlation exists between higher stress scores and DLQI scores ( $r = 0.53$ ;  $p < 0.05$ ). Researchers also found that stress had a positive correlation with sensations and symptoms ( $r = 0.41$ ;  $p < 0.05$ ) and everyday activities ( $r = 0.38$ ;  $p < 0.05$ ).<sup>4</sup>

Although psoriasis can affect people at any age,

it rarely appears before age 10. It most often develops between 20 and 30 and between 50 and 60.<sup>1,5,6</sup> The prevalence of psoriasis globally is estimated to range from 0.09% to 8.5%. Psoriasis vulgaris affects 20-30% of patients with psoriasis.<sup>1</sup> Data on the prevalence of psoriasis in Indonesia is around 2.5-3%.<sup>7</sup> Segar et al. did a retrospective study about psoriasis patients in Ngoerah Hospital from 2017 to 2018 and found the prevalence of psoriasis was 0.6–0.7%, with 142 new psoriasis patients.<sup>8</sup>

Consistent with Tang et al.'s findings, psoriasis patients reported a heightened risk of developing several co-occurring diseases. Their study revealed a significantly higher risk of organ-based comorbidities among all psoriatic patients (pRR=1.20; 95% CI 1.11–1.32;  $p < 0.001$ ).<sup>10</sup> Several studies also found that severe psoriasis has a risk of developing cardiovascular disease, cerebrovascular disease, and death from cardiovascular disease.<sup>11</sup> Psoriasis also significantly increases the risk of developing metabolic syndrome.<sup>2</sup> Ferdinando et al. study found that patients with psoriasis had a higher body mass index (BMI), higher blood pressure, higher blood sugar levels, larger abdominal circumference, lower HDL

levels, and a higher incidence of angina pectoris.<sup>12</sup> Adiguna et al. studied the relationship between psoriasis vulgaris severity and the HbA1C level at Ngoerah Hospital and discovered that psoriasis vulgaris participants had significantly higher HbA1C levels than non-psoriasis subjects ( $p=0.019$ ,  $PR=6.545$ ).<sup>13</sup> This article will provide further information about psoriasis data in Indonesia. This study aims to assess comorbidities profile in psoriasis patients at RSUP. Prof. Dr. IGNG. Ngoerah, Denpasar, Bali.

## MATERIALS AND METHODS

The cross-sectional-retrospective study occurred at Prof. Dr. I.G.N.G. Ngoerah General Hospital in Bali, Indonesia, between 2018 to 2022. The population in this study is psoriasis patients that came to dermatology and venereology polyclinic in Prof. Dr. I.G.N.G. Ngoerah General Hospital. The sampling method was non-probability sampling method, with total sampling of 124

patients. A structured data collection sheet and a manual medical record system were used to gather data through a retrospective chart review. Patients meeting the inclusion criteria were new psoriasis cases diagnosed clinically or histopathologically. The exclusion criteria were patients with missing or incomplete data. The data collecting sheet included clinical (various psoriasis and comorbidities) and sociodemographic (age, gender, and body mass index) characteristics. Microsoft Excel 2016 was used to enter the data collected from the collection sheet. Descriptive statistics were used to display qualitative variables as categories and to summarize them as frequencies and percentages. The Institutional Review Board at the Faculty of Medicine of Udayana University, Bali, Indonesia, granted ethical approval for this study with number 0596/UN14.2.2.VII.14/LT/2024. We ensured the confidentiality of all patient data.

## RESULTS

**Table 1.** Characteristics of the study.

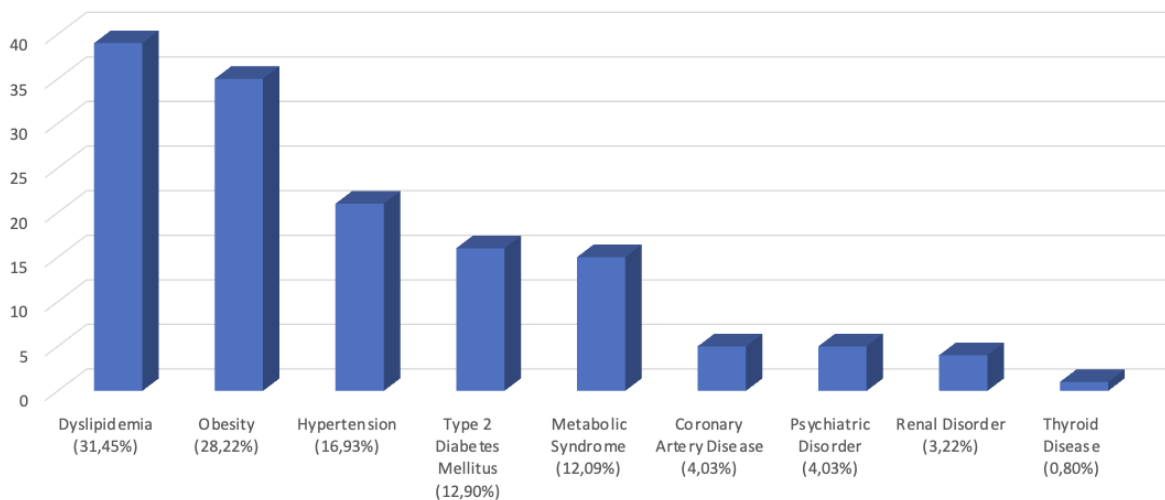
Variables	Sum (%) or mean $\pm$ SD
Total subjects	124
Age	2 – 77 years old (41.75 $\pm$ 16.83)
Sex	
• Male	71 (57.25%)
• Female	53 (42.71%)
Psoriasis Type	
• Psoriasis vulgaris	80 (64.51%)
• Guttate Psoriasis	23 (18.54%)
• Pustular psoriasis	10 (8.06%)
• Sebopsoriasis	6 (4.83%)
• Erythrodermic psoriasis	4 (3.22%)
• Inverse psoriasis	1 (0.80%)
Nail psoriasis	17 (13.70%)
Psoriasis-Arthritis	16 (12.96%)
Number of Comorbidity	
• No comorbidities	89 (71.77%)
• One comorbidity	18 (14.51%)
• More than one comorbidity	17 (13.70%)
Comorbidities:	
• Dyslipidemia	39 (31.45%)
- Hypertriglyceridemia (tryglyceride levels $\geq$ 150 mg/dL)	14 (11.29%)
- Low HDL cholesterol (HDL cholesterol level $<$ 40 mg/dL)	23 (18.54%)
- High LDL cholesterol (LDL cholesterol level $\geq$ 100 mg/dL)	27 (21.77%)
- Hypercholesterolemia (cholesterol total level $\geq$ 200 mg/dL)	16 (12.90%)
• Obesity	35 (28.22%)
- Underweight (BMI $<$ 18,5)	2 (1.61%)
- Normal (BMI 18,5 – 22,9)	87 (70.16%)
- Overweight with risk (BMI $\geq$ 23 – 24,9)	12 (9.67%)
- Stage 1 obesity (BMI 25 – 29,9)	12 (9.67%)
- Stage 2 obesity (BMI $\geq$ 30)	11 (8.87%)
• Hypertension	21 (16.93%)
- Normal (SBP 120-129 and/or DBP 80-84 mmHg)	92 (74.19%)
- Prehypertension (SBP 130-139 and/or DBP 85-89 mmHg)	11 (8.87%)
- Stage 1 hypertension (SBP 140-159 and/or DBP 90-99 mmHg)	19 (15.32%)
- Stage 2 hypertension (SBP 160-179 and/or DBP 100-109 mmHg)	1 (0.80%)
- Stage 3 hypertension (SBP $\geq$ 180 and/or DBP $\geq$ 110 mmHg)	1 (0.80%)

• Type 2 diabetes mellitus	16 (12.90%)
• Metabolic syndrome	15 (12.09%)
• Coronary Artery Disease	5 (4.03%)
• Psychiatric disorder	5 (4.03%)
• Renal disorder	4 (3.22%)
• Thyroid disease	1 (0.80%)

**Dyslipidemia:** one or more abnormalities in the lipid profile of triglyceride, HDL, LDL, and cholesterol; **Obesity:** body mass index > 23kg/m<sup>2</sup>; **Hypertension:** blood pressure > 130/85 mmHg; **Type 2 diabetes mellitus:** fasting plasma glucose ≥ 126 mg/dL or 2-hour postprandial blood glucose ≥ 200 mg/dL or HbA1c ≥ 6.5%; **Metabolic syndrome:** waist circumference (men > 102 cm and women > 88 cm), triglycerides ≥ 150 mg/dL, HDL cholesterol (men > 40 mg/dL and women < 50 mg/dL), blood pressure ≥ 130/ ≥ 85 mmHg, and fasting plasma glucose ≥ 100 mg/dL; **SBP:** systolic blood pressure; **DBP:** diastolic blood pressure.

This study included 124 psoriasis cases ranging from 2 to 77 years old (41.75 ± 16.83). The sex distribution of the patients was 71 (57.25%) males and 53 (42.71%) females, showing almost equal distribution between all sexes. The majority of patients (89 or 71.77%) lacked comorbidities, followed by those with one or more comorbidities (18 or 14.51%) and more than one comorbidity (17 or 13.70%). Psoriasis vulgaris was the most prevalent subtype in the study, identified in 80 patients (64.51%), followed by guttate psoriasis (23 patients, 18.54%), pustular psoriasis (10 patients, 8.06%), seborrheic psoriasis (6 patients, 4.83%),

erythrodermic psoriasis (4 patients, 3.22%), and inverse psoriasis (1 patient, 0.80%). Nail involvement (nail psoriasis) was 17 patients (13.70%), and joint involvement (psoriasis arthritis) was 16 patients (12.96%). The comorbidities of the psoriasis patients (Diagram 1) were dyslipidemia (31.45%), obesity (28.22%), hypertension (16.93%), type 2 diabetes mellitus (12.90%), metabolic syndrome (12.09%), coronary artery disease (4.03%), psychiatric disorder (4.03%), renal disorder (3.22%), and thyroid disease (0.80%).



**Diagram 1.** Variation of Psoriasis's Comorbidities in RSUP Prof. Dr. I.G.N.G. Ngoerah.

**Table 2.** Treatments of psoriasis and the comorbidities.

Variables	n (%)
Psoriasis	124
• Topical therapy	124 (100%)
• Fotherapy Nb-UVB	72 (58.06%)
• Methotrexate	40 (32.25%)
• CyclosporineA	9 (7.25%)
• Secukinumab	24 (19.35%)
Dyslipidemia	39
• Simvastatin	31 (79.48%)
• Atorvastatin	8 (20.51%)
Hypertension	21

• Calcium channel blocker	10 (47.61%)
• ACE inhibitor	5 (23.80%)
• Angiotensin receptor blocker	4 (19.04%)
• Diuretics	2 (9.52%)
Type 2 Diabetes Mellitus	16
• Biguanides	9 (56.25%)
• Sulfonylurea	1 (6.25%)
• Insulin	6 (37.50%)
Coronary Artery Disease	5
• Antithrombotic	5 (100%)
• Antiplatelet	5 (100%)
• Vasodilator	5 (100%)
• Diuretics	3 (60%)
Psychiatric disorder	5
• Selective serotonin reuptake inhibitor (SSRI)	5 (100%)
• Benzodiazepine	4 (80%)
• Psychotherapy	5 (100%)
• Cognitive behavioral therapy	5 (100%)

Treatments of psoriasis include topical therapy to all psoriasis patients (100%), 72 patients have Narrow-band Ultraviolet B (NB-UVB) phototherapy (58.06%), 40 patients have methotrexate (32.5%), 9 patients have cyclosporine A (7.25%), and 24 patients received secukinumab injection (19.35%). Patients with dyslipidemia received statin medication, whereas for hypertension conditions treated with calcium channel blocker (47.61%), angiotensin-converting enzyme (ACE) inhibitor (23.80%), angiotensin receptor blocker (19.04%), and diuretics (9.52%). Type 2 Diabetes Mellitus (DM) received biguanides (56.25%), sulfonylurea (6.26%), and insulin (37.50%). Antithrombotic, antiplatelet, and vasodilator medications were used to treat coronary artery disease. The psychiatrist gave selective serotonin reuptake inhibitor (SSRI), psychotherapy, and cognitive-behavioral therapy.

## DISCUSSION

This descriptive cross-sectional study of comorbidities in psoriasis patients' findings was consistent with previous studies. Previous studies showed that the mean age of psoriatic patients ranged from 12.0 to 69.5 years.<sup>10</sup> The authors found that psoriasis patients ranged in age from 2 to 77; this wide age distribution is consistent with previous studies. The sex distribution varied between each study; female sex ranged from 32.58% to 59.19%.<sup>10</sup> This finding is also similar to our study, which is 42.71% in females and 57.25% in males. A similar study from Fettahlioglu et al. showed that 32.3% detected no comorbidity, 24.2% was single comorbidity, and 43.5% was multimorbidity. The most common comorbidities found in the Fettahlioglu study were psoriatic arthritis, followed by diabetes and psychiatric disorders. These findings were different from our study, which may be due to the genetic and cultural diversity in the Bali population, which needs to be further studied.<sup>14</sup>

El-Komy et al. conducted a clinical and epidemiological study of the features of psoriasis patients

in Egypt. They found that 82.6% are psoriasis vulgaris, 11.7% are inverse psoriasis, 10.8% are guttate psoriasis, 3.1% are erythrodermic psoriasis, and 2.1% are pustular psoriasis.<sup>15</sup> This study supported our findings, which are psoriasis vulgaris is the most commonly found (64.51%), followed by other variations, such as guttate psoriasis (18.54%), pustular psoriasis (8.06%), sebopsoriasis (4.83%), erythrodermic psoriasis (3.22%), and inverse psoriasis (0.80%).

Psoriatic arthritis is a progressive inflammatory musculoskeletal disease occurring in people with psoriasis.<sup>16</sup> This inflammatory arthritis can occur in 6-42% of patients with psoriasis.<sup>17</sup> Our findings showed that 12.96% of psoriatic patients developed psoriatic arthritis, which is compatible with the previous study. In addition to skin and joints, psoriasis also commonly affects the nail.<sup>18</sup> The prevalence of nail psoriasis varies, around 6.4 to 81.8%.<sup>19</sup> The authors found that 13.70% of patients with psoriasis also have a nail involvement.

Dyslipidemia is defined as a lipid metabolism disorder characterized by an increase or decrease in plasma fraction levels (cholesterol total level  $\geq$  200 mg/dL; LDL cholesterol level  $\geq$  100 mg/dL; HDL cholesterol level  $<$  40 mg/dL; triglyceride levels  $\geq$  150 mg/dL).<sup>20</sup> Psoriasis patients tend to have more dyslipidemia than patients without psoriasis, with some studies finding that the odds ratio (OR) ranges from 1.04 to 5.55.<sup>17</sup> Mirghani et al also reported an association between psoriasis with dyslipidemia with an OR 1.63.<sup>21</sup> Kalfie et al. also conducted a study about dyslipidemia in psoriasis patients in Nepal, which showed that 96.7% psoriasis group had dyslipidemia compared to 61.7% from the non-psoriasis group, with an OR 1.709.<sup>22</sup> Several studies found that dyslipidemia can be more prevalent in psoriatic patients; nevertheless, dyslipidemia can also be a risk factor for developing psoriasis.<sup>23</sup> Wang et al. also conducted a systematic review and meta-analysis study regarding psoriasis with serum apolipoprotein A1 and B; it was found that there was a

decrease in serum apolipoprotein A1 and an increase in serum apolipoprotein B levels in psoriasis patients.<sup>24</sup> Apolipoprotein B was a protein for chylomicrons, very low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL), and low-density lipoprotein (LDL), while apolipoprotein A1 was a protein for high-density lipoprotein (HDL).<sup>20</sup> Dyslipidemia can be atherogenic, characterized by elevated triglycerides (TG), elevated LDL, and decreased HDL.<sup>25</sup> The exact pathogenesis of dyslipidemia in psoriasis remains unclear; however, some studies found a significant negative correlation between serum apolipoprotein A1 with the increase of TNF- $\alpha$ , IL-1, and IL-6. Apolipoprotein B will induce the production of TNF- $\alpha$  and IL-6 and exaggerate the inflammation.<sup>24</sup> In our study, we found that 31.45% of our psoriatic patients had a dyslipidemia condition.

Obesity is defined as excessive accumulation of adipose tissue<sup>26</sup> that can be an independent risk factor for psoriasis.<sup>17</sup> Obesity classification based on body mass index (BMI) from WHO were underweight (BMI < 18.5), normal (BMI 18.5 – 22.9), overweight with risk (BMI  $\geq$  23 – 24.9), stage 1 obesity (BMI 25 – 29.9), and stage 2 obesity (BMI  $\geq$  30).<sup>27</sup> In our research, we found that 28.22% of our psoriatic subjects were obese. A study by Czarnecka et al in Poland about overweight and obesity in psoriatic patients found that 39.46% of psoriatic patients were overweight and 37.41% were obese.<sup>28</sup> Armstrong et al's meta-analysis showed an OR of 1.66 for the association between psoriasis and obesity.<sup>17</sup>

Hypertension is one of the modifiable risk factors for cardiovascular disease and contributes to morbidity and mortality worldwide.<sup>29</sup> The classification of hypertension was as follows: stage 1 hypertension (SBP 140-159 and/or DBP 90-99 mmHg), stage 2 hypertension (SBP 160-179 and/or DBP 100-109 mmHg), stage 3 hypertension (SBP  $\geq$  180 and/or DBP  $\geq$  110 mmHg), and normal (systolic blood pressure (SBP) 120-129 and/or diastolic blood pressure (DBP) 80-84 mmHg). In our investigation, we discovered that 16.93% of psoriasis patients also had hypertension. A systematic review and meta-analysis study by Duan et al. on the relationship between psoriasis and hypertension found a significant association between psoriasis and the risk of hypertension, with an OR of 1.43. (95% CI 1.25–1.64;  $p=$ .000). In the sub-analysis of this study, there was a strong association between psoriasis and the risk of hypertension in Europeans with an OR of 1.46 (95% CI 1.20–1.77;  $p=$ .000) and Asians with an OR of 1.46 (95% CI 1.26–1.68;  $p=$ .000).<sup>30</sup> In psoriasis patients, T helper (Th)17 is more active and promotes collagen deposition in arteries, causing atherosclerosis and hypertension.<sup>31</sup>

The incidence and prevalence of type 2 diabetes Mellitus (DM) are increasing worldwide, and it contributes to cardiometabolic disease. Psoriasis shares comorbidities with type 2 DM, and both diseases share overlapping pathophysiologies, mainly in genes and susceptibility loci, which are PTPN22, ST6GAL1, and JAZF1 genes. These genes will affect T-cell receptor signaling pathways, T-cell activation, and glucose

metabolism. These defects will increase pro-inflammatory cytokines that will lead to insulin resistance.<sup>32</sup> Our study showed that 12.90% of psoriatic patients had type 2 diabetes mellitus. These findings are also supported by several studies about the association between psoriasis and type 2 diabetes mellitus, which showed that 12% of psoriatic patients are associated with type 2 DM.<sup>10</sup> A meta-analysis study showed an association between psoriasis and type 2 DM with a relative risk (RR) for diabetes is 1.27 (95% CI, 1.16 -1.40).<sup>17</sup>

Metabolic syndrome consists of several metabolic dysregulations, which are insulin resistance, atherogenic dyslipidemia, central obesity, and hypertension.<sup>33</sup> A systematic review by Liu et al. on the global prevalence of metabolic syndrome in psoriatic patients showed a prevalence of 32% (95% CI, 0.26 – 0.38).<sup>34</sup> The authors found 12.09% of metabolic syndrome in psoriatic patients. The association between psoriasis and metabolic syndrome is based on chronic inflammation from the cytokine production of Th17 cells that will induce insulin resistance, which is the main cause of metabolic syndrome and type 2 DM.<sup>35</sup>

Hypertension, obesity, dyslipidemia, insulin resistance, and metabolic syndrome in psoriasis patients will also increase the risk of cardiovascular disease.<sup>17</sup> A study in North America also showed an estimated prevalence of 14.3% of cardiovascular heart disease in psoriatic patients.<sup>36</sup> Our study showed a 4.03% of coronary artery disease in psoriatic patients, which is lower in our study, probably due to different populations. A systematic review and meta-analysis study by Liu et al found that patients with psoriasis tend to have an increase in developing myocardial infarction with an RR 1.17 (95% CI, 1.11 – 1.124).<sup>37</sup>

Other comorbidities of psoriasis in this study are psychiatric disease (4.03%), renal disorder (3.22%), and thyroid disease (0.80%). Our findings contrast with previous research indicating a prevalence of psychiatric comorbidities, renal disorder, and thyroid disease among psoriasis patients, ranging from 30 to 62.5%<sup>38</sup>, 13.46%<sup>39</sup>, and 8%<sup>40</sup>, respectively.

Correlation between treatment for comorbidities will also improve psoriasis condition and lower systemic complications. Studies have shown that anti-psoriatic therapy restores the HDL's function and composition.<sup>41</sup> A meta-analysis study by Mahil et al, found that weight loss with a lifestyle modification will improve psoriasis condition by a reduction in the PASI score, with a mean difference of -2.49.<sup>23</sup> The association between obesity and psoriasis is based on a chronic inflammatory condition from the increased levels of proinflammatory cytokines from the adipose tissue, such as IL-6, TNF- $\alpha$ , leptin-specific molecules, adiponectin, and resistin.<sup>25</sup> Other studies also showed that a one-year biological agent therapy could reduce 5% of the non-calcified plaque burden, especially with TNF- $\alpha$  and IL-12/23 antibodies. After two years, one psoriasis patient treated with IL-17 inhibitors showed improvements in coronary artery morphology and blood pressure.<sup>41</sup>

**CONCLUSION**

This study describes the characteristics of comorbid psoriasis diseases at Prof. Dr. I.G.N.G. Ngoerah Hospital. Psoriasis vulgaris is the predominant clinical manifestation. Dyslipidemia and obesity were the most frequent comorbidities, highlighting the need for a comprehensive approach to managing psoriasis and associated health risks. Proper management of comorbid conditions can improve psoriasis outcomes and reduce complications

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