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The positive correlation between psoriasis vulgaris severity degree with HbA1C level



Made Swastika Adiguna^{1*}, Made Wardhana¹, Fresa Nathania Rahardjo²

ABSTRACT

Introduction: Psoriasis is a skin abnormality based on chronic inflammation immune-mediated. Insulin resistance and psoriasis seem to have a connection, but it has not been explained clearly. HbA1c describe the glucose concentration and demonstrate the insulin resistance condition indirectly.

Objective: This study aims to understand the correlation between psoriasis vulgaris severity degree with HbA1c.

Material and methods: This study was using a cross sectional method. Psoriasis vulgaris diagnosed clinically and assessed with the PASI score. The HbA1c level examination done by drawing venous blood then analyzed with chromatography method. Samples were selected by using inclusion and exclusion criteria and

a consecutive sampling method.

Results: Total 51 subjects (33 subjects with psoriasis vulgaris and 18 subjects without psoriasis vulgaris) were included in this study. Mostly (57.6%) of the subject was mild, 24.2% moderate, and 18.2% severe psoriasis. HbA1c level of psoriasis vulgaris subjects is significantly higher than non-psoriasis vulgaris subjects ($p=0.019$, $PR=6.545$). Correlation between severity degree and HbA1c level found in positive course significantly with moderate strength of correlation ($r=0.580$, $p<0.001$).

Conclusion: HbA1c level on psoriasis vulgaris subjects are higher than non-psoriasis vulgaris. Psoriasis vulgaris severity degree positively correlated with HbA1c.

Keywords: Psoriasis vulgaris, psoriasis severity degree, HbA1c

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¹Dermatology and Venereology
 Departement, Faculty of Medicine,
 Udayana University, Sanglah
 General Hospital Denpasar, Bali-
 Indonesia

²Post-graduate in Dermatology
 and Venereology, Faculty of
 Medicine, Udayana University,
 Sanglah General Hospital
 Denpasar, Bali-Indonesia

*Correspondence to:
 Made Swastika Adiguna
 Dermatology and Venereology
 Departement, Sanglah General
 Hospital Denpasar, Bali-Indonesia
 adiguna_bali@yahoo.co.id

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INTRODUCTION

Psoriasis is a chronic inflammatory disease based on the autoimmune state with clinical manifestation of erythema plaque covered with grayish thick squamous layer.¹ Psoriasis vulgaris or plaque-type psoriasis is the most common form of psoriasis, seen in 90% of psoriasis patients. Lesions in the form of erythematous plaques with symmetrically distributed squares located in the extensors of the extremities, especially in the elbows and knees, are the manifestation of pathognomonic lesions.^{2,3} The incidence of this disease is estimated at 60 persons per 100,000 population per year. In studies in the United States, it was reported that there was a doubling of the incidence of psoriasis in the last 30 years.¹ The prevalence of psoriasis is reported to be 2% of the world population, but in America and Canada obtained at 4.6% and 4.7%, while in Asia it is estimated to be around 0.4-0.7%.²

Inflammation in psoriasis results from increased levels of cytokines such as TNF- α , Th-1, IL-1 β , IL-6, IL-7, IL-8, IL-17, IL-18, and IL-23, which

has been proven plays an important role in the pathogenesis of insulin resistance.^{4,5} IL-1 β acts as an insulin-mediated antagonist of glucose uptake by adipocyte cells, where IL-1 β is one of the direct products synthesized by TNF- α and can be bound to TNF- α receptors in fat tissue and cause inhibition of insulin action in glucose uptake. In insulin receptors, inflammatory mediators (TNF- α) give signals through the insulin receptor signal pathway, known as insulin receptor signal-1 (IRS-1). With reduced sensitivity to insulin, IRS-1 levels dropped dramatically. The effects of decreasing levels of IRS include endothelial dysfunction, which causes early atherosclerosis.^{6,7}

HbA1c (glycosylated hemoglobin or glycated hemoglobin) is a glucose bond with hemoglobin. HbA1c describes the average blood glucose concentration for three months. The amount of HbA1c formed according to blood glucose concentration. Compared to fluctuating blood sugar levels almost every time, HbA1c tends to be stable. Consequently, it can be used as an objective measurement to detect the occurrence

of insulin resistance.⁸ The mechanism for the occurrence of insulin resistance in psoriasis is a complex process and is not completely clear. Insulin resistance in psoriasis is associated with a continuous inflammatory process. Although psoriasis itself is a chronic inflammatory disease, with proper management in the form of avoidance of precipitating factors and appropriate topical and systemic treatment.⁹⁻¹¹

Insulin resistance in psoriasis patients is a result of binding to the insulin receptor (IRS-1) with inflammatory mediators that play a role in the pathogenesis of psoriasis and result in prolonged manifestations of the skin. The binding of insulin receptors results in inhibition of insulin action, induce glucose uptake from tissues (intracellular) to plasma membranes with the role of glucose transporters (GLUT-4). Inhibition of IRS-1 prevents glucose metabolism via the glycolysis pathway. This results in glucose stored in tissues could not be converted to ATP for cell metabolism, and circulating insulin could not bind to its receptors.¹² The purpose of this study was to prove the correlation between psoriasis vulgaris with HbA1c levels.

MATERIAL AND METHODS

This study used a cross-sectional study design conducted in the Dermatology and Venereology Outpatient Clinic of Sanglah General Hospital from December 2017 to March 2018. The inclusion criteria for psoriasis subjects were new psoriasis vulgaris or old psoriasis patients who had exacerbations and met the criteria for diagnosing psoriasis vulgaris clinically, aged \geq 15-65 years, and are willing to be included in the research and sign the informed consent. Subjects with a history or diagnosed with type 1 diabetes mellitus, obesity, hemolytic anemia, sickle cell anemia, acute or chronic bleeding, chronic renal failure, chronic liver disease, pregnancy, alcoholism, long-term corticosteroid consumption, consuming blood glucose-regulating drugs were excluded from this study. Diagnosis of psoriasis vulgaris is based on history and physical examination with or without histopathological examination. Non-psoriasis subjects were visitors to the Dermatology and Venereology Outpatient Clinic who were not psoriasis patient, taken by consecutive sampling and fulfilling the inclusion and exclusion criteria. The severity of psoriasis measurement have done objectively based on the clinical picture using the PASI (psoriasis area severity index) score. Mild psoriasis if the PASI score is <7, moderate degree if the PASI score is 7-12 and the degree is severe if the PASI score is > 12. The principle of HbA1c examination measured by immunoassay. Based on Indonesian Endocrinology Association (PERKENI) consensus, normal HbA1c level is <5.7%, prediabetes with 5.7-6.4%, and diabetes with \geq 6.5%. Collected data were analyzed with a descriptive and analytical method using SPSS Ver 22. This study was approved by the Research Ethical Commission of Udayana University/Sanglah General Hospital with number: 2350/UN-14/KEP/2017.

RESULT

Subjects that met the inclusion and exclusion criteria were 51 samples, consist of 33 patients with psoriasis vulgaris and 18 non-psoriasis patients. Subject characteristics such as age, gender, psoriasis vulgaris severity, HbA1c levels, and body mass index are presented in Table 1.

The results of the Spearman Rho correlation test ($r=0.490$, $p=0.004$) shows that there is a significantly medium strength positive correlation between HbA1c levels and the severity of psoriasis vulgaris. Comparative test results for HbA1c levels in subjects with psoriasis vulgaris and non-psoriasis were shown in Table 4. From the Chi-Square test results found a significant difference

Table 1. Overview of research subject characteristics

| Characteristic | Psoriasis N = 33 (%) | Non-psoriasis N = 18 (%) | p value |
|-----------------------------------|-------------------------|-----------------------------|--------------------|
| Age (years) | | | |
| 11 – 20 | 0 | 2 (11.1) | 0.239 ^a |
| 21 – 30 | 4 (12.1) | 2 (11.1) | |
| 31 – 40 | 6 (18.2) | 2 (11.1) | |
| 41 – 50 | 9 (27.3) | 7 (38.9) | |
| 51 – 60 | 10 (30.3) | 5 (27.8) | |
| 61 – 65 | 4 (12.1) | 0 | |
| Gender | | | |
| Male | 22 (66.7) | 6 (33.3) | 0.038 ^a |
| Female | 11 (33.3) | 12 (66.7) | |
| Psoriasis vulgaris severity index | | | |
| Mild | 19 (57.6) | N/A | N/A |
| Moderate | 8 (24.2) | | |
| Severe | 6 (18.2) | | |
| Chronicity | | | |
| <10 years | 17 (51.5) | N/A | N/A |
| \geq 10 years | 16 (48.5) | | |
| HbA1c level | | | |
| Normal | 21(63.6) | 17 (94.4) | 0.019 ^a |
| Elevated | 12 (36.4) | 1 (5.6) | |
| Body mass index | | | |
| Underweight (<18.5) | 0 (0) | 0 (0) | |
| Normal (18.5–24.9) | 20 (60.6) | 16 (88.9) | 0.130 ^b |
| Overweight (>25–29.9) | 13 (39.4) | 2 (11.1) | |

^aChi Square test, significant if p<0.05

^bIndependent T test, significant if p<0.05

N/A: Cannot be assessed

Table 2 Normality test between groups

| Variable | Group | Shapiro-Wilk | |
|-------------|------------------------|--------------|---------|
| | | Statistic | p-value |
| Severity | Psoriasis vulgaris | 0.778 | <0.001 |
| PASI score | Psoriasis vulgaris | 0.890 | 0.003 |
| HbA1c level | Psoriasis vulgaris | 0.756 | <0.001 |
| | Non-psoriasis vulgaris | 0.938 | 0.266* |

*Significant if p>0.05

Table 3 Correlation between HbA1c with psoriasis vulgaris severity

| Variable | Median | IQR | r | p-value |
|-------------|----------------------|------|-------|---------|
| HbA1c level | 5.4% (4.6 – 12.1%) | 1.9 | 0.490 | 0.004 |
| Severity | Mild : 19 (57.6%) | 5.95 | | |
| | Moderate : 8 (24.2%) | | | |
| | Severe : 6 (18.2%) | | | |

Spearman rho test. r=correlation coefficient, significant if p<0.05

IQR: Interquartile range

Table 4 Chi Square test HbA1c level on psoriasis vulgaris and non-psoriasis vulgaris

| Group | HbA1c | | p-value |
|------------------------|--------|----------|---------|
| | Normal | Elevated | |
| Psoriasis Vulgaris | 21 | 12 | |
| Non-psoriasis Vulgaris | 17 | 1 | 0.019* |

*Significant if p< 0.05

Table 5 Prevalence ratio elevated HbA1c level on psoriasis vulgaris compared with non-psoriasis vulgaris

| Variable | PR | 95%CI | |
|----------|-------|---------|---------|
| | | Minimum | Maximum |
| HbA1c | 6.545 | 0.924 | 46.352 |

PR=prevalence ratio, CI=confidence interval

between psoriasis vulgaris subjects with an HbA1c levels increase compared to subjects without psoriasis vulgaris ($p=0.019$). The calculation of prevalence ratio (PR) in the two groups was calculated as shown in Table 5.

DISCUSSION

The characteristics psoriasis severity was 19 subjects (57.6%) with mild psoriasis followed by eight subjects with moderate psoriasis (24.2%) and six subjects with severe psoriasis (18.2%). This result is consistent with the research conducted by Setyorini at the RSCM Jakarta resulted with the most psoriasis group was mild (40%) followed by moderate degrees (37.5%) and severe degree

(22.5%).¹³ Another study with similar results by Huerta et al. stated that psoriasis vulgaris was the highest with mild degrees with 45%.¹⁴ However this result is different from research in Japan in 2006-2008 which noted that most psoriasis subjects had moderate severity (34.6%), mild degrees (33.3%), and severe degrees (32.1%).¹⁵

Table 3 shows a significant correlation with positive direction and the strength of a medium correlation ($r=0.490$, $p=0.004$) These results answer the research hypothesis regarding the positive correlation between the severity of psoriasis vulgaris based on the PASI score with blood HbA1c levels. Our study result is supporting the results of a study by Aruna et al. stated that the severity of psoriasis significantly positively correlated with the incidence of metabolic syndrome. It is related to the pathogenesis of diseases associated with the involvement of inflammatory mediators in psoriasis, especially in chronic plaque-type psoriasis which shows the role of CD4 T cells and macrophages with inflammatory cytokines (IL-6, IL-8, IL-17, and TNF- α).¹⁵ In a study by Milcic et al., which examined metabolic syndrome in 244 psoriasis patients for two years, a significant correlation was found between the incidence of type 2 diabetes mellitus and psoriasis vulgaris with severe severity with a $p<0.001$. The pathogenesis of type 2 diabetes mellitus is thought to be related to the mechanism of insulin resistance associated with inflammation that occurs in psoriasis vulgaris.¹⁶ The results of similar studies have been mentioned previously in a study by Gisondi et al., that metabolic syndrome correlated significantly with the severity of psoriasis vulgaris with a value of $p<0.005$.¹⁷

Comparative analysis between the HbA1c levels of psoriasis subjects and non-psoriasis with Chi-Square test in the previous chapter in Table 4 found a significant increase in HbA1c levels in subjects with psoriasis vulgaris with a value of $p=0.019$ with Risk measurement resulted with PR=6.545. In this study psoriasis vulgaris was a factor of exposure that caused an increase in HbA1c levels, which in the calculation of PR obtained a result of 6.545. Subjects with psoriasis had a 6.5-fold higher risk of experiencing elevated HbA1c compared to non-psoriasis subjects. This result is supporting the study by Milcic et al. in Serbia who examined the relationship of psoriasis to metabolic syndrome in 407 patients and found the risk of psoriasis subjects having increased blood glucose levels by 1.9 times compared to non-psoriasis subjects (OR = 1.92 with 95% CI and $p<0.001$).¹⁶ This results also supported by Salunke et al. in India who examined the association of metabolic syndrome with psoriasis vulgaris in tertiary health facilities

and found that there was a 2.4-fold increased risk for subjects with psoriasis vulgaris to experience metabolic syndrome compared to subjects without psoriasis with OR=2.39 and p-value=0.007.¹⁸ Some proinflammatory cytokines play role in the insulin resistance and Psoriasis. An increase in blood glucose levels was described by increasing levels of HbA1c.^{19,20} Other factors that might affect HbA1c levels include genetic predisposition, also influenced by ethnicity and culture related to daily physical activity and a diet with a high glycemic index.^{15,21,22} This study does not evaluate the cytokines level or correlation with psoriasis.

CONCLUSION

Blood HbA1c levels were higher in subjects with psoriasis vulgaris compared to subjects, without psoriasis vulgaris. HbA1c have moderate positive correlation with psoriasis severity.

CONFLICT OF INTEREST

None declared.

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