Correlation between Expression of Interleukin-22 in Immunohistochemistry Examination with Epidermal Thickness in Psoriasis Vulgaris

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Abstract

Introduction: Psoriasis is a chronic residive inflammatory skin disease that can occur in all age, characterized with erythematous plaque and thick scales. Interleukin-22 (IL-22) is a cytokine pro-inflammatory that has an important role in inflammatory diseases. IL-22 induces migration of keratinocytes, causing hyperplasia of the keratinocyte layer resulting in thick epidermis. There was correlation between expression IL-22 with psoriasis severity.
Objective: To determine correlation between expression of IL-22 in immunohistochemistry examination in psoriasis vulgaris patients with psoriasis severity.
Methods: This study is an observational analytic study with cross-sectional design involving 30 psoriasis vulgaris patients. The diagnosis is based on anamnesis and clinical examination, the severity of the disease is measured with PASI score. Skin biopsy was taken from psoriatic plaque for immunohistochemistry examination for expression of IL-22.
Results: In this study we found that there was a mild positive correlation (r=0.466) between expression of IL-22 in immunohistochemistry in psoriasis vulgaris patients with psoriasis severity with p= 0.009. The mean expression of IL-22 in immunohistochemistry examination is 1.57±2.4. The median of PASI score is 10.2 (1.2 - 40.5). There was no significant correlation between expression of IL-22 with gender, age and duration of the disease.
Conclusion: There is a correlation between expression of IL-22 in immunohistochemistry examination in psoriasis vulgaris patients with psoriasis severity.

Keywords: psoriasis vulgaris, interleukin-22, immunohistochemistry, PASI

I. INTRODUCTION

Psoriasis is an inflammatory skin disease that is chronic recidive, can affect all ages, is characterized by reddish plaques coverd by thick silvery white scales.[1,2] Psoriasis lesions are distributed symmetrically with predilection especially in the elbow and knee area, scalp, lumbosacral, buttocks and genitalia. This typical lesion caused by excessive keratinocyte proliferastion. The causes of psoriasis are not fully understood, but multifactorial causes such as the immune system, genetics and envirnoment cause the complexity of psoriasis.[2,3]

The prevalence of psoriasis in the world population varies between 0.09% until 11.4%. in some developing countries, the prevalence is between 1.5% and 5%.[2] Based on medical records from Haji Adam Malik Central General Hospital in Medan, Indonesia from January to December 2012, from 5.342 patients in Dermatovenereology Department there was 36 patients (0.67%) diagnosed as psoriasis vulgaris.[4] The average age of onset varies from various studies, but nearly 75% psoriasis patients have onset before age 46, and 12% have onset at the age 50-60.[2,5]

Psoriasis treatment is still unsatisfactory, and the result is decrease in quality of life and became a socioeconomic burden. The absence of animal model that can produce psoriasis lesions de novo, make it hard to understand the pathogenesis of psoriasis.[6,7] The pathogenesis of psoriasis is differentiation and proliferation of keratinocytes accompanied by an inflammatory process in the epidermis and dermis. This process mediated by T cells. Abnormalities in inflammatory cytokines cells such as interleukin-1 (IL-1), IL-6, Tumor Necrosis Factor-α (TNF-α) and pro-inflammatory transcription factors such as, NF-kB and AP-1 can caused psoriasis. The presence of TNF-α, TGF-β, IL-6 make T cells differentitate into Th17.[3,5] Production of Th17 induced by IL-23,that has an important factor in pathogenesis of psoriasis. Th17 cells that produce IL-22 alone, but not produce IL-17 called

Th22 cells.[11,12] Based on the structural and gene coding, IL-22 is a group of IL-10 cytokines families. IL-22 functions are defense against microbes, regeneration and protection against damage, and an important role in chronic inflammatory disease.[8,9]

IL-22 receptors are expressed in various tissures and mediate the non-specific immune systm. IL-22 is produced by active CD4+ T cells and serve to regulate keratinocytes proliferation.[10] IL-22 cause hyperproliferation of keratinocytes and production of antimicrobal peptide, such as S100A7-psoriasin, S100A8, S100A9. IL-22 induces the migration of keratinocytes, causeing hyperplasia of keratinocyte layer resulting in thick epidermis.[8,10,11] Increased levels of IL-22 caused an abnormality and abnormal differentation of keratinocytes.

There are several studies that show an increased of IL-22 serum and expression in psoriasis patients comapred to healthy individuals. De Oliveira's study in Brazil, showed a significant increase of IL-17A, IL-22, and IL-6 serum in psoriasis patients. However, this study did not find a significant correlation between IL-22 level serum and disease severity. In Benham's study, there was no significant difference in IL-22 level serum in psoriasis patients, but an increase in IL-22 level serum in psoriasis arthritis patients compared with non-psoriasis.[12] Local production of IL-22 was measured from the supernatant skin biopsy, and there was a significant increase of IL-22 in psoriasis patients.[10,11]

Detection of IL-22 on the skin of psoriasis patients can be assessed using immunohistochemistry examination. The principe of this examination is antibody-antigen reactions on the tissue. Immunohistochemistry examination is a good detection technique and can preciesly showing certain proteins thath will be examined directly in tissues. The severity of psoriasis is measured using Psoriasis Area and Severity Index (PASI) which is the gold standard to determine the severity and the progress of therapy.

From this data, there was still controversy regarding correlation between the expression of IL-22 and severity of psoriasis need for further understanding of the pathogenesis of psoriasis. The present study was aimed to determine correlation between expression of IL-22 in immunohistochemistry examination in psoriasis vulgaris patients with psoriasis severity.

II. METHODS

The present study was a cross-section based observational study which included 30 patients of psoriasis vulgaris from February 2018 to February 2019 in the Department of Dermatovenereology, H. Adam Malik General Hospital Medan and Dr.Pirngadi General Hospital Medan, were enrolled in the study. The diagnosed of psoriasis vulgaris based on history taking and clinical examination by dermatovenereologist. The skin 4-mm skin biopsy performed by dermatovenereologist. The histologic and immunohistochemistry was performed and read by two Pathologist that blinded by the severity of the patients. The immunohistochemistry score with the Immuno Reactive Score (IRS) multiplication of score percentage of positive cells and intensity of staining. The reagen of IL-22 from GeneTex that diluted 1:100. This study has been approved by the Health Research Ethics Commission of the Faculty of Medicine, Universitas Sumatra Utara/H. Adam Malik General Hospital Medan.

III. RESULTS

Total 30 subjects, with the highest proportion was male (56.7%) and female (43.3%), the highest distribution in the age group of 36-45 years (23.3%), the mean of age 38.53±14.4 years. The most common level of education of the patients is high school graduate (63.3%). The highest distribution in the duation of the disease is 1-5 years (50%) and followed by 6-10 years (30%) with the mean duration is 5.58±4.34 years.

Tabel 1. Characteristics of the subyek

	Descriptions	**n**	**%**	**Mean ±SD**
Sex	Man	17	56.7%	
	Woman	13	43.3 %	
Age (years)	17-25	8	26.7	**38.53±14.4**
	26-35	5	16.7	**years**
	36-45	7	23.3	
	46-55	5	16.7	
	56-65	5	16.6	
	>65	0	0	
Level of education	Middle School Graduate	3	10	
	High School Graduate	19	63.3	
	University Graduate	8	26.7	
Duration of the disease (years)	< 1	1	3.3	**5.58±4.34**
	1 -5	15	50	**years**
	6-10	9	30	
	>10	5	16.7	

The median score of IL-22 expression is 1, with minimum score is 0 and maximum score is 9. The median score of PASI is 10.2 and minimum score is 1.2 and maximum score is 40.5. The correlation strength is moderate.

Table 2. Correlation between IL-22 expression and PASI

	Mean±SD	**Median (min-max)**	**p**	**r**
IL-22 Expression	1.57±2.4	1 (0-9)	0.009	0.466
PASI	12,880±9,1959	10.2 (1.2 -40.5)		

There was no significant correlation between IL-22 expression and age, sex, duration of the disease.

Table 3. Correlation between IL-22 expression and sex, age, duration of the disease

	p	**r**
IL-22 Expression and sex	0.931	0.016
IL-22 Expression and age	0.732	0.065
IL-22 Expression and duration of the disease	0.201	0.240

IV. DISCUSSION

Out of 30 subjects of psoriasis vulgaris in this study, the highest proportion 17 were male (56.7%) and 13 were female (43.3%), the highest distribution in the age group of 36-45 years (23.3%), the mean of age 38.53±14.4 years. A similar study by Putri et al in Medan, Indonesia also the proportion of male (54.5%) is higher than female (45.5%).[13] Sinniah et al in Malaysia in Tengku Ampuan Rahimah Klang Hospital whitin 2 years there were 11.6% (316/2613) male and 7.2% (215/2994) female.[14] Study by Affandi et al, based on Malaysian Psoriasis Registry (MPR) from 15.794 psoriasis patients from 2007 to 2016, showed the male percentage 56.6% is higher than female 43.3%. The ratio between male and female 1.3 : 1.[15] Similar study Bohm et al in German reported from 381 psoriasis patients, proportion of male were 60.6% and female 39.4%. Generaly, the propotion of male is higher than female, but there were no phenotype difference between male and female.[16]

The highest proportion group age 17-25 years and followed by group age 36-45 years. The mean and the standard deviation 38.53±14.4. Parisi et al rarely occur before 9 year, with prevalence 0% to 0.55%. Parisi et al also stated that there was a tendency an increase of psoriasis incidence with the increasing age.[17] Similar to Darjani et al, the highest proportion age group is < 35 years (49.1%).[18] Olsen et al in Norway from 8045 patients the highest incidences in male age group 24-27 years and female age group is 16-19 years.[19] It is consistent with psoriasis onset, that have two bimodal onset, first 16-22 years and 57-60 years. This result can caused by the sampling method and small sample. Furthermore, this disease has multifactorial causeses, so the distribution of age can also vary.

The most common level of education of the patients is high school graduate (63.3%) so we can assumed that the education is pretty good. Knowing the education level is important for assess the knowledge of the patients about the diseases, quality of life and compliance for treatment. Milcic et al stated that higher education associate with a good quality of life and manage the disease.[20]

The highest distribution in the duation of the disease is 1-5 years (50%) and followed by 6-10 years (30%) with the mean duration is 5.58±4.34 years. Similar to Milcic et al in Serbia from 201 psoriasis patient, the mean duration on the disease is 4 years.[20] As well as de Oliveira in Brazil, there was 65% patient who has the disease for more than 5 years.[21] Little bit different from Sjahrir et al in Medan, where the most common duration is 11-15 years (34.8%).[22] Egeberg et al staed that the average duration from 87.161 psoriasis patients was 7.8 years with standard deviation 5.2 years.[23] This shows the chonic and persistence of psoriasis. The difference from this study due to most of the sample is younger than other study.

Our study showed a correlation between expression of IL-22 in immunohistochemistry examination in psoriasis vulgaris patients with psoriasis severity. This correlation is moderate. Study from Nograles et al reported that IL-22 expression in skin biopsy was increased in dermatitis atopic (DA) and psoriasis compared to healthy skin, which is 16.62±8.10 for DA, 3.02±0.91for psoriasis, 0.00±0.00 for healthy skin.[24] Similar to Boniface et al that observed in supernatant psoriasis patients compared to blood serum and compared to healthy subjects, there was a increase is IL-22 level.[11] Study from de Oliveira et al also showed that IL-22 serum level is higher in psoriasi 7.8(7.8-103.9)pg/mL compared to healthy skin 4.6 pg/mL.[21]

Wolk et al observed from 47 blood plasma psoriasis patients, there was a positive correlation between IL-22 level and disease severity, with coefficient correlation was 0.73. Same with Liu et al found that IL-22 mRNA was expressed in psoriatic skin (0.929±0.054) and not found in healthy skin.[25] Study coundected by Hofny et al, showed a positive correlation between IL-22 serum and PASI, with coefficient correlation 0.688.[26] Cengiz et al in Turkey in 2015, compared IL-22R1 in psoriasis, vitiligo and healthy subjects. The IL-22R1 expressed in healthy skin and vitiligo patients. This study also observed the correlation between PASI and IL-22R1 expression, the result is the higher the intensity of IL-22 expression have the higher PASI score.[27] Wawryzkci et al reported the serum level of IL-22 in psoriasis patients compared to healthy individu and the association with PASI. The result is there was a correlation between PASI and IL-22 level serum.[28] This showed that IL-22 is not olny bystander phenomena, but also have a role in psoriasis pathogenesis.

IL-22 secreted by Th1, Th17 and Th22. IL-22 has a major three function, antimicrobial peptide, protein related to differentiation and protein that regulate the mobility and migration of keratinocytes. IL-22 have to bind to its receptors to start the function. Furthermore, these protein for differentiation of keratinocytes, especially for cornification, decreasce the thickness of granular layer and epidermal acanthosis.

From our study, we also observed there was no correlation between age, sex and duration of the disease with IL-22 expression.

V. CONCLUSION

IL-22 have a role in psoriasis pathogenesis, mainly for differentiation of keratinocyte to produce typical psoriatic skin. There is a correlation between expression of IL-22 in immunohistochemistry examination in psoriasis vulgaris patients with psoriasis severity.

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