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ApaI Vitamin D Receptor Gene Polymorphisms in Psoriasis

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Abstract: Psoriasis is a chronic autoimmune skin disorder that is an autoimmune disease and still considers a global problem. This condition is suspected to be contributed by genetic and environmental factors. Several studies have shown an association between vitamin D gene receptor polymorphisms and the risk of psoriasis. This study was an observational study, which involved 64 research subjects, who were psoriasis patients. Each subject was interviewed and went through physical examination, also Polymerase Chain Reaction - Restriction Fragment Length Polymorphism (PCR-RFLP) examination to determine ApaI (rs7975232) vitamin D receptor gene polymorphism. After the tabulation of the data, we found that the age of psoriasis onset in this study was 21 to 40 years old with an average of 34.40 ± 14.98 years old. The majority of our subjects ApaI VDR gene polymorphism genotype was aa (53.1%). This is consistent with the results of several studies conducted in Asia.

Keywords: ApaI, gene polymorphisms, psoriasis, vitamin D receptor.

INTRODUCTION

Psoriasis is a chronic inflammatory skin disorder in the form of papules and erythema plaques with a thick white scale, including an autoimmune disease played by T cells.[1,2] Psoriasis can be found in 2% of the world's population but its prevalence varies from 0.09% to 11.4% so it is a global problem.[3,4] Until now the etiology is unclear, but it is suspected that there is genetic involvement.[3] Environmental factors also play a role, including obesity, alcohol consumption, psychological pressure, smoking, and vitamin D.[1]

Vitamin D is a prohormone that not only plays a role in calcium regulation but also plays an important role in several physiological systems.[5] In the skin, vitamin D can act as an antiproliferative and promote keratinocyte differentiation, and modulate the humoral and cellular immune systems.[6,7,8] To be able to carry out its role, vitamin D must bind to its receptors (vitamin D receptor or VDR) in the target cell.

There are several types of polymorphisms in VDR that have been found, namely Cdx2, FokI, TaqI, ApaI, BsmI, Tru9I, and EcoRV, and several studies have found an association of VDR polymorphisms with psoriasis and response to treatment..[6,9] Until now, there has not

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been any research on the distribution of VDR gene polymorphisms on the risk of psoriasis events that have not been carried out in Indonesia. Therefore, researchers are interested in conducting this study to determine the role of vitamin D receptor gene polymorphisms, especially ApaI and TaqI, on the risk of psoriasis.

METHODS

This study is observational in psoriasis patients. Each patient who had agreed to participate in this study and signed informed consent, underwent anamnesis, physical examination, and blood sampling. Blood sampling was carried out at the Outpatient Unit of the Allergy and Immunology Division of the SMF, Dermatology and Venereology, H. Adam Malik Hospital Medan, and several other hospitals. Polymerase Chain Reaction - Restriction Fragment Length Polymorphism (PCR-RFLP) examination was conducted to examine the polymorphism of the ApaI vitamin D receptor gene (rs7975232) at the Integrated Laboratory of the Faculty of Medicine, Universitas Sumatera Utara. The collected data is then presented in a frequency distribution table.

RESULTS

There are 64 subjects involved in this study. The distribution of study subjects based on the age of onset and polymorphisms of the VDR ApaI gene can be seen in Table 1.

Information regarding age onset is divided into several age groups. Most age groups were found in the age group 21-30 years with 15 people (23.44%) and the age group 31-40 years with 15 people (23.44%). Meanwhile, the genotype frequency was mostly found with 34 people (53.1%), followed by Aa genotype, namely 25 people (39.1%) and AA with 5 people (7.8%).

Table 1. Distribution of study subjects based on age-onset and genotype of the VDR ApaI gene polymorphism

Characteristics	Subject n (%)
Age onset	
≤ 10 year old	3 (4.69)
11 - 20 year old	9 (14.06)
21 - 30 year old	15 (23.44)
31 - 40-year-old	15 (23.44)
41 - 50-year-old	12 (18.75)
51 - 60-year-old	6 (9.38)
> 60 years old	4 (6.25)
ApaI VDR gene polymorphisms	
AA	5 (7.8)
Aa	25 (39.1)
aa	34 (53.1)
Total	64 (100.0)

The mean age of onset in genotype AA, Aa, and aa groups was 38.8 ± 14.5 years, 30.3 ± 16.8 years, and 36.8 ± 13.3 years, respectively. In general, the mean age of onset was 34.40 ± 14.98 years.

Table 2. Distribution of onset age of vitamin D gene polymorphisms in ApaI VDR

ApaI VDR gene polymorphisms	Mean age onset (years)
AA	38.8 ± 14.5
Aa	30.3 ± 16.8
aa	36.8 ± 13.3

In the study subjects, calculations were performed to assess the Hardy-Weinberg balance for the ApaI VDR gene and showed a p-value = 0.89. Then, the allele frequencies of A and C in the study subjects were 0.27 and 0.73. Through these

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calculations, it can be found that the VDR ApaI gene genotype does not deviate from the Hardy-Weinberg balance so that it can be concluded as a polymorphism.

Table 3. *Hardy-Weinberg Equilibrium* (HWE) *Apa*I (rs7975232)

Genotype	Observed	Expected
AA	5	4.8
AC	25	25.4
CC	34	33.8
Var allele freq	0.73	

$X^2 = 0.018$ X^2 test *p* value = 0.892

DISCUSSION

In this study, it was found that the greatest age-onset was found in the 21-30 year age group and the 31-40 year age group. This is not following several large studies to get two peaks of age onset in patients, namely at the age of 15 to 20 years and 55 to 60 years.[10] The study by Henseler and Christopher distinguished psoriasis into two groups based on age onset, namely, type I psoriasis with an onset of fewer than 40 years of age which is the most common type, and type II psoriasis with an onset of more than 40 years. Individuals with type I psoriasis usually have a family history of psoriasis with a more severe degree of disease than type II psoriasis.[11]

Psoriasis can appear at any age and can be found after birth and in the elderly age group. It is often difficult to determine the age of psoriasis onset because it usually depends on the patient's memory which can be inaccurate.[10] The mean age of onset of psoriasis patients in this study was 34.40 ± 14.98 years. This is consistent with an epidemiological study by Affandi et al in Malaysia which found that the mean age of onset was 35.14±16.16 years.[12] The youngest mean age of onset was found in genotype Aa, namely 30.3 ± 16.8 years. Research by Park et al showed that there was a significant relationship between VDR gene polymorphisms and psoriasis.[13] However, in this study we did not look for the correlation within.

Several studies have found an association between VDR polymorphisms and susceptibility to psoriasis.[6] The polymorphism variant of ApaI is located on intron 8 with nucleotide A like the A allele and nucleotide C as the allele. It is not yet known with certainty the function of this polymorphism, but several studies have found a relationship between ApaI and several diseases.[9] A study in South Korea by Park et al in 1999 found that the ApaI polymorphism had a significant association with psoriasis.[13] Kaya et al also found an association between ApaI polymorphism and psoriasis in a population in Turkey and this association was more pronounced in the Psoriasis Vulgaris group than in the acute guttate psoriasis. However, there are differences in genotype frequency between the two populations.[14]

Genotype aa is a type of polymorphism that is mostly found in the subjects of this study. A similar view was found by Pontoriero et al in the South American population and Park et al in the South Korean population.[13,15] However, research conducted by Rucevic et al in Croatia found that the most genotypes found were Aa.[16] In a meta-analysis study by Liu et al, it can be seen that research conducted on East Asian races shows the majority of genotypes are aa, whereas in Caucasian and African races the genotype of ApaI is mostly found is Aa..[17] The differences in distribution obtained from these studies are caused by differences in the population under study. Therefore, it is advisable to carry out a similar study in other populations and carry out further studies to see the relationship of

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VDR gene polymorphisms with the risk of psoriasis.

CONCLUSION

In this study, we found that age-onset psoriasis was found in the 21 to 40 years age group with a mean of 34.40 ± 14.98 years. Also, it was found that the most genotypes of the VDR ApaI gene polymorphisms in this study were aa.

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