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Research Article

Relationship of Stress to Recurrence of Atopic Dermatitis in Adults

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Abstract

Atopic Dermatitis is a chronic disease common in children but can also reoccur in adults. Atopic dermatitis cases in Indonesia is five of the most common skin disease. Atopic Dermatitis is mainly caused by genetic factors and specific environments, including neurological and immunological factors. Of the many factors associated with atopic dermatitis, psychological stress can cause a recurrence of atopic dermatitis in adults and could cause an increase in the severity of atopic dermatitis symptoms. This research aims to find out if stress is related to the recurrence of atopic dermatitis in adults. This research is a correlation study done in February 2017 with 53 respondents that have passed the restriction criteria made by the researcher. The results from the statistical test show that $p=0.003$ ($p<0,05$) and $r=0,398$, which means that there is a significant correlation between stress and the recurrence of atopic dermatitis in adults, with low correlation strength.

Keywords: Stress, Atopic Dermatitis

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INTRODUCTION

Atopic dermatitis (AD) is a typical skin inflammatory disease, chronic residif, with characteristic itching and frequent recurrence. It occurs most often in infancy and childhood but can continue into adulthood. Skin disorders can be in the form of pruritus, erythema, papules, oedema, and vesicles in the acute and chronic stages characterized by lichenification. This disease is often associated with elevated serum IgE levels and a history of atopy in patients and their families, such as allergic rhinitis, bronchial asthma, allergic conjunctivitis, or atopic dermatitis itself. ^{1, 2, 3}

Atopic dermatitis is a multifactorial process, so many factors play a role in the occurrence of this disorder. The aetiology and pathogenesis of atopic dermatitis are still unknown, but several factors are considered the trigger for this disorder, including genetic, immunologic, psychological, and environmental factors. Of these factors, psychological stress is considered one of the things that can cause atopic dermatitis to relapse because stress causes changes in the balance of stress hormones such as cortisol and norepinephrine, which have an impact on the balance of T-helpers which play a role in increasing hypersensitivity to allergens, thereby increasing the severity of atopic dermatitis ⁴.

Epidemiological research shows that in recent years in developing countries, the prevalence of AD has increased quite high, namely 2 to 3 times. The prevalence is 15-30% in children and 2-10% in adults. The increase in the incidence of

AD follows the level of community welfare ^{3, 5}. Based on the background of this research, the formulation of the problem in this study was formulated in the form of the following questions "Is there a relationship between stress and AD recurrence in adults?" with the aim of the study, namely to find out whether stress can be a trigger for AD recurrence in FK UKI students class 2013.

LITERATURE REVIEW

The skin is the outermost organ. The area of the skin of an adult is about 2 m², with a weight of approximately 16% of body weight. The skin is a vital organ and is a mirror of health and life. The skin is also very complex, elastic and sensitive, varying in climatic conditions, age, sex, and race. The skin has various protective, absorbent, sense of taste, and defence functions. The skin division comprises three main layers, namely the epidermis, dermis and subcutis ^{1, 6}.

The epidermis consists of the stratum corneum, stratum lucidum, stratum granulosum, stratum spinosum, and stratum basale. The stratum corneum is the outermost layer of skin which is the end product of epidermal cell differentiation, forming 15-25 layers of strong and dense cells. Every day one layer of the uppermost stratum corneum is desquamated, and a replacement layer is synthesized in the stratum basale. This barrier protects the body from the environment and normally prevents the penetration of irritants and allergens through the skin ⁷.

Corneocytes are composed of keratinized threads and are covered by a tough and flexible substance called the cornified envelope. The horned sheath consists of proteins (involucrin and loricrin). Corneocytes covered by this sheath bind to fat, forming structures such as brick and mortar, and in this analogy, bricks represent corneocytes filled with keratin filaments and the proteolytic products of filaggrin, surrounded by a tightly bound protein coat. The cement mortar represents an intercellular matrix composed mostly of nonpolar lipids forming a hydrophobic covering. These lipids consist of 50% ceramides, 25% cholesterol, and 10-20% long-chain free fatty acids arranged in a repeating array of lamellar layers. These lamellar lipids are very important in normal barrier function; otherwise, they will disrupt barrier function⁵. In addition, on high brick walls, some corneodesmosomes attach skin cells, which is analogous to an iron rod^{5,8}.

The stratum lucidum is located directly under the corneum layer, a layer of flattened cells without a nucleus with protoplasm that turns into a protein called eleidin. These layers appear more clearly on the palms and soles^{3,5}. The stratum granulosum is 2 to 3 layers of flattened cells with a coarse-grained cytoplasm and a nucleus. Filaggrin is formed in the granular layer of the epidermis. Filaggrin has an important role in the initial thinning of keratinocytes in corneocyte formation and intact skin barrier. The proteolysis of filaggrin occurs in the stratum corneum. Proteolysis of filaggrin releases histidine, which is then deaminated to form trans-urocanic acid, converted to cis-urocanic acid by ultraviolet irradiation. The glutamic acid released by filaggrin is converted into pyroglutamic acid, a natural moisturizing agent. In addition, filaggrin also contains several hydrophilic amino acids that can retain water⁶.

Stratum spinosum consists of several layers of polygonal-shaped cells that vary in size due to mitosis. The protoplasm is clear because it contains much glycogen, and the nucleus is located in the middle. These cells are closer to the surface, the more flattened they are. Between the cells of the stratum spinosum, there are bridges between cells consisting of protoplasm and keratin. The adhesions between these bridges form small round thickenings called Bizzozero nodules. Among the spinous cells are Langerhans cells and stratum spinosum cells contain a lot of glycogen⁹.

The stratum basale or germinativum consists of cuboidal cells arranged vertically on a dermo-epidermal junction based on a palisade. This layer is the lowest layer of the epidermis. These basal cells undergo mitosis and function reproductively. This layer consists of two types of cells: columnar cells with basophilic protoplasm, oval and large nuclei connected by intercellular bridges, and melanin-forming cells or clear cells, light-coloured cells with basophilic cytoplasm and dark core, and contains pigment grains (melanosomes).

The layer below the epidermis is the dermis, thicker than the epidermis. This layer consists of a dense elastic and fibrous layer with cellular elements and hair follicles. It is divided into two parts, namely the papillary part, which is the part that protrudes into the epidermis and contains the ends of nerve fibres and blood vessels, and the reticular part, which is the lower part that protrudes subcutaneously. This part consists of supporting fibres such as collagen, elastin and reticulin. The base of this layer consists of a viscous fluid of hyaluronic acid and chondroitin sulfate, in which fibroblasts also form, forming bonds containing hydroxyproline and hydroxycillin. Young collagen is flexible with age. It becomes less soluble so that it becomes stable. Reticulin is similar to young collagen. Elastic fibres are usually wavy, amorphous in shape and easily expand and are more elastic.

The subcutis layer is a continuation of the dermis, which consists of loose connective tissue containing fat cells. Fat cells are round cells, large, with the nucleus pushed to the edge of the cytoplasm of the increased fat. These cells form clusters separated from one another by fibrous trabeculae. Layers of fat cells called adipose panniculus serve as food reserves. There are peripheral nerve endings, blood vessels, and lymph in this layer. Fat tissue thickness is not the same, depending on its location. The abdomen can reach 3 cm in the eyelid area, and the penis is very thin. This fat layer also functions as a cushion^{1,3,5}.

Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by recurrent pruritus, lichenification and history of atopies such as allergic rhinitis, asthma, or allergic conjunctivitis in patients and their families. Skin disorders that arise can be pruritus, erythema, oedema, vesicles in the acute stage, and lichenification in the chronic stage. This skin disease often occurs in infancy and childhood but can continue into adulthood. Atopic dermatitis causes a considerable psychological burden, leading to sleep disturbances, feelings of anxiety, feelings of unattractiveness, and depression. AD is a multifactorial process, so many factors influence this skin disorder. The exact aetiology and pathogenesis of AD are also unknown. However, several factors are considered the cause or trigger of atopic dermatitis. AD as a specific inflammation of the dermo-epidermal compartment that occurs in atopic skin that reacts abnormally with clinical manifestations. The onset of itching and eczematous inflammatory skin lesions¹⁰.

Atopic dermatitis is a skin disease that often affects children, with a prevalence in children of 10-20% and adults of 1-3% in America, Japan, Europe, Australia, and other industrialized countries. Meanwhile, in agrarian countries such as China and Central Asia, the prevalence of AD is lower. AD is more common in women than men by approximately 1.3:1¹¹. The aetiology of AD is still unknown, and the pathogenesis is complex, but several factors are thought to play a role as a trigger for this disorder, such as genetic, immunologic, environmental and lifestyle factors, and psychological factors.

Atopic dermatitis is a multifactorial syndrome. Until now, the cause of AD in children is not known with certainty. However, AD disease is influenced by genetic (intrinsic) and environmental (extrinsic) factors that can regulate gene expression at a certain level. Genetic factors can be identified using a good history, but in some studies, it turns out that 15-30% of cases do not have a genetic history. Environmental factors act as trigger factors for genetic predisposition. Environmental factors include socioeconomic conditions, number of family members, lactation, the introduction of foods containing allergens in the early stages, environmental pollution, exposure to cold air and psychological stress^{12,13}.

Atopic dermatitis is closely related to atopy, which is a term that indicates an individual and familial tendency to be sensitized and produce IgE antibodies in response to exposure to allergens, which are usually proteins and cause typical allergic symptoms. Hereditary factors in individuals are believed to cause atopic tendencies in infants and children. Several studies have shown that half to two-thirds of patients with AD have a history of atopy in one or both parents, and this percentage is higher when the sibling also has a history of atopy. A family history of allergic disease is useful as an early marker of atopic disease.

Many epidemiological studies have proven that genetic factors have a role in causing atopy. Children born to families with a history of atopy are more likely to suffer from atopy. If one parent has a history of atopy, the probability of their child becoming atopy is 19.8%. If atopy affects both parents, then

the frequency of the possibility of their child suffering from atopy becomes 42.9%, 72.2% becomes atopy if both parents have the same atopy history, and 85% becomes atopy if both parents and siblings have a history of atopy ^{14,15}.

The pathogenesis of atopic dermatitis is still unknown, but several factors are considered triggers of this disorder, including genetic factors, neuroimmunological factors, skin barrier function dysfunction, psychological factors, and environmental factors ^{8; 16}. Psychological stress is one of the internal factors triggering several skin disorders related to impaired defence function in the epidermis layer of the skin, such as psoriasis and atopic dermatitis. However, not many studies have been able to explain the pathogenesis clearly. Based on several further studies, three potential theories can explain the negative effects of psychological stress on host defence function ¹⁷, namely psychoneuroimmunoendocrine dysfunction, elevated plasma endogenous glucocorticoid levels, and the skin steroidogenic system.

The detrimental effect of psychological stress and increased plasma levels of endogenous glucocorticoids on skin permeability function is due to the mechanism of inhibition of lipid synthesis in the epidermis. It causes a decrease in the production of epidermal lamellar bodies, a functional organelle in charge of delivering fat, desquamating enzymes and antimicrobial peptides to the crevices of the stratum corneum, which play a role in maintaining permeability and defence functions against microorganisms ^{17; 18}. Psychological stress conditions cause changes in the structure and function of the stratum corneum layer of the epidermis, which causes changes in the expression of antimicrobial peptides in the epidermis, thereby directly increasing the risk of skin infections. Robles assessed the response to psychological stress on skin barrier function by measuring Transepidermal Water Loss (TEWL). TEWL is an indication of the skin's ability to prevent water loss from the deep layers of the skin. Psychological stress causes a delay in the restoration of skin barrier function and an increase in plasma cortisol, norepinephrine, interleukin, and Tumor Necrosis Factor (TNF) levels ¹⁹.

These changes in skin permeability induced by psychological stress are mediated by increased levels of endogenous glucocorticoids. Psychological stress in the form of insomnia causes the impaired function of the stratum corneum in the form of a decrease in the proliferation of epidermal cells, interferes with epidermal differentiation and decreases the density and size of the corneodesmosome. Impaired skin permeability barrier function is associated with decreased production and secretion of lamellar bodies, which will affect epidermal fat synthesis ²⁰. Atopic skin inflammation is mediated by a complex temporal-spatial expression of cytokines and chemokines. Wounds from trauma, infection, or even scratching during itching are associated with atopic skin, stimulating local production of primary proinflammatory cytokines, such as interleukin 1 (IL-1) and tumour necrosis factor- α (TNF- α). These cytokines bind to vascular endothelial receptors, activate cellular signalling, and induce endothelial cell adhesive molecules, thereby causing the extravasation of inflammatory cells into the skin ²¹.

The main symptom of AD is itching or pruritus that appears throughout the day and worsens at night which can cause insomnia and decreased quality of life. The intense itching sensation causes the sufferer to scratch his skin so that it gives a scratch mark which secondary abnormalities will follow in the form of papules, erosions or excoriations and then lichenification will occur if the process becomes chronic ^{15; 22}. The appearance of eczematous lesions can be acute

(erythematous plaques, prurigo papules, papulovesicular), subacute (thickening and plaque excoriations), and chronic (lichenification). Eczematous lesions can become erosive when scratched, and exudation occurs, resulting in crusted lesions. Weeping and crusted skin lesions are common in advanced diseases ²³.

Until now, the management of atopic dermatitis is mainly aimed at reducing the signs and symptoms of the disease, preventing/reducing recurrence so that it can overcome the disease in the long term, and changing the course of the disease. The management of atopic dermatitis is adjusted to the state of the disease, consisting of basic adjuvant therapy (skin protection) and, if necessary, anti-inflammatory and identification and avoidance of precipitating factors. Treatment is mainly symptomatic, i.e. hydration of the skin and reducing itching ²⁴. Effective early treatment must be given to prevent the disease from getting worse. Management emphasizes long-term-control, not just relapse ²⁴.

It is difficult to predict the prognosis of AD in a person. The prognosis will be worse if both parents suffer from atopic dermatitis. There is a tendency for spontaneous improvement in childhood, and there is often a recurrence in adolescence to adulthood. Most cases persist at the age of over 30 years. Spontaneous healing of atopic dermatitis suffered from infancy occurs after the age of 5 years by 40-60%, especially if the disease is mild. Atopic dermatitis in children followed from infancy to adolescence 20% disappeared, and 65% reduced symptoms. More than half of treated atopic dermatitis in adolescents relapses into adulthood ^{4; 24}.

Stress is a universal phenomenon that occurs in everyday life and cannot be avoided and will be experienced by everyone. Stress can be defined as a state we experience when a mismatch exists between accepted demands and our ability to cope ²⁵. Stress can also be defined as an unavoidable reality of everyday life caused by changes that require adjustment ²⁶. Stress is a set of physiological changes resulting from the body being exposed to a threat. Stress has two components, namely physical changes, namely physiological and psychological changes, namely how a person feels about the circumstances in his life. These changes in physical and psychological states are referred to as stressors, namely experiences that induce a stress response ²⁷.

Stress is divided into two based on individual perceptions of the stress they experience, namely distress (negative stress) and eustress (positive stress) ²⁸. Stuart and Sundeen classify stress levels: as mild stress, moderate stress and severe stress ^{29; 30}. Sources of stress are all stimulatory conditions that are noxious and produce a stress reaction, i.e. the sum of all nonspecific physiological responses that cause damage to a biological system. Acute stress reaction (acute stress reaction) is a temporary disorder that appears in an individual without other obvious mental disorders and occurs due to very severe physical and mental stress, usually subsides within a few hours or days. A person's vulnerability and coping capacity play a role in the occurrence of acute stress reactions and their severity ^{31; 32}. There are four sources or causes of psychological stress: frustration, conflict, pressure, and crisis.

RESEARCH METHOD

This research is an analytic study with a cross-sectional design. The study was carried out at the UKI Medical Faculty from 6-10 February 2017. The research population was 248 UKI Medical Faculty students from the 2013 batch. The samples in this study were those who met the inclusion criteria. This study uses 1 data source, namely data taken directly from respondents using questionnaires. The data

collection process was carried out by a) the existing respondents were given an explanation regarding the course of the research to be carried out by the researcher and ensured that all had signed the informed consent form; b) researchers interviewed respondents using a questionnaire tool, and c) the completed questionnaire will be used as a data source and will be processed using the SPSS (Statistical Product and Service Solutions) program. Data processing is done through editing, coding, transferring, and tabulating stages. Research data will be analyzed using univariate and bivariate analysis.

RESULT AND DISCUSSION

This study of the relationship between stress and recurrence of atopic dermatitis was conducted on university students aged over 17 years at the UKI Faculty of Medicine who had met the inclusion criteria. This research took place on 6 – 10 February 2017, with 53 respondents. The characteristics used in this study were based on age and gender.

Table 1: Characteristics of Respondents by Age

Age	Number	%
21 years old	49	92,5
22 years old	4	7,5
Total	53	100

From the table above, information is obtained that most respondents are 21 years old, as many as 49 people or 92.5%.

Table 2: Characteristics of Respondents by Gender

Sex	Number	%
Male	13	24,5
Female	40	75,5
Total	53	100

From the table above, information is obtained that most respondents are female, as many as 40 people or 75.5%. Based on data processing, the results obtained that stress levels can be categorized as stress and not stress are as follows (Table 3).

Table 3: Stress Frequency Distribution

Stress	Number	%
No	14	26,4
Yes	39	73,6
Jumlah	53	100

Based on the table above, it is known that of 53 respondents, the majority of 39 people (73.6%) experienced stress. Based on the respondents' answers, the level of atopic dermatitis can be categorized as mild, moderate and severe, as shown in table 4.

Table 4: Frequency Distribution of Atopic Dermatitis

Atopic Dermatitis	Number	%
Mild	32	60.4
Severe	21	39.6
Heavy	0	0
Jumlah	53	100

Based on the table above, it is known that of 53 respondents, 32 people (60.4%) suffered from mild atopic dermatitis. In

this study, to examine the relationship between stress and recurrence of atopic dermatitis in adults, nonparametric statistics were used using the Pearson Rank. Analysis of the relationship of stress with atopic dermatitis recurrence in adults.

Table 5: Correlation test between stress and recurrence of atopic dermatitis in adults.

		Atopic Dermatitis	Stress
Atopic Dermatitis	<i>Pearson Correlation</i>	1.000	0,398
	Sig. (2-tailed)		0,003
	N	53	53
Stress	<i>Pearson Correlation</i>	0,398	1.000
	Sig. (2-tailed)	0,003	
	N	53	53

Based on the results of statistical tests using the Pearson Rank above, from the tests carried out, the results obtained r (correlation) = 0.398, which means the strength of the relationship between stress and recurrence of atopic dermatitis in adults is low. It has a positive or unidirectional relationship, while the p -value (probability of) = 0.003 or $p < 0.05$, which means a significant relationship.

Characteristics of respondents described from the study results include demographic data in the form of age and gender. Based on the study results, it was found that the majority of respondents were 21 years old (92.5%), and respondents aged 22 years (7.5%) were included in the young adult age group. In young adulthood, individuals have an increased habit of rational thinking, have adequate life experience and education and are psychosocially considered more capable of solving personal and social tasks. According to Notoatmodjo, the older a person is, the better his mental development processes are, but at a certain age, this mental development process is not as fast as when he was in his teens ³³.

Based on the results of the study, it was found that the majority of respondents were female (75.5%) and male respondents (24.5%). According to the American Psychological Association (APA), men and women react to stress differently, physically and mentally. Based on the APA study, women experience symptoms of stress more often, but women are also easier to deal with stress than men. About half of the women studied by the APA complained of increased stress in the past five years. The incidence of atopic dermatitis in women in young adults is higher than in men, while at the age of children, the incidence is more in men ^{34,35}.

Analysis of the Relationship between Stress and Recurrence of Atopic Dermatitis - Based on the results of the Pearson Rank statistical test above, the results obtained r (correlation) = 0.398, which means the relationship between stress and recurrence of atopic dermatitis in adults is low and has a positive or unidirectional relationship, while the p -value (probability) = 0.03 or $p < 0.05$, which means that there is a significant relationship. So it can be concluded that there is a correlation between stress and recurrence of atopic dermatitis in adults. The result of the correlation coefficient is 0.398, which means that the correlation is positive, so if the respondent is stressed, the severity of atopic dermatitis gets worse.

CONCLUSION

There is a direct relationship between stress and recurrence of atopic dermatitis in adults with moderate strength. Thus, young adults with atopic dermatitis are expected to increase further their knowledge about atopic dermatitis and what factors can trigger recurrences in young adults by seeking information about atopic dermatitis through electronic media, print media, and in consultation with a dermatologist so that the symptoms of atopic dermatitis do not get worse. Health agencies are also expected to increase their attention in disseminating information about atopic dermatitis so that people who experience symptoms of atopic dermatitis can know about their disease. Then they are not going to be stressed because there are symptoms of atopic dermatitis in their bodies and also so that people with atopic dermatitis know the factors anything that can trigger a relapse.

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