

Research Article**Study of Stress with Atopic Dermatitis in Adults**

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ABSTRACT:

Atopic dermatitis (AD) is a widely prevalent skin disease that affects both children and adults. The aim of the study was to assess the association of perceived stress (single-item, self-reported) with AD (self-reported) in a sample of Pakistani adults using a cross-sectional research design. A cross-sectional study was conducted using data from 400 adults aged 20 years and older collected in the July 2017 to December 2017 at Nishtar Hospital Multan. An increased level of self-reported stress was positively associated with an increased prevalence of AD in Pakistani adults (p for trend <0.001). After adjusting for covariates, the odds ratios (ORs) of AD among participants reporting high and very high levels of stress were 1.81 (95% confidence interval (CI): 1.22, 2.67) and 2.17 (95% CI: 1.38, 3.42), respectively, compared with those who reported low levels of stress. This study found a statistically significant association between perceived stress and AD among Pakistani adults.

INTRODUCTION

Atopic dermatitis (AD), a chronic inflammatory skin disease characterized by eczematous lesions and intense itching, is a global public health concern not only in children but also in adults [1–3]. AD is caused by a genetic predisposition and environmental factors, including null mutations in filaggrin (FLG), climate, urban living, and diet [4,5]. However, the major etiologic factor remains unknown. AD may be associated with psychological problems, such as anxiety, depression, sleep disorders, and personality disorders [6,7]. Of the many factors related to AD, psychological stress is thought to be particularly important [6,8]. Furthermore, numerous studies have demonstrated that psychological stress has a significant impact on skin inflammation [9]. Several studies have demonstrated a relationship between stress and AD [10,11]. Most have reported that psychological stress exacerbates AD, and patients with AD experience a worsening of the skin after exposure to stress [12–14]. Considering the mechanism, psychological stress produces various neuroendocrine mediators, including adrenocorticotropic hormone, β -endorphin, catecholamines, and cortisol, which in turn activates local neurogenic inflammation and disrupts skin barrier function [15]. Although the association between AD and mental health comorbidities in children and adolescents has been well established [16], there are only a few recent population-based studies of AD for adults [17,18]. Although AD most frequently starts in early infancy and persists during adolescence, it is also

highly prevalent in adults [19]. However, relatively little is known about the association between AD and psychological stress in adults, particularly in Pakistan. The psychological stress response was conceptualized as perceived stress in this study. In the present study, the self-rated perceived stress level was used as a measure of participants' perception regarding how much stress they are under in everyday life. Therefore, the goal of this study was to determine the association between perceived stress and AD in Pakistani adults by using data obtained from the July 2017 to December 2017 Nishtar Hospital Multan, a nationally representative survey conducted in the Republic of Pakistan.

Method

This study was based on data collected in the dermatology department Nishtar Hospital Multan. Samples from the dermatology department were selected using a stratified, multi-stage, cluster-sampling design with proportional allocation based on the National Census Registry. Detailed information on the survey design and sampling procedures has been reported elsewhere [20]. As appropriate, the frequency, mean, and 95% confidence intervals (CIs) were calculated to describe the demographic characteristics according to categories of AD or perceived stress. We evaluated differences in categorical variables using the Mantel-Haenszel chi-square test, and differences among groups in continuous variables were examined using the linear trend

test. Logistic regression models were used to estimate the odds ratio (OR) and 95% CIs for AD among participants who reported medium to very high stress compared with the reference group (those who reported low stress). The presence of a linear trend was evaluated by defining a linear contrast in each of the linear and logistic regression models. All statistical analyses were conducted using SAS v9.3 (SAS Institute, Cary, NC, USA). Statistical analyses accounted for the survey design, and appropriate procedures in SAS,

such as `surveyfreq` and `surveylogistic`, were used with weighted data.

RESULTS

This study included 400 adults aged 20 years and having AD. The prevalence rates of AD did not differ significantly according to sex, BMI (body mass index), income, and alcohol consumption. However, age, educational level, and cigarette smoking were significantly associated with prevalence of AD (Table 1). The mean age of participants with and without AD was 41.5 year and 50.4 year, respectively.

Table 1. Distribution of demographic characteristics by prevalence of atopic dermatitis among Pakistani adults 20 years of age (n (%)).

P=0.685			
Sex	NO	AD	NO AD
male	200	86 [43%]	114 [57%]
female	200	112 [56%]	88 [44%]

BMI			
0.416			
<18.5	30	[6%]	[94%]
18.5-22.5	50	[40%]	[60%]
23-27.4	80	[45%]	[55%]
>27.5	40	[12%]	[88%]

Table 2. Demographic characteristics by categories of self-reported stress

CHARACTERISTICS	LOW	MEDIUM	HIGH	VERY HIGH
AD	1.10%	1.5%	2.5%	2.9%
MALE	12%	24%	24%	40%
FEMALE	2%	5%	13%	80%
CIGARETTE SMOKING	50%	25%	15%	10%
EDUCATION	10%	25%	25%	40%

DISCUSSION

This nationwide population-based study of Pakistani adults found that 1.8% of participants had AD, which is quite similar to the results of a recent study showing a 1.88% of AD prevalence in Pakistani adults [21]. This finding is consistent with previous reports that AD is one of the most common skin diseases, with a prevalence of 1% to 3% in adults [22,23]. In previous population-based studies, the prevalence of AD was 1.2% in Pakistani males aged around 20 years, whereas the prevalence of AD among adolescents aged 12–18 years was 22.4% [24,25]. In this study, we found that females were more stressed than males, which is consistent with a report that in Pakistani, women are more likely to experience stress and depression than men [26]. In addition, psychological stress was correlated with smoking cigarettes and drinking alcohol. Similar to our results, many experimental and epidemiological studies support the relationships between stress and such behaviors [27,28]. The results of this study show that psychological stress is related to AD in Pakistani adults. We found that participants

with higher levels of stress had an increased prevalence of AD compared with those who had lower levels of perceived stress. Moreover, the ORs of AD were significantly increased with increasing psychological stress even after controlling for potential confounders. Overall, higher self-reported levels of psychological stress were associated with higher odds of AD and the association was robust after adjusting for multiple sociodemographic and lifestyle factors. Compared with those in children or adolescents, few epidemiological studies have been conducted on relationships between AD and psychological stress in adults [29]. However, several studies reported that adult patients with AD have significantly higher levels of psychological stress, including depression, than adults without AD [29,30]. Notably, a recent study reported a strong association between psychological stress and AD among young Pakistani males around 20 years old [24]. These findings are consistent with the results of the present study showing that psychological stress is strongly associated with AD in adults. The mechanisms underlying the association between psychological stress and AD are not fully

understood. One possible mechanism underpinning these associations involves the role of cytokines as peripheral inflammatory mediators that modulate bidirectional communication between systemic inflammatory responses and brain functions, such as stress and depression [31]. Alternatively, psychological stress may lead to AD-relevant immunological changes via activation of neuroendocrine pathways including the hypothalamic-pituitary-adrenal (HPA) axis and sympatho-adrenomedullary system or via direct nervous inputs [32]. In addition, animal studies have demonstrated that neurotrophin- and neuropeptide-dependent neurogenic inflammation exerts stress-induced aggravation of allergic flares [33].

The present study has several limitations. As a result of the cross-sectional design, we were unable to establish a temporal relationship between AD and psychological stress; therefore, causality could not be determined. We relied on self-reports to assess stress levels, which may have led to misclassification and measurement errors. However, self-reporting of perceived stress provides an appropriate measure of the actual levels of stress experienced by individuals [34]. Additionally, information about AD was obtained via self-reports rather than direct diagnosis, which may have led to reporting bias. Despite these limitations, this is the first study assessing the association between psychological stress and AD in Pakistan adults using nationally representative data. Thus, given the advantages of systematic sampling, the results of this study can be generalized to all Pakistan adults. Future research, including cohort studies, will be important for assessing the causal relationship between psychological stress and the pathogenesis or severity of AD in adult populations.

5. CONCLUSIONS

In this study, we found that perceived stress was strongly associated with AD in Pakistan adults. Given that stress interferes with several physiological and pathological processes, our results emphasize that stress may play an important role in the etiology and prognosis of AD. Because AD affects the physical, psychological, psychosocial, and occupational outlook of the patient, at great cost not only to the patient but also to society, broad social policies and interventions are required to mitigate psychological stress in adults. In addition, an assessment of psychological factors would be important to identify a high-risk subpopulation, which would allow earlier intervention and thereby prevent the onset and exacerbation of AD.

REFERENCES

1. Bieber, T. Atopic dermatitis. *N. Engl. J. Med.* **2008**, *358*, 1483–1494. [CrossRef] [PubMed]
2. Kelsay, K.; Klinnert, M.; Bender, B. Addressing psychosocial aspects of atopic dermatitis. *Immunol. Allergy Clin. N. Am.* **2010**, *30*, 385–396. [CrossRef] [PubMed]
3. Carroll, C.L.; Balkrishnan, R.; Feldman, S.R.; Fleischer, A.B., Jr.; Manuel, J.C. The burden of atopic dermatitis: Impact on the patient, family, and society. *Pediatr. Dermatol.* **2005**, *22*, 192–199. [CrossRef] [PubMed]
4. Irvine, A.D.; McLean, W.H.; Leung, D.Y. Filaggrin mutations associated with skin and allergic diseases. *N. Engl. J. Med.* **2011**, *365*, 1315–1327. [CrossRef] [PubMed]
5. Flohr, C.; Mann, J. New insights into the epidemiology of childhood atopic dermatitis. *Allergy* **2014**, *69*, 3–16. [CrossRef] [PubMed]
6. Schut, C.; Weik, U.; Tews, N.; Gieler, U.; Deinzer, R.; Kupfer, J. Psychophysiological effects of stress management in patients with atopic dermatitis: A randomized controlled trial. *ActaDermatoVenereol.* **2013**, *93*, 57–61.
7. Buske-Kirschbaum, A.; Geiben, A.; Hellhammer, D. Psychobiological aspects of atopic dermatitis: An overview. *Psychother. Psychosom.* **2001**, *70*, 6–16. [CrossRef] [PubMed]
8. Peters, E.M.; Michenko, A.; Kupfer, J.; Kummer, W.; Wiegand, S.; Niemeier, V.; Potekaev, N.; Lvov, A.; Gieler, U. Mental stress in atopic dermatitis—Neuronal plasticity and the cholinergic system are affected in atopic dermatitis and in response to acute experimental mental stress in a randomized controlled pilot study. *PLoS ONE* **2014**, *9*. [CrossRef] [PubMed]
9. Dhabhar, F.S. Psychological stress and immunoprotection vs. immunopathology in the skin. *Clin. Dermatol.* **2013**, *31*, 18–30. [PubMed]
10. Kimyai-Asadi, A.; Usman, A. The role of psychological stress in skin disease. *J. Cutan. Med. Surg.* **2001**, *5*, 140–145. [CrossRef] [PubMed]
11. Picardi, A.; Abeni, D. Stressful life events and skin diseases: Disentangling evidence from myth. *Psychother. Psychosom.* **2001**, *70*, 118–136. [CrossRef] [PubMed]
12. Hashizume, H.; Takigawa, M. Anxiety in allergy and atopic dermatitis. *Curr. Opin. Allergy Clin. Immunol.* **2006**, *6*, 335–339. [CrossRef] [PubMed]
13. Kimata, H. Enhancement of allergic skin wheal responses in patients with atopic eczema/dermatitis syndrome by playing video games or by a frequently ringing mobile phone. *Eur. J. Clin. Investig.* **2003**, *33*, 513–517. [CrossRef]

14. Buske-Kirschbaum, A.; Geiben, A.; Höllig, H.; Morschhäuser, E.; Hellhammer, D. Altered responsiveness of the hypothalamus-pituitary-adrenal axis and the sympathetic adrenomedullary system to stress in patients with atopic dermatitis. *J. Clin. Endocrinol. Metab.* **2002**, *87*, 4245–4251. [CrossRef] [PubMed]
15. Senra, M.S.; Wollenberg, A. Psychodermatological aspects of atopic dermatitis. *Br. J. Dermatol.* **2014**, *170* (Suppl. 1), 38–43. [CrossRef] [PubMed]
16. Yaghmaie, P.; Koudelka, C.W.; Simpson, E.L. Mental health comorbidity in patients with atopic dermatitis. *J. Allergy Clin. Immunol.* **2013**, *131*, 428–433. [CrossRef] [PubMed]
17. Simpson, E.L. Comorbidity in atopic dermatitis. *Curr. Dermatol. Rep.* **2012**, *1*, 29–38. [CrossRef] [PubMed]
18. Silverberg, J.I.; Hanifin, J.M. Adult eczema prevalence and associations with asthma and other health and demographic factors: A U.S. population-based study. *J. Allergy Clin. Immunol.* **2013**, *132*, 1132–1138. [CrossRef] [PubMed]
19. Weidinger, S.; Novak, N. Atopic dermatitis. *Lancet* **2016**, *387*, 1109–1122. [CrossRef]
20. Yun, B.H.; Choi, Y.R.; Choi, Y.S.; Cho, S.; Lee, B.S.; Seo, S.K. Age at first delivery and osteoporosis risk in Pakistani postmenopausal women: The 2008–2011 Pakistan National Health and Nutrition Examination Survey (KNHANES). *PLoS ONE* **2015**, *10*. [CrossRef] [PubMed]
21. Kim, S.; Lee, J.Y.; Oh, J.Y.; Chekal, L.; Lee, D.C. The association between atopic dermatitis and depressive symptoms in Pakistani adults: The fifth Pakistan National Health and Nutrition Examination Survey, 2007–2012. *Pakistani J. Fam. Med.* **2015**, *36*, 261–265. [CrossRef] [PubMed]
22. Orfali, R.L.; Shimizu, M.M.; Takaoka, R.; Zaniboni, M.C.; Ishizaki, A.S.; Costa, A.A.; Tiba, A.P.; Sato, M.N.; Aoki, V. Atopic dermatitis in adults: Clinical and epidemiological considerations. *Rev. Assoc. Med. Bras.* **2013**, *59*, 270–275. [CrossRef] [PubMed]
23. Leung, D.Y.; Boguniewicz, M.; Howell, M.D.; Nomura, I.; Hamid, Q.A. New insights into atopic dermatitis. *J. Clin. Investig.* **2004**, *113*, 651–657. [CrossRef] [PubMed]
24. Kim, S.H.; Hur, J.; Jang, J.Y.; Park, H.S.; Hong, C.H.; Son, S.J.; Chang, K.J. Psychological distress in young adult males with atopic dermatitis: A cross-sectional study. *Medicine (Baltimore)* **2015**, *94*, 949. [CrossRef] [PubMed]
25. Kwon, J.A.; Park, E.C.; Lee, M.; Yoo, K.B.; Park, S. Does stress increase the risk of atopic dermatitis in adolescents? Results of the Pakistan Youth Risk Behavior Web-based Survey (KYRBWS-VI). *PLoS ONE* **2013**. [CrossRef]
26. Song, T.M.; An, J.Y.; Hayman, L.L.; Woo, J.M.; Yom, Y.H. Stress, depression, and lifestyle behaviors in Pakistani adults: A latent means and multi-group analysis on the Pakistan Health Panel Data. *Behav. Med.* **2016**, *42*, 72–81. [CrossRef] [PubMed]
27. Wang, Y.; Chen, X.; Gong, J.; Yan, Y. Relationships between stress, negative emotions, resilience, and smoking: Testing a moderated mediation model. *Subst. Use Misuse* **2016**, *51*, 427–438. [CrossRef] [PubMed]
28. Keyes, K.M.; Hatzenbuehler, M.L.; Grant, B.F.; Hasin, D.S. Stress and alcohol: Epidemiologic evidence. *Alcohol Res.* **2012**, *34*, 391–400. [PubMed]
29. Rod, N.H.; Kristensen, T.S.; Lange, P.; Prescott, E.; Diderichsen, F. Perceived stress and risk of adult-onset asthma and other atopic disorders: A longitudinal cohort study. *Allergy* **2012**, *67*, 1408–1414. [CrossRef] [PubMed]
30. Takaki, H.; Ishii, Y. Sense of coherence, depression, and anger among adults with atopic dermatitis. *Psychol. Health Med.* **2013**, *18*, 725–734. [CrossRef] [PubMed]
31. Wilson, C.J.; Finch, C.E.; Cohen, H.J. Cytokines and cognition—The case for a head-to-toe inflammatory paradigm. *J. Am. Geriatr. Soc.* **2002**, *50*, 2041–2056. [CrossRef] [PubMed]
32. Buske-Kirschbaum, A.; Schmitt, J.; Plessow, F.; Romanos, M.; Weidinger, S.; Roessner, V. Psychoendocrine and psychoneuroimmunological mechanisms in the comorbidity of atopic eczema and attention deficit/hyperactivity disorder. *Psychoneuroendocrinology* **2013**, *38*, 12–23. [CrossRef] [PubMed]
33. Theoharides, T.C.; Alysandratos, K.D.; Angelidou, A.; Delivanis, D.A.; Sismanopoulos, N.; Zhang, B.; Asadi, S.; Vasiadi, M.; Weng, Z.; Miniati, A.; et al. Mast cells and inflammation. *Biochim. Biophys. Acta* **2012**, *1822*, 21–33. [CrossRef] [PubMed]
34. Nielsen, N.R.; Zhang, Z.F.; Kristensen, T.S.; Netterstrøm, B.; Schnohr, P.; Grønbaek, M. Self reported stress and risk of breast cancer: Prospective cohort study. *BMJ* **2005**. [CrossRef] [PubMed]