# Psychosocial burden of patients with atopic dermatitis at two tertiary referral centres in Malaysia

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## ABSTRACT

**Background: Atopic dermatitis (AD) is a chronic pruritic skin disorder that affects up to 20% of children and 10% of adults. The disease course is unpredictable with periods of exacerbation and remission, thus having a significant impact on the mental health and quality of life (QOL). We evaluated the prevalence of anxiety and depression and their association with disease severity, QOL and their associated factors in adolescents (≥ 13 years old) and adults with AD.**

**Methods: A cross-sectional study was conducted involving patients aged ≥ 13 years with AD who fulfilled the Hanifin and Rajka diagnostic criteria. These patients were recruited from Hospital Queen Elizabeth, Kota Kinabalu and Hospital Kuala Lumpur between January 2020 to March 2021. Assessment instruments used were Scoring for Atopic Dermatitis (SCORAD), Patient-Oriented Eczema Measure (POEM), Dermatology Life Quality Index (DLQI) and Hospital Anxiety and Depression Scale (HADS).**

**Results: Of the 217 participants, 75 (34.6%) had mild eczema, 116 (53.5%) moderate eczema and 26 (12.0%) severe eczema with a mean SCORAD score of 30.4 (standard deviation [SD] = 4.70). Twenty-six (12.0%) and 17 (7.8%) had anxiety and depression, respectively. Patients with moderate to severe disease reported higher HADS-A (HADS-anxiety component), HADS-D (HADS-depression component), POEM, DLQI, itch, sleep loss and skin pain scores ($p < 0.001$ for all). Severe sleep loss (adjusted odd ratio [AOR] 12.41, $p < 0.001$) and hospitalisation in the past year (AOR 6.44, $p = 0.004$) were significant predictors for anxiety whereas those aged 41 to 60 (AOR 10.83, $p = 0.020$), having severe skin pain (AOR 6.12, $p = 0.028$), DLQI ≥ 10 (AOR 5.27, $p = 0.002$) and history of hospitalisation in the past year (AOR 12.73, $p = 0.002$) had increased risk for depression.**

**Conclusion: The prevalence of anxiety was 12.0% while depression was 7.8% in our cohort. AD renders a significant burden on mental health and QOL with a higher impact on those with more severe disease. The use of screening tools such as HADS and DLQI for assessment of mental health and QOL should be considered to address the multidimensional burden of AD.**

**KEYWORDS:**
*Psychiatric comorbidities, mental health, anxiety, depression*

## INTRODUCTION

Atopic dermatitis (AD) is a chronic pruritic skin disorder that affects up to 20% of children and 10% of adults.[1] In acute AD, the cutaneous lesions are characterised by weepy, oedematous and erythematous papules or vesicles. On the other hand, chronic dermatitis presents with itchy, xerotic skin with lichenification. It commonly occurs in childhood and is often associated with a personal or family history of atopy. The prevalence of AD among children in Malaysia was reported to be 12.6%.[2] As AD is a chronic disorder with periods of exacerbation and remission, it has a great impact on the patient's quality of life (QOL).[3] It does not only affect a person physically but also psychologically.[4-6]

Mental health which is recognised as an important element in comprehensive care has often been overlooked in the management of AD. The World Health Organization (WHO) defines health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity".[7] People with mental disorders are more likely to suffer from disability and have a higher mortality rate.[5] According to the National Health and Morbidity Survey (NHMS) in 2015, 29.2% of Malaysians aged 16 and above were found to have mental health problems compared to 10.7% in 1996.[8]

Previous studies demonstrated a higher prevalence of anxiety and depression in patients with AD compared to the general population,[5,6] which correlated to the severity of the AD.[9,10] A multicentre study in 13 European countries by Dalgard et al.[6] reported 10.1% of patients with AD had depression and 15% had anxiety. Moreover, a study conducted in our neighbouring country, Singapore reported that 18% had anxiety and 5% had depression in their cohort.[9] A meta-analysis by Ronnstad et al. concurred with these findings and demonstrated a positive association with suicidal behaviour.[11] In addition, Cheng CM et al. reported that having AD in adolescence or adulthood predisposes a patient to develop anxiety and depression later in life.[4] However, a causal relationship has not been established. Stressful events solely may lead to exacerbation of AD.

Sleep disturbance and the severity of itch and skin pain have been associated with impaired quality of life.[12,13] Approximately 50% of patients complain of skin itch, and 10% have sleep disturbance and skin pain.[14] Skin lesions on the head and neck and lower limbs are associated with

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inadequate control of AD.[13] Chronic itch leads to sleep deprivation and results in poor concentration at school or work. With the increasing severity, it leads to absenteeism and loss of work productivity. Ring J et al. conducted a study involving nine European countries among patients with AD and reported a high burden of disease and its negative effect on relationships, restriction to employment and leisure activities and direct and indirect financial costs imposed on the individual.[15]

In Malaysia, several studies on the impact of AD on QOL in children[16] and adults[17] have been published in the recent years. However, to date, there are no local studies assessing the association of AD with psychiatric comorbidities such as anxiety and depression. We aim to evaluate the prevalence of anxiety and depression, association of anxiety and depression with disease severity, QOL and their associated factors in adolescents (≥ 13 years old) and adults with AD in two tertiary hospitals in Malaysia.

## MATERIALS AND METHODS

This was a cross-sectional study conducted from January 2020 till March 2021 at the dermatology clinics of Hospital Queen Elizabeth and Hospital Kuala Lumpur, Malaysia both which are the state dermatology referral centres. A total of 217 patients aged ≥ 13 years old who fulfilled the Hanifin and Rajka diagnostic criteria for AD (refer to Table I) were recruited during the study period. The Hanifin and Rajka criteria is a diagnostic standard published in 1980 and widely considered to be the gold standard for AD diagnosis requiring 3 of 4 major criteria and 3 of 23 minor criteria to be met for diagnosis.[18] Patients were recruited by consecutive sampling based on their clinic appointments. Those who were not able to understand the questionnaire, illiterate and declined participation were excluded.

Approval from the Malaysian Research and Ethics Committee (MREC) was obtained prior to the study commencement (NMRR-19-3035-51334). Written informed consent was obtained from all patients who agreed to participate in the study. Parental written consent was obtained for participants < 18 years old. Demographics and clinical information were obtained from each patient using a structured clinical research form by the investigators. AD severity was determined by assessment using the Scoring for Atopic Dermatitis (SCORAD). SCORAD is a widely used tool to assess disease severity in atopic dermatitis in randomised controlled trials.[19,20] The scoring includes the extent of the disease, severity of pruritus and sleep disturbance related to dermatitis with a maximum score of 103. Mild eczema is defined as a score of < 25, moderate eczema 25 to 50 and severe eczema > 50.

The average skin pain score over the past 3 days was evaluated using the visual analogue scale (VAS; 0 = no skin pain, 10 = unbearable skin pain). Average itch score and sleep loss scores over the past 3 days were also evaluated with VAS (0 = no itch/insomnia, 10 = unbearable itch/total insomnia, respectively). Subjects were questioned on the average time spent daily on topical application of medication (minutes) and the average amount of monthly expenditure spent on the treatment of AD. They were subsequently subjected to three self-administered questionnaires which were the Patient Orientated Eczema Measure (POEM), Dermatology Life Quality Index (DLQI), and Hospital Anxiety and Depression scale (HADS) questionnaires in either Malay or English language.

POEM is a tool that is used to measure disease severity based on the patient's own experience. It has been recommended for use in the National Institute for Health and Care Excellence (NICE) guidelines.[21] It consists of seven items with each item having a score of 0 to 4; ranging from 0 (no day) to 4 (every day) with a maximum score of 28. A score of < 8 indicates clear to mild eczema, 8 to 16 indicates moderate eczema and > 16 indicates severe eczema.[22]

DLQI is a self-administered questionnaire that measures the QOL over the past one week in patients with skin disease.[23] It consists of 10 questions which cover 6 domains which are, symptoms and feeling, daily activities, leisure, work and school, personal relationships and treatment. Each question is scored 0 to 3; ranging from 0 (not at all) to 3 (very much) with a maximum score of 30. A total score of 0 to 1 indicates "no effect on patient's life", 2 to 5 "small effect on patient's life", 6 to 10 "moderate effect on patient's life", 11 to 20 "very large effect on patient's life" and 21 to 30 as "extremely large effect on patient's life". For subjects < 17 years old, the Children's DLQI was used. A DLQI score of ≥ 10 indicates significant impairment of QOL.

HADS was chosen as it has good psychometric properties and has been used in multiple studies worldwide to evaluate the psychological impact of atopic dermatitis in adults[14,24-26] and adolescents.[9] The Malay version of HADS has been validated for use in adults.[27] HADS consists of seven items that assess anxiety (HADS-A) and depression (HADS-D) separately. Each item is scored 0 to 3. Each subscale has a total score that ranges from 0 to 21. A score of ≤ 7 indicates no anxiety or depression, 8 to 10 indicates borderline anxiety or depression and ≥ 11 indicates clinical anxiety or depression. Participants with scores of ≥ 11 for either component were considered to have anxiety or depression.

*Statistical Analysis*

All statistical analyses were performed using the Statistical Package for Social Sciences for Windows, SPSS 22.0 (SPSS Inc., IBM Corp). Categorical data were expressed as frequencies and percentages. Continuous data were expressed in means and standard deviations if they were normally distributed, or median and interquartile range if they were not normally distributed. Analysis of categorical data was done with simple logistic regression. Pearson coefficient or Kendall's tau b correlation coefficient were used to assess the correlation (r) between numerical variables. Simple Logistic Regression was run for anxiety score and depression score. A p-value of < 0.05 was considered statistically significant. In multivariate logistic regression analysis, both forward and backward Likelihood Ratio were applied for selection of independent variables. Those with p-value of < 0.05 were included in the model. The preliminary model was checked for any interaction terms between the selected variables and its multicollinearity. Hosmer-Lemeshow goodness-of-fit test was

**Table I: Diagnostic criteria for atopic dermatitis[18]**

**Must have 3 major and ≥3 minor features for diagnosis of atopic dermatitis**

Major
- Pruritus
- Typical morphology and distribution:
  - flexural lichenification or linearity in adults
  - facial and extensor involvement in infants and children
- Chronic or chronically relapsing dermatitis
- Personal or family history of atopy (asthma, allergic rhinitis, atopic dermatitis)

Minor
- Xerosis
- Ichthyosis/ palmar hyperlinearity/ keratosis pilaris
- Immediate (type I) skin test reactivity
- Elevated serum IgE
- Early age of onset
- Tendency toward cutaneous infections (esp. Staph aureus and Herpes simplex)/ impaired cell-mediated immunity
- Tendency towards non-specific hand or foot dermatitis
- Nipple eczema
- Cheilitis
- Recurrent conjunctivitis
- Dennie-Morgan infraorbital fold
- Keratoconus
- Anterior subcapsular cataract
- Orbital darkening
- Facial pallor/ facial erythema
- Pityriasis alba
- Anterior neck folds
- Itch when sweating
- Intolerance to wool and lipid solvents
- Perifollicular accentuation
- Food intolerance
- Course influenced by environmental/ emotional factors
- White dermographism/delayed blanching

**Table II: Demographic and clinical characteristics of study participants**

| Demographic and clinical characteristics | Number, n=217 (%) |
|---|---|
| Gender | |
| Male | 104 (47.9) |
| Female | 113 (52.1) |
| Ethnicity | |
| Ethnic Sabahans | 111 (51.2) |
| Malay | 42 (19.4) |
| Chinese | 60 (27.6) |
| Indian | 4 (1.8) |
| Marital status | |
| Single | 117 (53.9) |
| Married | 92 (42.4) |
| Divorced/separated | 6 (2.8) |
| Widow/widower | 2 (0.9) |
| Education | |
| Up to secondary | 99 (45.6) |
| Tertiary and above | 118 (54.4) |
| Employment status | |
| Unemployed | 20 (9.2) |
| Employed/Student | 166 (76.5) |
| Homemaker, retired | 31 (14.3) |
| Monthly Income (RM) | |
| <RM3000 | 88 (40.6) |
| RM3000-RM9999 | 112 (51.6) |
| >RM10000 | 17 (7.8) |
| Personal history of atopy | 144 (66.4) |
| Family history of atopy | 146 (67.3) |
| Systemic treatment in the past 1 year | |
| Systemic corticosteroids | 98 (45.2) |
| Azathioprine | 31 (14.3) |
| Methotrexate | 16 (7.4) |
| Phototherapy | 16 (7.4) |
| Cyclosporin | 5 (2.3) |
| Mycophenolate mofetil | 2 (1.0) |

**Table III: Factors associated with anxiety, depression and significant impairment of quality of life (QOL) (using multivariate logistic regression)**

| | Anxiety | | | | Depression | | | | Significant impairment of QOL | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Crude odds ratio (COR) | 95% CI | | p-value[a] | Crude odds ratio (COR) | 95% CI | | p-value[a] | Crude odds ratio (COR) | 95% CI | | p-value[a] |
| | | Lower value | Upper value | | | Lower value | Upper value | | | Lower value | Upper value | |
| Age (years) | | | | 0.299 | | 0.98 | 1.02 | 0.022 | | | | 0.002 |
| 20 or less | | | | | 1.00 | | | | 1.00 | | | |
| 21-40 | 1.84 | 0.84 | 4.03 | 0.128 | 4.00 | 1.45 | 11.06 | 0.007[b] | 2.46 | 1.28 | 4.85 | 0.009[b] |
| 41-60 | 1.01 | 0.37 | 2.70 | 0.992 | 4.11 | 1.33 | 12.66 | 0.014[b] | 1.89 | 0.84 | 4.23 | 0.123[b] |
| 61 and above | 1.02 | 0.29 | 3.77 | 0.950 | 1.15 | 0.20 | 6.50 | 0.872[b] | 0.30 | 0.08 | 1.14 | 0.076[b] |
| Ethnicity | | | | 0.462 | | | | 0.010[b] | | | | 0.032 |
| Malay | 1.55 | 0.72 | 3.36 | 0.262[b] | 3.23 | 1.48 | 7.06 | 0.026[b] | 2.04 | 0.97 | 4.26 | 0.059[b] |
| Chinese | 0.95 | 0.45 | 1.97 | 0.881[b] | 1.19 | 0.54 | 2.63 | 0.003[b] | 0.68 | 0.36 | 1.28 | 0.229[b] |
| Others | 1.00 | | | | 1.00 | | | | 1.00 | | | |
| SCORAD score | | | | <0.001 | | | | 0.006 | | | | <0.001 |
| Mild eczema | 1.00 | | | | 1.00 | | | | 1.00 | | | |
| Moderate eczema | 3.47 | 1.51 | 8.00 | 0.003 | 3.05 | 1.32 | 7.08 | 0.009 | 3.76 | 2.00 | 7.06 | <0.001[b] |
| Severe eczema | 9.77 | 3.37 | 28.31 | <0.001 | 5.23 | 1.78 | 15.38 | 0.003 | 15.13 | 4.64 | 49.32 | <0.001[b] |
| Pruritus score | | | | <0.001 | | | | 0.015 | | | | <0.001 |
| None | 1.00 | | | | 1.00 | | | | 1.00 | | | |
| Mild | 1.46 | 0.16 | 13.37 | 0.741[b] | 2.46 | 0.29 | 21.20 | 0.412[b] | 6.86 | 0.84 | 55.68 | 0.072[b] |
| Moderate | 5.90 | 0.74 | 47.25 | 0.095[b] | 4.80 | 0.60 | 38.72 | 0.141[b] | 15.20 | 1.92 | 120.28 | 0.010[b] |
| Severe | 14.06 | 1.76 | 112.66 | 0.013[b] | 8.80 | 1.09 | 70.85 | 0.041[b] | 83.20 | 9.88 | 700.56 | <0.001[b] |
| Sleep loss score | | | | <0.001 | | | | <0.001 | | | | <0.001 |
| None | 1.00 | | | | 1.00 | | | | 1.00 | | | |
| Mild | 3.62 | 1.24 | 10.55 | 0.019[b] | 5.50 | 1.82 | 16.63 | 0.003 | 3.93 | 1.75 | 8.83 | 0.001[b] |
| Moderate | 5.65 | 1.96 | 16.32 | 0.001[b] | 5.43 | 1.74 | 16.95 | 0.004 | 12.66 | 5.15 | 31.16 | <0.001[b] |
| Severe | 13.75 | 5.04 | 37.53 | <0.001[b] | 10.21 | 3.50 | 29.76 | <0.001 | 33.27 | 11.87 | 93.30 | <0.001[b] |
| Skin pain score | | | | <0.001 | | | | <0.001 | | | | <0.001 |
| No pain | 1.00 | | | | 1.00 | | | | 1.00 | | | |
| Mild | 4.06[b] | 1.67 | 9.90 | 0.002[b] | 6.30 | 2.31 | 17.18 | <0.001[b] | 2.56 | 1.29 | 5.10 | 0.007[b] |
| Moderate | 6.14[b] | 2.48 | 15.21 | <0.001[b] | 7.91 | 2.84 | 22.06 | <0.001[b] | 10.91 | 4.63 | 25.70 | <0.001[b] |
| Severe | 16.38[b] | 5.15 | 52.14 | <0.001[b] | 16.48 | 4.85 | 55.96 | <0.001[b] | 47.77 | 6.07 | 376.13 | <0.001[b] |
| Medical conditions[c] | | | | 0.424 | | | | 0.809 | | | 0.067 | |
| No | 1.00 | | | | 1.00 | | | | 1.00 | | | |
| Yes | 0.73 | 0.34 | 1.58 | | 0.91 | 0.41 | 2.00 | | 0.54 | 0.28 | 1.04 | |
| Lesions at visible areas[d] | | | | 0.406 | | | | 0.022 | | | | 0.001 |
| No | 1.00 | | | | 1.00 | | | | 1.00 | | | |
| Yes | 1.43 | 0.62 | 3.33 | | 4.18 | 1.23 | 14.23 | | 3.63 | 1.67 | 7.91 | |
| Time spent on treatment daily (mins) | | | | 0.002 | | | | 0.023 | | | | 0.002 |
| ≤15 mins | 1.00 | | | | 1.00 | | | | 1.00 | | | |
| 16-30 mins | 3.05 | 1.57 | 5.94 | 0.001[b] | 2.20 | 1.10 | 4.41 | 0.023 | 2.51 | 1.38 | 4.56 | 0.003[b] |
| ≥30 mins | 3.10 | 1.08 | 8.87 | 0.035[b] | 3.27 | 1.14 | 9.42 | 0.028 | 3.85 | 1.30 | 11.45 | 0.015[b] |

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**Table III: Factors associated with anxiety, depression and significant impairment of quality of life (QOL) (multivariate logistic regression) (cont.)**

| | Anxiety | | | | Depression | | | | Significant impairment of QOL | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Crude odds ratio (COR) | 95% CI | | p-value[a] | Crude odds ratio (COR) | 95% CI | | p-value[a] | Crude odds ratio (COR) | 95% CI | | p-value[a] |
| | | Lower value | Upper value | | | Lower value | Upper value | | | Lower value | Upper value | |
| Number of clinic visits in the past year | | | | 0.054 | | | | 0.005 | | | | 0.098 |
| 1-4 | 1.00 | | | | 1.00 | | | | 1.00 | | | |
| 5-8 | 1.45 | 0.72 | 2.92 | 0.305[b] | 2.46 | 1.16 | 5.21 | 0.019 | 1.91 | 1.04 | 3.50 | 0.036 |
| ≥9 | 2.70 | 1.20 | 6.04 | 0.016[b] | 3.81 | 1.62 | 9.01 | 0.002 | 1.55 | 0.73 | 3.28 | 0.250 |
| Hospitalisation in the past year | | | | <0.001 | | | | <0.001 | | | | 0.015 |
| No | 1.00 | | | | 1.00 | | | | 1.00 | | | |
| Yes | 8.53 | 2.56 | 28.48 | | 10.51 | 3.13 | 35.29 | | 6.56 | 1.43 | 30.04 | |
| Money spent on treatment monthly (RM) | | | | 0.874 | | | | 0.046 | | | | 0.003 |
| <RM50 | 1.00 | | | | 1.00 | | | | 1.00 | | | |
| RM51-150 | 1.21 | 0.59 | 2.50 | 0.605[b] | 1.83 | 0.86 | 3.88 | 0.115[b] | 2.37 | 1.22 | 1.22 | 0.011 |
| >RM150 | 1.07 | 0.39 | 2.92 | 0.897[b] | 2.94 | 1.15 | 7.52 | 0.024[b] | 3.90 | 1.45 | 10.47 | 0.007 |
| DLQI score | | | | <0.001 | | | | <0.001 | | | | |
| < 10 | 1.00 | | | | 1.00 | | | | | | | |
| ≥ 10 | 5.42 | 2.66 | 11.03 | | 11.08 | 4.47 | 27.48 | | | | | |

[a] Likelihood Ratio (LR) test [b] Wald test

[c] Medical conditions include hypertension, dyslipidemia, ischemic heart disease, cardiac arrhythmias, gastrointestinal diseases, respiratory diseases, neurological diseases, rheumatological diseases, osteoporosis

[d] Visible areas include face, neck, hands and feet

**Table IV: Factors associated with anxiety and depression (Multivariate Logistic Regression)**

| | Anxiety | | | | Depression | | | |
|---|---|---|---|---|---|---|---|---|
| | Adjusted odds ratio (AOR) | 95% CI | | p-value[a] | Adjusted odds ratio (AOR) | 95% CI | | p-value[a] |
| | | Lower value | Upper value | | | Lower value | Upper value | |
| Age group | | | | | | | | 0.020 |
| 20 or less | | | | | 1.00 | | | |
| 21-40 | | | | | 6.06 | 1.59 | 23.06 | 0.008 |
| 41-60 | | | | | 10.83 | 2.22 | 52.90 | 0.003 |
| 61 and above | | | | | 1.51 | 0.07 | 26.87 | 0.778 |
| Skin pain score | | | | | | | | 0.028 |
| None | | | | | 1.00 | | | |
| Mild | | | | | 5.68 | 1.70 | 18.97 | 0.005 |
| Moderate | | | | | 4.03 | 1.16 | 13.99 | 0.028 |
| Severe | | | | | 6.12 | 1.44 | 25.96 | 0.014 |
| Sleep loss score | | | | <0.001 | | | | |
| None | 1.00 | | | | | | | |
| Mild | 3.25 | 1.10 | 9.67 | 0.034[b] | | | | |
| Moderate | 4.58 | 1.54 | 13.66 | 0.006[b] | | | | |
| Severe | 12.41 | 4.49 | 34.30 | <0.001[b] | | | | |
| Hospitalisation in the past year | | | | 0.004 | | | | 0.002 |
| No | 1.00 | | | | 1.00 | | | |
| Yes | 6.44 | 1.79 | 23.21 | | 12.73 | 2.62 | 61.80 | |
| DLQI score | | | | | | | | 0.002 |
| < 10 | | | | | 1.00 | | | |
| ≥ 10 | | | | | 5.27 | 1.84 | 15.12 | |

[a] Likelihood Ratio (LR) test [b] Wald test
Both models have no interaction terms, no multicollinearity and no outliers.
Hosmer-Lemeshow goodness-of-fit test for both models were not significant.
For depression model, 83.8% cases were predicted correctly whether they have depression or not and AUC of ROC was 86.5% (excellent discrimination) whereas for anxiety model, 76.5% cases were predicted and AUC of ROC was 77.7% (acceptable discrimination).

**Table V: Comparison of current study with previous studies**

| Characteristics | Current study | Silverberg et al[14] | Dieris-Hirche et al[25] | Lim VZY et al[9] | Chiesa Fuxench et al[24] |
|---|---|---|---|---|---|
| Country | Malaysia | United States | Germany | Singapore | United States |
| Number of Participants | 217 | 602 | 181 | 100 | 93 |
| Female | 113 (52.1%) | 349 (58.0%) | 137 (75.7%) | 22 (22.0%) | 58 (62.4%) |
| Age | 31.0 (IQR 22.0) (range 13-87) | 46.6 | 27.6 (SD 8.3) (range 18-60) | 25.7 (SD 10.1) (range 14-58) | 51.8 (SD 18.2) |
| Severity tool | SCORAD | PO-SCORAD | PO-SCORAD | SCORAD | POEM |
| Mean SCORAD | 30.4 (SD 14.7) | 27.5 (SD 1.8) | 48.8 (SD 16.8) | 55.0 (SD 16.2) | - |
| Severity | | | | | |
| Mild | 75 (34.6%) | 289 (59.4%) | 19 (10.5%) | 1 (1.0%) | 362 (60.1%) |
| Moderate | 116 (53.5%) | 172 (34.8%) | 73 (40.3%) | 39 (39.0%) | 174 (28.9%) |
| Severe | 26 (12.0%) | 34 (6.9%) | 89 (49.2%) | 60 (60.0%) | 66 (11.0%) |
| Mean DLQI | 10.3 (SD 6.7) | 4.9 (SD 0.6) | 8.3 (SD 5.9) | - | 4.7 (SD 6.4) |
| HADS-A | | | | | |
| Borderline | 30 (13.8%) | 112 (19.8%) | - | - | - |
| Abnormal | 26 (12.0%) | 150 (28.6%) | 47 (26.0%) | 18 (18.0%) | 23 (24.7%) |
| Mean HADS-A | 5.3 (SD 4.1) | 7.7 | 8.2 (SD 4.1) | 7.2 (SD 3.7) | 7.0 (SD 4.8) |
| HADS-D | | | | | |
| Borderline | 32 (14.7%) | 115 (21.0%) | - | - | - |
| Abnormal | 17 (7.8%) | 79 (13.5%) | 16 (8.8%) | 5 (5.0%) | 13 (14.0%) |
| Mean HADS-D | 4.6 (SD 3.8) | 6.0 | 4.9 (SD 3.8) | 5.0 (SD 3.4) | 5.8 (SD 4.5) |

Abbreviations: IQR, interquartile range; SD, standard deviation; SCORAD, scoring for atopic dermatitis; PO-SCORAD, patient-oriented scoring for atopic dermatitis; POEM, patient-oriented eczema measure; DLQI, dermatology life quality index; HADS-A, hospital anxiety and depression scale-anxiety component; HADS-D, hospital anxiety and depression scale-depression component

checked, not significant value means the model fits well. The sensitivity and specificity of the model's prediction of the model were determined, above 70% is considered a good model. The ROC (receiver operating characteristics) curve was checked to see the model's ability to discriminate between 2 outcomes. Finally, the Cooks influential statistic was checked and values above 1.0 were considered outliers.

## RESULTS

*Demographics*

We recruited a total of 217 participants during the study period. Their median age was 31.0 years (interquartile range [IQR] = 22.0; range, 13 to 87). The demographics of our study participants are summarised in Table II.

*Eczema severity – SCORAD and POEM tool, pruritic score, pain score and sleep loss score*

The mean SCORAD score was 30.4 (standard deviation [SD] = 14.70) with 75 (34.6%) reporting mild eczema, 116 (53.5%) moderate eczema and 26 (12.0%) severe eczema. The median POEM score was 11.0 (IQR = 12.0); 72 (33.2%) mild eczema, 88 (40.6%) moderate eczema and 57 (26.3%) severe eczema. The mean pruritus score was 4.7 (SD = 2.59), median skin pain score was 2.0 (IQR = 4.0) and median sleep loss score was 2.0 (IQR = 6.0). Higher SCORAD scores were strongly correlated with higher scores for pruritus ($r$ = 0.740, $p$ < 0.001), sleep loss ($r$ = 0.702, $p$ < 0.001) and skin pain ($r$ = 0.539, $p$ < 0.001).

*Quality of life (QOL) – DLQI tool*

Sixteen (7.4%) patients reported no effect, 50 (23.0%) small and moderate effect, 83 (38.2%) very large effect and 18 (8.3%) had extremely large effect on their QOL. The mean DLQI was 10.3 (SD = 6.73). The most affected domain was symptoms ($r$ = 0.444, $p$ < 0.001), followed by interference with leisure activities ($r$ = 0.390, $p$ < 0.001), treatment-related factors ($r$ = 0.366, $p$ < 0.001) and effect on daily activities ($r$ = 0.334, $p$ < 0.001).

*Anxiety and Depression - HADS tool*

Our cohort had a mean HADS-A score of 5.3 (SD = 4.07) and HADS-D score of 4.6 (SD = 3.83). Thirty (13.8%) of the study participants had borderline anxiety and 26 (12.0%) had clinical anxiety whereas 32 (14.7%) had borderline depression and 17 (7.8%) had clinical depression. Eleven (5.1%) participants had both anxiety and depression, whereas fifteen (6.9%) and six (2.8%) had anxiety and depression only respectively. Of those with severe eczema, half of them (53.8%) had borderline or clinical anxiety and a third (38.5%) had borderline or clinical depression.

Logistic regression analysis of variables associated with HADS-A, HADS-D and DLQI are summarised in Table III. Unadjusted analysis revealed that patients with severe eczema were more likely to have anxiety (crude odd ratio [COR] 9.77, $p$ < 0.001), depression (COR 5.23, $p$ = 0.006) or significant impairment of quality of life (COR 15.13, $p$ < 0.001) compared to those with mild eczema. Besides that, those with DLQI ≥ 10 were more likely have anxiety (COR 5.42, $p$ < 0.001) or depression (COR 11.08, $p$ < 0.001) compared to those with DLQI < 10.

Age group of 21 to 40, Malay ethnicity and having lesions at visible areas were associated with symptoms of depression and significant impairment of QOL. Treatment-related factors such as more time spent on treatment, hospitalisation in the past year, higher pruritus, sleep loss and skin pain scores were associated with higher risk of anxiety, depression and significant impairment of QOL. In addition, lesions at visible areas and more money spent on treatment monthly were associated with increased risk of depression or significant impairment of QOL. Increased frequency of clinic reviews was also associated with increased risk of depression. On the other hand, gender, employment status, education level, monthly household income, marital status, early onset AD (≤ 5 years old), duration of AD, personal or family history of atopy and underlying medical conditions were not associated with symptoms of anxiety or depression.

Following multivariate analysis (refer to Table IV), only severe sleep loss and hospitalisation in the past year were significant predictors for anxiety whereas age 41 to 60, severe skin pain, DLQI ≥ 10 and hospitalisation in the past year were significant predictors for depression.

The DLQI domain most affected by anxiety was symptom (r = 0.446, $p$ < 0.001), followed by interference with leisure activities ($r$ = 0.401, $p$ < 0.001). For depression, the DLQI domain that was most affected was related to treatment ($r$ = 0.431, $p$ < 0.001), followed by symptoms ($r$ = 0.043, $p$ < 0.001). Anxiety scores were strongly correlated with depression scores ($r$ = 0.751, $p$ < 0.001). Anxiety score significantly predicted depression score (constant = 0.888, $p$ = 0.002) and anxiety score accounted for 70.6% of the explained variability in the total depression score.

## DISCUSSION

Mental health is recognised as an essential component in a person's health and well-being. Therefore, it is imperative to recognise the psychological impact of AD on patients to provide comprehensive care. This study was conducted to demonstrate the psychological impact of AD among Malaysians. HADS was selected for evaluation of anxiety and depression as it has been used in multiple similar studies.[9,14,24,25] Furthermore, validation of the Malay version of HADS in our population showed good sensitivity and specificity.[27]

The prevalence of anxiety (12.0%) in our study was lower compared to previous studies[9,14,24,25] In contrast, our prevalence of depression (7.8%) was comparable to the studies in Singapore[9] and Germany,[25] whereas a higher prevalence was reported in United States.[14,24] The mean HADS-A (5.3) and HADS-D (4.6) in our study were lower compared to the study conducted in Singapore[9] owing to the cohort in Singapore having moderate to severe eczema. Studies by Silverberg et al.[14] in The United States and Dieris-Hirche et al.[25] in Germany also documented higher anxiety and depression scores. This may be explained by the cross-cultural differences between Eastern and Western countries. A review by De Vaus et al.[28] reported differences in interpretation and response to negative emotion were critical in determining mental health well-being. Easterners have a more holistic way of thinking whereby contradictions are more accepted

resulting in adaptation to the negative emotion. In contrast, Westerners adopt a more analytical style of thinking that views positive and negative emotions as exclusive entities. In addition, Easterners are more likely to cope with high levels of negative emotions before they become overwhelmed, leading to clinical disorder. Good social support in collectivist cultures is also associated with better health outcomes.[28] Furthermore, the cost of medical treatment in Malaysia is not a barrier to obtain medical care as it is subsidised by the government. Patients only need to pay a minimal amount for medical care in the public setting thus relieving the mental stress of financial burden. Comparison of our results with previous studies are summarised in Table V.

The mean DLQI (10.3) in our study was higher compared to the studies by Silverberg et al.[14] and Chiesa Fuxench et al.[24] This could be due to the higher proportion of mild AD in their study cohorts. A study in Malaysia[17] on the impact of skin disorders on patients' QOL reported a mean DLQI of 12.9 (SD = 7.9) in AD patients. Climate differences between our country and the temperate countries may subject our patients to more AD flares due to frequent perspiration resulting in aggravation of itch and sleep disturbance thus restricting leisure, sports activities and social interactions. A review by Nguyen et al.[29] reported that with increasing temperature and humidity, sweating is enhanced which leads to skin irritation and worsening of AD. Moreover, pruriceptive nerve fibres are more activated at higher temperatures. However, ultraviolet radiation has immunosuppressive effects by enhancing T regulatory cells which leads to downregulation of T helper 2 (Th2) response. These contrasting views on the effect of climate on AD will need to be further clarified.[29,30] Additionally, our study was conducted during the COVID-19 pandemic whereby the patients may suffer from AD flares due to the use of personal protective equipment, hand sanitizers and frequent hand washing.

There was a stepwise increase in the SCORAD score with increasing anxiety, depression, DLQI, pruritus, sleep loss and skin pain scores which was also reported in previous studies [9,14,15,24,25,31] Symptoms such as itch, sleep loss, skin pain, excessive dryness, scaling and skin inflammation as well as restricted daily activities and social interactions are important factors that affect QOL, more so in those with moderate to severe disease.[14] Having AD on the visible parts of the body such as the face, neck, hands and feet were also associated with higher DLQI and depression scores. Patients often feel stigmatised, discriminated and less accepted due to the visible skin lesions. This leads to avoidance of social interaction and reduced social activities.[14] Moreover, self-esteem and confidence are affected which may lead to social isolation. Treatment-related factors such as spending more time on daily treatment, spending more money to purchase products to improve the skin condition and a higher number of clinic visits and hospitalisations were associated with greater disease severity. Understandably, patients with more severe disease will need more time to apply topical medications, to travel to the hospital for clinic reviews and blood investigations.

Besides that, with increasing AD severity, poor concentration and poor work performance at school or work leads to poor mental health.[11] Perceived social stigmatisation and the need to adapt to lifestyle changes are also contributory factors.[32] Similarly, the presence of anxiety or depression may exacerbate AD. Studies have shown that patients with psychological distress were less likely to adhere to their chronic medical illness treatment. This leads to poor control of the disease which further aggravates psychological distress.[33] Dysregulation of the hypothalamic-pituitary-adrenal axis due to chronic inflammation has been hypothesized to contribute to psychiatric comorbidities. Additionally, greater sympathetic overactivity was observed in patients with AD regardless of stress level which may lead to poor sleep quality and exacerbation of neuropsychiatric conditions.[33,34] Current data also demonstrates an increased risk of suicidal ideation in patients with severe AD.[25]

We found that AD had the highest impact on QOL and depression scores in the age group of 41 to 60 years. This age group consists of working adults. Poorly controlled AD may lead to difficulty in securing employment due to fear of stigmatisation, restricted occupational choices, presenteeism and absenteeism. A study by Andersen et al.[35] found that a higher disease severity was associated with a worse impact on work productivity. This may result in hindrance of career advancement and less fulfilling life achievements. On the other hand, the older age group was associated with lower DLQI, anxiety and depression scores. The older age group may have better coping mechanisms[17] and less daily life stress.

In our cohort, the ethnic distribution reflects the diverse ethnic groups in Malaysia. Two-thirds were recruited from Kota Kinabalu, Sabah, thus more than half of the subjects were of the ethnic groups from Sabah, followed by Chinese, Malays and Indians. In contrast, subjects from Kuala Lumpur were predominantly Malays, followed by Chinese and Indians.[36] The Malay ethnicity was associated with higher DLQI and depression scores which was also reported by Lim et al.[9] in Singapore. However, a local study on the impact of skin disorders on QOL demonstrated that QOL was most impaired in Indians followed by Malays and Chinese.[17] The differences may be due to the under-representation of the Indian and Malay ethnic groups in our cohort.

SCORAD has been widely used for the objective assessment of AD severity. However, studies have reported discrepancies between patient and clinician regarding disease severity. Those who perceived their disease to be more severe had more impaired QOL. Generally, a higher severity was reported by patients as compared to their clinicians.[37] This was also noted in our cohort where almost half of the patients who perceived they had severe disease, had moderate disease based on SCORAD assessment. These patients also had higher DLQI, anxiety and depression scores. It would be judicious then for clinicians to consider patients' perception of disease severity in deciding treatment plans as self-assessed severity has a significant impact on the psychological well-being of the patient.[38]

Awareness of the importance of recognising psychological disorders in patients with AD is essential to provide comprehensive care. The burden of disease is no longer a

measurement of physical disease only; it needs to consider the psychosocial burden and impact on QOL. Psychosocial intervention with multi-disciplinary team involvement is useful to address the psychological aspect of the disease.[10] Education on strategies to interrupt the itch-scratch cycle, good sleep habits, stress management, positive thinking and better communication skills should be incorporated in the care plan. Patient empowerment is important to equip them with the necessary resources to face challenges in their work and social life.[39] Linnet et al.[10] have reported that AD patients with high anxiety levels had improvement in mental health and skin condition after psychotherapy treatment. On the other hand, failure to recognise and provide psychological treatment to these patients may lead to poor treatment compliance.[10] Patients with anxiety and depression due to AD should be treated more aggressively as better control of AD will result in better control of the psychological comorbidities.[40] Furthermore, with new targeted treatments such as biologics and JAK (januse kinase) inhibitors, most patients can achieve good to excellent disease control.

## RECOMMENDATIONS

The incorporation of screening tools such as HADS and DLQI in our daily practice should be considered especially for patients with moderate to severe disease. Patients who have abnormal anxiety or depression scores (HADS-A or HADS-D ≥ 8) should be referred for psychological assessment and counselling. These patients should be followed up closely with early consideration for systemic treatment to achieve rapid eczema control.

## LIMITATIONS

As this was a cross-sectional study, we were only able to evaluate the association between psychosocial burden and AD, not causation. A study extension to compare the improvement in the SCORAD, POEM, DLQI, and HADS score after adequate control of AD would be more accurate to evaluate the impact of AD on mental health. In addition, having an age and sex-matched control group would help to better gauge the effect of AD on the psychosocial comorbidities.

## CONCLUSION

This study demonstrated that AD has a significant impact on mental health and quality of life, more so with severe disease. The prevalence of anxiety was 12.0% and depression was 7.8% in our cohort. Factors that afflicted the psychological well-being of patients with AD included middle age group, higher skin pain or sleep loss scores, hospitalisation in the past year and significant impairment of QOL (DLQI ≥ 10).

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## CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

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