

## Materials and Methods

The study population of this retrospective case-control study consisted of inpatients who were hospitalized in the dermatology service at the Tan Tock Seng Hospital, Singapore, between 1 May 2013 and 31 May 2015. The cases were patients who were diagnosed with idiopathic GED. The diagnosis of GED was based on the following criteria: (1) typical clinical features of diffuse erythema and scaling affecting a body surface area greater than 80% as assessed by dermatologists, and (2) consistent findings on histology with features of spongiotic or psoriasiform dermatitis with or without eosinophils. These cases were classified as idiopathic GED if evaluation could not reveal an apparent cause such as an associated malignancy, a pre-existing dermatosis or culprit drug. Controls in a 1:1 ratio were randomly selected from inpatients with other dermatological conditions admitted during the same period. Patients who had similar chronic dermatoses (such as extensive atopic dermatitis or psoriasis), adverse drug reactions (such as exanthematous drug eruptions) or diagnoses possibly related to an adverse drug reaction (such as erythema multiforme) were not included in the control group.

All patients in the study were screened for a history of treatment with angiotensin-converting enzyme inhibitors, angiotensin receptor blockers,  $\beta$ -blockers, calcium channel blockers, thiazides and statins in the past 4 years. The drug history was included into the analysis if the patient was taking the medication at the time of GED diagnosis for cases or date of admission for controls. Confirmation of these chronic medications was made using the prescription section of the patients' medical records.

Variables included in the analysis as possible confounding factors were age, gender, racial group, related medical conditions such as hypertension, hyperlipidaemia, diabetes mellitus, asthma or eczema. Racial groups were categorized into "Chinese", "Malay", "Indians" and "other races". Comorbid conditions were determined based on the International Classification of Diseases (ICD) diagnosis codes in the patients' medical records.

The relationship between GED and the use of antihypertensive drugs or statins was analysed using the  $\chi^2$  or Fisher exact tests. Multivariate logistic regression analysis was performed with GED as the dependent variable, and age, gender, racial groups, aforementioned related medications (such as treatment with antihypertensive drugs and statins), hypertension, hyperlipidaemia, diabetes mellitus, asthma and eczema as the independent variables. Multicollinearity between the independent variables was assessed using the variation inflation factor. The Statistical Package for Social Sciences (IBM SPSS Version 22) was utilized for the analysis of the above-mentioned variables to evaluate statistical significance. Odds ratio, 95% confidence interval and  $p$  values were calculated to test the null hypothesis of the association between GED with a positive current drug use of antihypertensive drugs or statins. A two-sided  $p$  value of  $<0.05$  was considered statistically significant. The study was approved by our institution's ethics review board.