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Report

Autoimmune skin disease among dermatology outpatients in Botswana: a retrospective review

Pamela N. Madu[1], MD, Victoria L. Williams[2,3], MD, Megan H. Noe[2], MD, Bernard G. Omech[4], MD, Carrie L. Kovarik[2], MD, and Karolyn A. Wanat[5], MD

[1]Department of Dermatology, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA, [2]Department of Dermatology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA, [3]Botswana Ministry of Health, Gaborone, Botswana, [4]Department of Internal Medicine, University of Botswana School of Medicine, Gaborone, Botswana, and [5]Department of Dermatology, University of Iowa Carver College of Medicine, Iowa City, IA, USA

Correspondence
Karolyn A. Wanat, MD
Department of Dermatology, University of Iowa Carver College of Medicine, 40027 Pomerantz Family Pavilion, 200 Hawkins Drive, Iowa City, IA 52242, USA
E-mail: kwanat@gmail.com

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Abstract

Background There is a paucity of data describing autoimmune skin diseases in sub-Saharan Africa and in HIV positive cohorts. We describe the incidence of autoimmune skin diseases in public dermatology clinics in Botswana.

Methods New patient records from public dermatology clinics were reviewed retrospectively for the period of September 2008 to December 2015. New diagnoses of cutaneous lupus erythematosus, systemic lupus erythematosus (SLE) with cutaneous involvement, dermatomyositis, systemic sclerosis, lichen sclerosus, bullous pemphigoid, pemphigus foliaceus, pemphigus vulgaris, and pemphigus vegetans were identified. Demographic data were recorded, and incidence was determined.

Results A total of 262 patients were diagnosed with autoimmune skin disease (4% of all new patients) with an incidence rate of 28.8 (per 1,000,000). Cutaneous lupus was the most common diagnosis with discoid lupus occurring most frequently (12.6). The incidence of systemic sclerosis (2.2), morphea (1.6), lichen sclerosus (1.5), SLE with cutaneous involvement (1.3) and dermatomyositis (1.2) was relatively lower. Bullous pemphigoid was the most common bullous disease (3.8). Pemphigus foliaceus (0.9), pemphigus vulgaris (0.6), and pemphigus vegetans (0.2) were observed at a lower rate. At least 19.8% of these patients were also HIV positive.

Conclusions The incidence of autoimmune skin diseases in Botswana is lower compared to other published studies in other geographic areas, which may be reflective of a younger population, barriers to access, genetic differences, and a lack of comparative studies in sub-Saharan Africa. The hygiene hypothesis and helminth infections may also contribute to these differences. Further studies are needed to understand these disorders in this region.

Background

Autoimmune skin diseases develop because of an inappropriate immune response to self-antigens and broadly include both connective tissue diseases and immunobullous diseases. These diseases can be associated with significant morbidity and even mortality if not properly diagnosed, evaluated, and managed.[1–3]

The incidence and severity of some autoimmune skin diseases can vary depending on gender, age, and ethnicity of the population.[4–6] Previous studies of connective tissue diseases, particularly discoid lupus erythematosus (DLE), have shown a predilection for patients of African descent, and black patients have been shown to experience skin damage early in their disease course.[4]

Large studies on autoimmune skin disease in sub-Saharan Africa are limited. A retrospective review in Ibadan, Nigeria ($n = 1091$), demonstrated that 1.1% of patients had DLE and 0.5% had systemic sclerosis.[7] The incidence of autoimmune subepidermal blistering disease in southwestern Uganda has been reported as 5.34 per 1,000,000.[8] Aboobaker *et al.* reported a greater prevalence of pemphigus foliaceus in black patients compared to Indian patients in Kwa-Zulu Natal, South Africa.[9] Given the paucity of data in this region, especially in HIV positive cohorts, we reviewed the autoimmune skin diseases in our public dermatology clinics in Botswana.

Botswana is a country with an estimated population of 2,024,904[10] and a 22.2% prevalence of HIV.[11] Dermatological care in Botswana is limited with 1–2 public dermatologists and a

small number of private dermatologists, mostly clustered in the capital city of Gaborone. Public dermatologic care in Botswana has been provided by a combination of providers including local Botswana dermatologists and other trained healthcare providers, volunteer dermatologists from Cuba, rotating American Academy of Dermatology (AAD) sponsored US and Canadian dermatology residents, and recently a full-time staff dermatologist from the US.[12] Our dermatology clinics see approximately 4000 patients per year. There are no dermatopathologists in the country; histopathological diagnoses are made by a local pathologist and by teledermatopathology through a partnership with the University of Pennsylvania. Diagnostic studies such as direct immunofluorescence, indirect immunofluorescence microscopy, and immunoblotting are extremely limited in availability.

Materials and methods

The study was approved by the institutional review boards of the Botswana Human Research and Development Committee, Princess Marina Hospital, the University of Pennsylvania, and the University of Iowa. A retrospective chart review was performed on new patients seen by the public dermatology clinics associated with the Botswana-UPenn Partnership and Botswana Ministry of Health (in Gaborone, Kanye, Mochudi, Lobatse, Mahalapye) from September 2008 through December 2015. These clinics are located in South and South-Eastern Botswana and are located in districts with a total population of 1,300,652 persons[10] (Fig. 1). Although dermatologic care is not limited to patients in these districts, Fig. 1 is most representative of the population with the greatest proximity to our clinics.[10] The following diagnoses were recorded: subacute cutaneous lupus erythematosus (SCLE), discoid lupus erythematosus (DLE), cutaneous lupus NOS, systemic lupus erythematosus (SLE) with cutaneous involvement, dermatomyositis (DM), systemic sclerosis, lichen sclerosus, (LS), bullous pemphigoid (BP), pemphigus foliaceus (PF), pemphigus vulgaris, and pemphigus vegetans. Both clinical and histopathological diagnoses were accepted. Age, gender, and HIV status were collected for all patient records.

Descriptive statistics were used to examine the age, gender, HIV status, and diagnosis of individuals in the study population. The relative frequencies of each autoimmune disease were calculated based on the total number of new patients seen over the study period. An estimated incidence of each autoimmune disease was calculated using the number of new cases divided by the population of the districts where our clinics are located. All statistical analyses were performed using STATA 14.0 (College Station, TX, USA).

Results

There were 5897 new patient visits from September 2008 to December 2015; of these, 2605 (44%) patients were male and 3292 (56%) were female. A total of 262 (4%) patients were diagnosed with an autoimmune skin disease. The baseline characteristics of these patients are shown in Table 1.

Cutaneous lupus was the most common disease accounting for 2.6% of new patient visits and 58% of autoimmune skin diseases observed. DLE was the most frequently diagnosed form of cutaneous lupus (Table 2). Bullous and sclerosing disorders were seen less frequently. The estimated incidence of all cutaneous autoimmune diseases is 28.8 per 1,000,000 with discoid lupus being the highest at 12.6 per 1,000,000 people (Table 3).

Discussion

Autoimmune skin diseases in the dermatology clinics in Botswana accounted for 4% of all new patient appointments. Connective tissue disorders accounted for a majority of these diseases (80.5%) with DLE as the most common diagnosis within this group (54.5%). Less commonly reported diseases included the fibrosing disorders.

Autoimmune blistering diseases were also observed at a lower rate accounting for 0.8% of new patient visits. Bullous pemphigoid was the most common, accounting for 0.6% of new patient visits.

Autoimmune skin disease affected significantly more female than male patients (77.5% vs. 22.5%), despite the male clinic population of 44%. This gender distribution is in agreement with epidemiologic studies suggesting that cutaneous lupus and bullous pemphigoid, the most common diagnoses in our cohort, are more prevalent in females than in males.[6]

The proportion of the autoimmune skin disease observed in our clinics was relatively lower compared to other published reports, primarily in US white and black populations.[13–18] Potential explanations include the hygiene hypothesis which associates decreased incidence of infection in developed regions with increased autoimmunity.[19] As sub-Saharan Africa has one of the highest concentrations of helminth infections worldwide, its inverse relationship with inflammatory disorders could play a role in our observation.[20,21] The incidence of autoimmune skin disease in Botswana is likely an underestimation, given inherent barriers to access, e.g. only 1-2 public dermatologists in the country, difficult transportation from rural areas, and potential use of alternative sources of medical care such as traditional medicine. Botswana was also severely impacted by the HIV epidemic and has a disproportionately young population. According to the 2011 census, males and females over the age of 70 account for only 3.6% of the population.[10] Diseases most commonly seen in the elderly, such as bullous pemphigoid, may not be seen with as much frequency.

We attempted to evaluate the presence of any correlation between autoimmune skin disease and HIV status, as prior studies have suggested.[22,23] As a result of inconsistent recording of HIV status over the 7-year period, 40.1% of patients with autoimmune skin disease had either an unknown

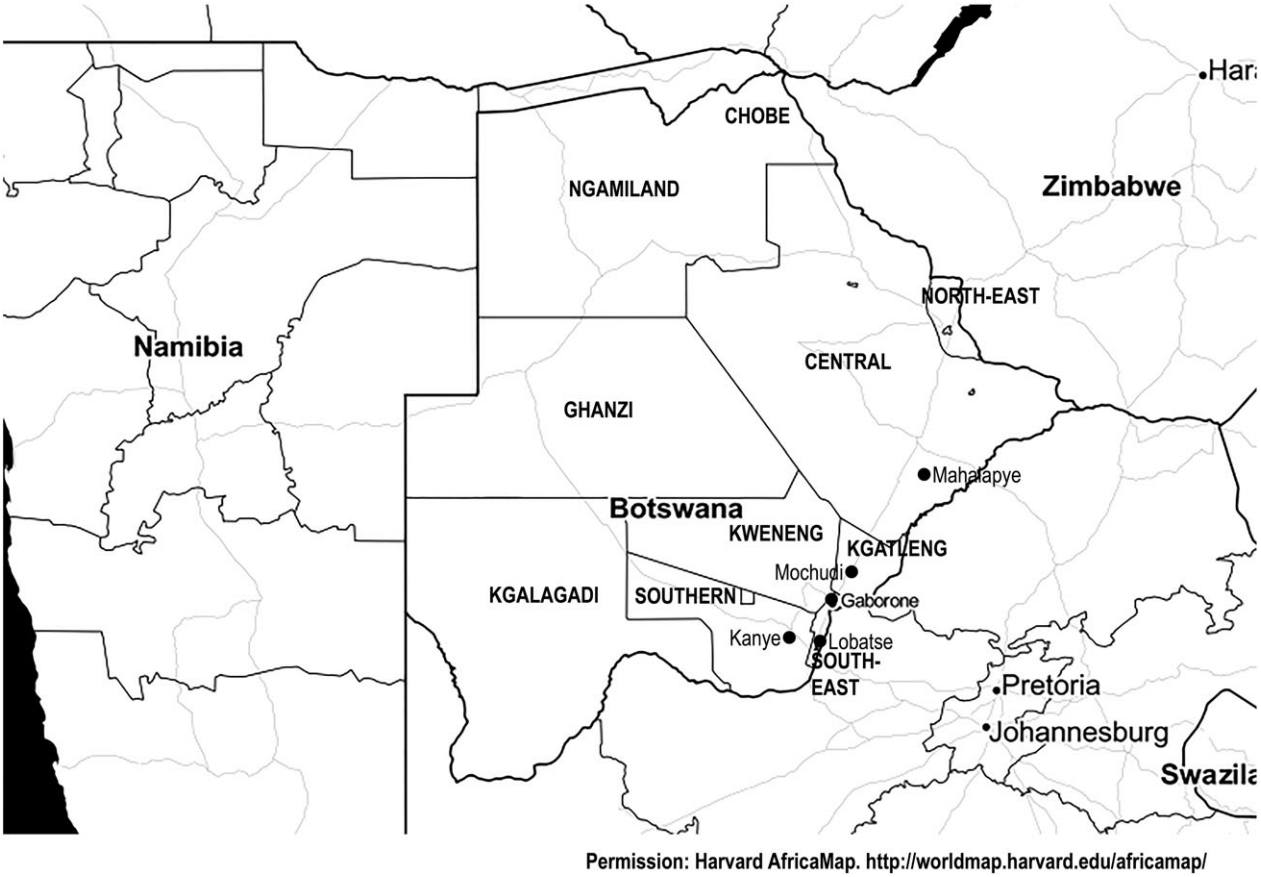

Figure 1 Map of Botswana and Location of Public Dermatology Clinics: Central (Mahalapye), Southern (Kanye), South-East (Gaborone, Lobatse), and Kgatleng (Mochudi) Districts

Table 1 Characteristics of patients seen in the dermatology clinic with a cutaneous autoimmune disease between September 2008 and December 2015

Gender, *N* (%)	***N* = 262**
Male	59 (22.5)
Female	203 (77.5)
Age in years, mean (SD)	46.7 (18.3)
HIV Status, *N* (%)	
Positive	52 (19.8)
Negative	105 (40.1)
Unknown	105 (40.1)

HIV, human immunodeficiency virus.

or nonrecorded HIV status, which is a significant limitation. We found that at least 19.8% of patients with autoimmune skin disease are also living with HIV, which is on par with the prevalence of HIV in Botswana.[11] This is important given the potential for drug interactions between antiretroviral medications and therapeutics for autoimmune skin disease[24] and the additional morbidity associated with a second chronic

Table 2 Frequency of autoimmune disease in Botswana dermatology clinics

Diagnosis	**% New patients *N* = 5897 *N* (%)**
Connective tissue diseases	
Cutaneous lupus erythematosus	152 (2.6)
DLE	115 (2.0)
CLE NOS	25 (0.4)
SLE with cutaneous involvement	12 (0.2)
Systemic sclerosis	20 (0.3)
Morphea	15 (0.3)
Lichen sclerosus	14 (0.2)
Dermatomyositis	11 (0.2)
Bullous diseases	
Bullous pemphigoid	35 (0.6)
Pemphigus foliaceus	8 (0.1)
Pemphigus vulgaris	5 (0.1)
Pemphigus vegetans	2 (0.03)

DLE, discoid lupus erythematosus; CLE, cutaneous lupus erythematosus; NOS, not otherwise specified; SLE, systemic lupus erythematosus.

Table 3 Estimated incidence of cutaneous autoimmune disease in Botswana

	New Cases	Incidence[a] per 1,000,000 people
All cutaneous autoimmune diseases	262	28.8
Any Connective Tissue Diseases	212	23.3
Discoid lupus erythematosus	115	12.6
CLE NOS	25	2.8
Systemic sclerosis	20	2.2
Morphea	15	1.6
Lichen sclerosus	14	1.5
SLE with cutaneous involvement	12	1.3
Dermatomyositis	11	1.2
Any bullous diseases	50	5.5
Bullous pemphigoid	35	3.8
Pemphigus foliaceus	8	0.9
Pemphigus vulgaris	5	0.6
Pemphigus vegetans	2	0.2

CLE, cutaneous lupus erythematosus; NOS, not otherwise specified; SLE, systemic lupus erythematosus.
[a]Calculated based on the population of districts where our clinics are located 1,300,652.

disease. Additional limitations of our study include its retrospective nature and lack of set diagnostic criteria, lack of availability of immunological diagnostic studies, and lack of comparative studies in ethnically and geographically similar populations.

We describe the incidence of autoimmune skin disease in our dermatology clinics in Botswana, which accounts for about 4% of all the new patient diagnoses. Healthcare practitioners in Botswana can benefit from further education about these diseases, particularly cutaneous lupus, which occurs more frequently than the other diagnoses. Education can highlight the need for sun protection and early referrals to specialty care. Additional data are needed to further illuminate the true prevalence of these diseases globally and better define the roles that ethnicity, race, geography, and HIV play in autoimmune skin disease.

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