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**Abstract**

**Background:** There is no epidemiologic data regarding autoimmune pemphigus in the Afro-Caribbean population.

**Objectives**: To describe the epidemiology of autoimmune pemphigus on the island of Guadeloupe (French West Indies, 400736 inhabitants, mostly black Caribbean of African European descent).

**Methods**: 5-year prospective study . Inclusion of the incident cases when directly referred to the Dermatology Department or secondarily referred by they private practice dermatologist once identified by the computerized databases of the guadeloupean pathology laboratories.

**Results:** World-population-standardized incidence was 6.96 (95% CI: 3.41-10.52) for pemphigus vulgaris and 3.75 (95% CI: 1.12-6.39) for pemphigus foliaceus. Patients usually live in the rural countryside whereas 75% of the population of Guadeloupe Island live in a urban environment.

**Conclusion**: We report a high incidence of auto immune pemphigus in Guadeloupe, especially for the foliaceus type and particular epidemiological features such as the rural countryside habitat.

## Introduction

Pemphigus is an autoimmune blistering disease involving the skin and or mucosa. It is due to pathogenic autoantibodies directed against keratinocytes surface antigens: desmoglein 1 (Dsg 1) and desmoglein 3 (Dsg 3). Both genetic and environmental factors have been associated with the occurrence of autoimmune pemphigus [1]. For example, the association between pemphigus vulgaris (PV) and pemphigus foliaceus (PF) with HLA class II alleles (ie: DR4 and DR14) is now clearly demonstrated [1,2]. Moreover, various epidemiological studies have identified environmental antigens linked to endemic PF [1,3,4]. For these reasons, annual incidence of the disease differs among ethnic groups and in parts of the world [1-7]. Little is known about the epidemiology of autoimmune pemphigus in black patients. Indeed, most studies concern Caucasians from Mediterranean Basin or Asia Minor and from Western Europe [1,5,6,7]. Only 2 studies concerning Black patients from South Africa and from Mali are available [8,9]. There is no epidemiologic data regarding autoimmune pemphigus in the Afro-Caribbean population. Moreover, all the studies performed with calculation of the world standardized incidence of autoimmune pemphigus are retrospective and few include an individual validation of the cases in their design [1,6].

Guadeloupe, an overseas department of France, is the greater island of the Lesser Antilles within the West Indies ( 400736 inhabitants, mostly black Caribbean of African European descent). Recent studies have reported a high incidence of autoimmune diseases in the French West Indies but autoimmune pemphigus has not yet, to our knowledge, been reported [10].

We performed a prospective study to estimate the world standardized incidence rate of autoimmune pemphigus on the island of Guadeloupe during the 5–year period between 1/11/2005 and 1/11/2010 and describe the epidemiological characteristics of the disease in this Afro-Caribbean population.

## Materials and methods

Incident cases of autoimmune pemphigus were prospectively included when referred to the Dermatology Department of Guadeloupe Island University Hospital. Possible cases of autoimmune pemphigus diagnosed exclusively in private consultation during the study period, were identified using the computerized databases from the 3 pathology laboratories of the island. Identified patients were secondarily referred to the Dermatology Department by their private practice dermatologists to be enrolled in the study. Inclusion criteria were the followings: i) patients with clinical and histological characteristics of autoimmune pemphigus ii) positive direct immunofluorescence (ie: deposition of IgG, C3 or both on the keratinocyte membrane), iii) patients who lived on the island of Guadeloupe for at least 6 months prior to their skin disease occurrence. The exclusion criterion was an age inferior to fifteen.

The following data were recorded for all the patients included in the study: gender, phototype according Fitzpatrick classification, socio professional category, habitat, age at diagnosis of pemphigus, clinical manifestations and histological features of the disease, medical history focused on neoplasia, auto-immunity and chronic inflammatory diseases, current treatment with special regards to medications known to induce autoimmune pemphigus [11].

### Laboratory studies

HLA tests were performed with the autorization of patients on a signed consent form. Antileishmaniasis activity and anti-HIV, HCV, HBV, HTLV-1 as well as syphilis serology were recorded for each included patient.

To determine anti-Dsg 1 and anti-Dsg3 antibodies titers, Dsg1- and Dsg3-ELISA tests (MESACUP Desmoglein test; Medical and Biological Laboratories, Nagano, Japan) were performed with 1:100 diluted serum samples according to the manufacturer's instructions. The cut-off values were set at 14 and 7 for anti-Dsg-1 et anti Dsg-3 ELISAs respectively.

**Statistical evaluation**

The crude and world-population-standardized incidences were determined using Stata/SE 10.0 for Windows software (StatCorp LP, College Station, TX, USA) and the 95% confidence interval was calculated assuming a Poisson distribution [12]. Statistical analysis was done using SPSS 17.0 software (IBM SPSS Statistics, Chicago, IL).

**Results**

Fifteen cases of autoimmune pemphigus were included in the study (PV n=7; PF n=8). No pediatric cases were identified. The crude annual incidence of autoimmune pemphigus on Guadeloupe Island was 7.49 cases per million inhabitants (95% CI: 4.19-12.35) over the study period. The world-population-standardized incidence was 6.96 cases per million inhabitants (95% CI: 3.41-10.52).

Characteristics of patients at baseline are sumarized in table 1. Mean age of patients was 53+/-19 years. Male/female sex ratio was 0.9. All patients were black Caribbean of African European descent with a dark phototype (ie: V or VI based on the Fitzpatrick classification).They all belonged to middle or low socio professional categories. The entire series of patients had lived on Guadeloupe Island since birth. Habitat was the rural countryside in 75% (9/12) of cases (i.e.: sugar cane fields and banana plantations, tractor farming) whereas 75% of the population of Guadeloupe Island live in a urban environment [13]. Lesions were exclusively localized in the oral cavity in 2 of the 7 patients with PV. Interestingly, most of the PV patients (4/5:80%) exhibited some pustules with hypopyon on the trunk and limbs (Fig.1). For these patients a specific skin biopsy specimen of the pustule was analyzed in addition with a standard skin biopsy specimen of a PV typical lesion. Histological examination of the pustule showed suprabasal acantholysis; direct

immunofluorescence (DIF) showed epithelial cell surface staining predominantly on the basal layers of the epidermis with IgG (n=3) or IgA (n=1). PF patients had typical skin lesions located on the classical sites (ie. central chest, scalp and face). Dsg1 Elisa test was positive in 7/8 cases ( PF: n=4, PV: n=3) and negative in the 2 cases of mucosal PV. Dsg3 Elisa test was positive in the 6 tested PV patients, and negative in PF patients, as expected. The HLA class II alleles associated with autoimmune pemphigus (i.e.: DR4 and/or DR14) were found in 9/12 (75%) tested patients (PF n=4; PV n=5). Anti-HIV, HCV, HBV, HTLV-1 antibodies as well as anti-leishmaniasis activity and syphilis serology were negative in all patients.

**Discussion**

This first epidemiological study about auto-immune pemphigus in the Afro-Caribbean population showed a high world-population-standardized incidence of 6.96 cases per million inhabitants per year , (95% CI:2.97-10.97). This incidence rate is higher than that reported in the US and in Western Europe, where the incidence rate varies from 0.6 to 1.55 cases per million inhabitants per year according to the most recent studies [5,6]. It is also greater than world-population- standardardized incidence rates reported in studies performed in Mediterranean Basin where values are the most high (ie: 3 cases per million inhabitants per year in Italy and 6.7 in Tunisia). [ 1,7 ]

Moreover, our study showed a high world-population-standardized incidence of PF (i.e.: 3.59 cases per million inhabitants per year (95% CI: 0.67-6.51) as compared to the incidence of sporadic PF in the US and in Europe (i.e: less to 1 case per million inhabitants per year) [ 1]. Despite the lack of familial cases, this latter result prompted us to investigate a link between pemphigus from Guadeloupe Island and endemic pemphigus from Brazil which is geographically near. We found 3 similarities between these 2 forms of autoimmune pemphigus: i) the HLA class II alleles DR4 and DR14 were observed in 75% of tested

patients, ii) about half of the patients lived in the rural countryside and ; iii) belung to low and middle socio professional categories. Interestingly, the endemic parasitosis of leishmaniasis that was recently suspected to trigger Brazilian endemic pemphigus is also present on Guadeloupe Island [ 3]. Unfortunately we did not find any positive serological tests for leishmaniasis. The second finding of our study, is that special clinical features ( i.e.: pustules with hypopyon) previously reported in African people from Mali, and from South Africa suffering from autoimmune pemphigus were observed in our series of Guadeloupean PV patients [ 8,9]. This point led to discuss the existence of clinical particularities of auto immune pemphigus in African and Afro-Caribbean people.

**Conclusion**

On the island of Guadeloupe (French West Indies), autoimmune pemphigus seems to have particular epidemiological and clinical features. These initial results prompted us to perform a larger prospective study including patients from several islands of the West Indies .

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**Legends:**

**Table 1:** Baseline characteristics of patients

**Figure 1:** Erosions and pustule with hypopyon in a patient with PV.

**Figure 2a/b:** histological examination of the pustule showing suprabasal acantholysis; direct immunofluorescence showing epithelial cell surface staining predominantly on the basal layers of the epidermis with IgG