

## Research Article

# Drug Eruptions at Patients in Consultation at the Dermatology Department of the Dermatology Teaching Hospital in Bamako, Mali: Epidemiological, Clinical and Etiological Study

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## Introduction

The administration of a drug substance is an essential step in the management of a patient. It aims either to cure the patient, to prevent a given disease or sometimes to help with the diagnosis. Unfortunately, the action of the drug can go beyond the desired effect, and cause skin-mucous accidents. These accidents, also known as drug-induced attacks, can be isolated or associated with systemic manifestations [1]. Drug eruption is a real public health issue because of the high frequency. In Europe, drug eruption is responsible for about 20% of spontaneous reports of drug accidents. They complicate 2% to 3% of hospital treatments and motivate 1% of consultations, 5% of hospitalizations in dermatology [2]. Some African authors were interested in the subject. Reported prevalence in hospital settings ranges from 0.4% to 1.53% [3,4]. In Mali, there are no national figures. Old statistics from the Department of Dermatology show that about thirty cases occur each year, most of which are represented by severe forms. However, the risk of drug eruption is thought to be very high due to increased local use of drugs without medical advice, the illegal proliferation of drug outlets ('Street Medicine'). And the lack of enforcement of existing regulations. In addition, some authors believe that the advent

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of antiretrovirals and the use of anti-infectious infections used to treat opportunistic infections have increased the risk of Drug eruption by 4 to 30 times, particularly in subjects infected with the acquired human immunodeficiency virus (HIV) [2]. This same risk can be observed in leprosy patients on combination chemotherapy. Clinically, the diagnosis of drug eruption is not as easy as one might think because of clinical polymorphism. The responsibility of a drug for the onset of a reaction is also not easy to establish, as in most cases several drugs are administered simultaneously before the onset of the rash. Because of illiteracy, patients find it difficult to make a complete list of the molecules consumed. To this must be added the high frequency of counterfeit medicines circulating both on the street and in private pharmacies. Given the scarcity of African studies and due to local specificities, it seemed interesting to us to undertake a study on Drug eruption in the dermatology department of the Dermatology teaching hospital of Bamako whose purpose is to study epidemiological aspects, clinical, etiological and to identify the molecules responsible in these patients.

## Patients and methods

The dermatology department of the Dermatology Teaching Hospital served as a framework for our study. The

Dermatology Teaching Hospital is a public scientific and technological institution (EPST). Its activity centre covers research on endemic diseases, vaccine research, clinical research, programme support, continuing education and teaching. It is located in 6th arrondissement of the district of Bamako precisely in the neighborhood of djicoroni para. This is a descriptive cross-sectional survey of all new patients consulting in the Dermatology Teaching hospital from 01 January 2019 to 31 December 2020. The study population consisted of consulting patients in the dermatology department during the study period.

The case was defined as any patient, regardless of age and sex, for a skin rash due to oral administration of a molecule. The imputability criteria used to search for the drug probably in question were those recommended by the French pharmacovigilance [5].

This was a systematic sampling to include all cases of toxiderma over a 2-year period in a specialized centre. We have included all patients consulted in the dermatology department of the Dermatology teaching hospital of Bamako and having the following characteristics: Rash compatible with a clinical presentation of toxidermis, appearance in the aftermath of the administration of a drug, agreeing to participate in the study. We systematically excluded: Autoimmune bullous diseases, too long time between eruption and administration of the molecule. All patients included were thoroughly interviewed. Socio-demographic data were collected on a survey sheet (Appendix). The chronological list of all recently taken medications (4 weeks prior) was carefully noted (molecule, dosages, reason for taking, duration, start and end of use). The notion of the occurrence of a similar episode was also sought. All patients were subjected to a complete dermatological examination. Retroviral serology was also prescribed.

TZANCK cytodiagnosis and skin biopsy were performed in the event of a new bubble. Stevens Johnson Syndrome and toxic epidermal necrolysis were routinely hospitalized. The informed consent of each patient was obtained before its inclusion. The iconography scrupulously respects the anonymity of the patients.

## Results

In total, during the study period 62 consultant cases for toxidermis were included in a sample of 2,129 patients, a prevalence of 2.91%. There were as many men (31 cases, 50%) as women, a sex ratio equal to 1 (Figures 1,2) (Table 1).

Patients came mainly from the regions of Bamako (71%), Koulikoro (14.5%), Sikasso (6.4%) and Ségou (4.8%) (Table 2).

Clinically, only 3.2% of patients had a history of atopy (Table 3).

Conditions that led to drug use: Approximately one-third

of patients (31.5%, 22 cases) became acutely ill as a result of drug use for malaria or suspected malaria fever. For the rest, toxidermis occurred in the course of treatment for rhino-bronchitis (7 cases), angina (4 cases), gout (4 cases), epilepsy (3 cases) and headache (3 cases), leprosy (1 case), HIV and HIV-related opportunists (2 cases) (Table 4).

Number of drugs consumed: The number of drugs consumed per patient ranged from 1 to 5 drugs, with an average of 1.8 1.6. Note that all had received at least one molecule (Tables 5,6).

The molecules to which patients were allergic were essentially chloroquine (6 times) and amoxicillin (1 time). The main molecules involved were: antibacterial sulfamides (24 cases), allopurinol (8 cases), antimalarials (22 cases). This was self-medication in 29 cases or 46.77% (Table 7).

This was self-medication in 29 cases or 46.77% (Table 8).

The clinical aspects observed were fixed erythema pigment or EPF (26 cases), Steven Johnson (16 patients including 7 with ocular involvement), - skin rash (15 cases), toxic epidermal necrolysis (4 cases) and finally a Drug reaction with eosinophilia and systemic syndrome (DRESS) 1 case (Table 9).

More than half of the patients visited the first few days after the first symptoms (Tables 10,11 ).

The progression of the disease was marked by healing without sequelae in 56 patients (90.3%), death in one patient (75-year-old patient). Finally, three patients were lost sight of.

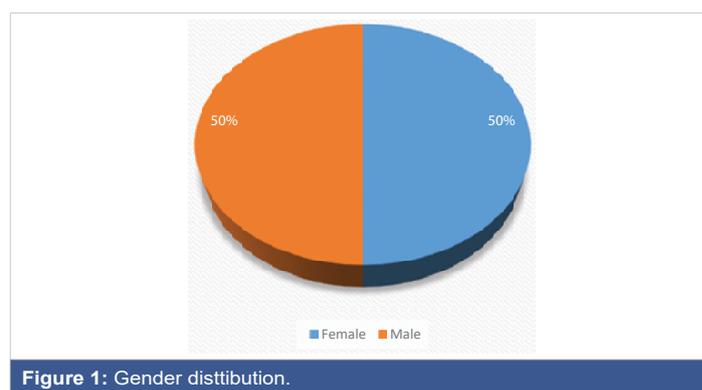


Figure 1: Gender distribution.

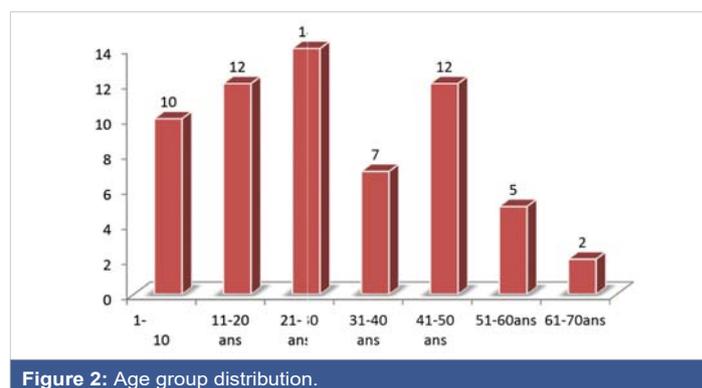


Figure 2: Age group distribution.



**Table 1:** Ethnic group distribution.

Ethnic	Frequency	Percentage
Peulh	14	22,6%
Bambara	13	21%
Soninke	9	14,5%
Senoufo	2	3,2%
Sonrhaï	2	3,2%
Bozo	1	1,6%
Dogon	1	1,6%
Minianka	1	1,6%
Autres	19	30,6%
Total	32	100%

**Table 2:** Distribution by place.

Number	Frequency	Percentage
Bamako	44	71%
Kayes	1	1,6%
Koulikoro	9	14,5%
Ségou	3	4,8%
Sikasso	4	6,5%
Autres	1	1,6%
Total	62	100%

**Table 3:** Distribution of patients accordant to the concept of drug allergy.

drug allergy	frequency	Percentage
Allergic	7	11,3%
No allergic	55	88,7%
Total	62	100%

**Table 4:** Distribution by reason of drug used.

Reason of drug used	Frequency	Percentage
Angina	4	6,5%
Malaria	22	31,5%
Rhinobronchitis	7	11,3%
Gout	4	6,5%
Epilepsy	3	4,8%
Headache	3	4,8%
HIV	2	3,2%
Fever	2	3,2%
Anemia	1	1,6%
Cancer	2	3,2%
Lupus	1	1,6%
Parasitosis	1	1,6%
IST	1	1,6%
Sexial disorder	1	1,6%
Gastralgia	1	1,6%
Diarrhea	11	1,6%
Paraplégia	11	1,6%
Leprosis	1	1,6%
Nephrotic Colic	1	1,6%
No found	1	1,6%
Preventive	2	3,2%
Total	62	100%

**Table 5:** Distribution by number of drugs kaked.

Number de médicament	Frequence	Percentage
One Drug	22	35,5%
Two Drugs	28	45,2%
Three Drugs	10	16,1%
Four Drugs	1	16,1%
Five Drugs	1	16,1%
Total	62	100%

**Table 6:** Distribution by Drug Involved.

Type of Drug	Frequency	Percentage
Amoxicillin	1	1,6%
Chloroquine	6	9,7%
No known allergy	55	88,7%

**Table 7:** Distribution by Drug Intake.

Médicaments suspects	Frequency	Percentage
Co-trimoxazole	16	25,85%
Sulfadoxine/ pyrimethamine	12	19,35%
Allopurinol	5	8,06%
None	3	4,83%
Lactam Coumpounds	3	4,83%
Neuroleptics	3	4,83%
Antiretrovirals	2	3,22%
Trioleandomycin	2	3,22%
Dapsone	1	1,6%
Plaquenil	11	1,6%
Authers	14	22,58%
Total	62	100%

**Table 8:** Distribution by Type of Drug Intake.

Type of Drug Intake	Frequency	Percentage
medical Prescription	33	53,22%
Self-medication	29	46,77%
Total	62	100%

**Table 9:** Distribution by clinical diagnosis.

Diagnosis	Frequency	Percentage
Fixed drug eruption	26	41,9%
Rash	15	24,2%
Steven Johnson Syndrome	16	25,8%
Lyell Syndrome	4	6,5%
DRESS syndrome	1	1,6%
Total	62	100%

**Table 10:** Distribution by Time Taken Prior to Consultation.

Time	Frequence	Percentage
0-1 day	35	56,4%
2-6 days	15	24,19%
7-15 days	12	19,35%
Total	62	100%

**Table 11:** Distribution by evolution.

Evolution	Frequence	Percentage
Healing with sequelae	2	3,2%
Death	1	1,6%
Healing without sequelae	56	90,3%
Lost sight of	3	3,2%
Total	62	100%

## Discussion

The average age of our patients was 30 years. This young age found in our series is comparable to that of Safiatou, et al. who reported an average age of 31.4 [6]. On the other hand, in the European and Asian series, toxidermis predominates in older subjects because of the frequent poly medication in these subjects [2,7]. In our series, as in the one reported by Özkaya-Bayazit and Harugeri [7, 8], the frequency of toxidermis was the same in both sexes. On the other hand, in the European series,



there was a predominance of women probably explained by their susceptibility to develop a toxidermy [2]. The Peuhl ethnic group was the most represented, with a frequency of 22.6%. There is no explanation for this predominance which could be a reflection of the consulting population or a mere coincidence. The majority of the patients came from Bamako. This is related to the proximity of the service, which represents, at the national and even sub-regional level, the largest centre for skin disease management. Clinically, Atopy: A notion of atopy was found in 3.2% of subjects. This result differs from that of Weeranut which reported an atopy rate of 20.9% [9]. This low proportion of atopic in our study may be explained by the difficulty of collecting information. Among the reasons for taking drugs, malaria was the main reason for taking drugs in our patients. This is easily explained by the high prevalence of this condition and the easy attribution of all the conditions to this source. Self-medication is a common practice in developing countries, particularly in Mali. In our series it was 46.77% against 51% in the study of Safiatou [6]. The proliferation of street drug outlets (on-street pharmacies) and the easy availability of non-prescription drugs make self-medication a common practice. Maculopapular exanthema is the most commonly reported clinical form of toxiderma in the literature [2]. However, in our series, fixed erythema pigment was the most common clinical form. Similar results were observed by other authors [6,7]. The onset of lesions ranged from 1 to 3 weeks. These data are compatible with the results of previous work, notably those of Roujeau, et al. and Krebs, et al. [2,10]. They generally correspond to the time required for the body to become aware of the drug. The majority of our patients consulted from the first day of the rash. This is related to the disturbing and brutal nature of the affection. Among the severe clinical forms of toxiderma in our series, Steven Johnson syndrome was the most common form. This predominance of the SJS is found in India [8] and Madagascar [11].

With 34.37% and 61.53% respectively. On the other hand, our results contradict those reported by Safiatou who found 2.35% of SJS (2/85) and Weeranut who found 8.4% (16/191) [6,10]. These differences are explained by the specificities of these different studies. The anti-infectious sulfamides were the most incriminated molecules in the occurrence of toxidermies in our patients: cotrimoxazole was found 16 times (25.85%), sulfadoxine pyrimethamine 12 times (19.35), Allopurinol 5 times (8%) and betalactamines 3 times. Our results are in line with the work carried out by Özkaya and Collaborateurs who found cotrimoxazole in 63.8% of patients with fixed erythema pigment [7]. In the study of Safiatou [6]. Paracetamol was responsible for toxicity in 23.08% of patients; penicillin was found in several authors [12-14]. This predominance of anti-infectious sulfamides is explained on the one hand by the high consumption of these molecules linked to its use in palustrine syndromes, respiratory and digestive diseases, and on the other hand, because of its availability both in the stores and in

the parallel market of our cities. In our series, 45.2% (28/62) of patients had consumed at least 2 medications before the onset of the rash. In the series published by Aguèmon on Lyell syndrome in intensive care settings, the majority of patients used several medications (27.42%) [13]. The seroprevalence of HIV in our study was 6.5% (4/62). In the Weeranut study, it was 22% (22/1541) [9]. The relationship between immunosuppression and HIV has been the subject of much work [4]. The risk of developing toxiderma is increased in HIV-infected patients. Recovery without sequelae was noted in 90.3% (56/62) of cases. For the rest, 2 patients had ocular sequelae (1 woman aged 60 and 1 man aged 17), 3 patients were lost of sight and 1 patient died during hospitalization (woman aged 70). The incidence of eye damage was estimated at 30.81% in France and 56% in Morocco.

## Conclusion

At the end of our study, it is clear that toxidermis remains common in developing countries such as sub-Saharan Africa. This high frequency is probably related to malaria endemicity in this region requiring the use of the antimalarial responsible for the toxidermis and the high frequency of self-medication.

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