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Epidemiological Profile of *Clostridium tetani* Portals of Entry in Tetanus Patients at the Point-G University Hospital Center, Bamako, Mali

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Abstract

Introduction: Tetanus remains a serious medical emergency and a major public health problem in developing countries. The presence of portal of entry (POE) remains an essential condition for the bacterium (*Clostridium tetani*) to enter the body. **Objective:** To determine the frequency and main tetatogenic profiles of bacterial POE and describe their topography. **Patients and Method:** We conducted a descriptive and analytical cross-sectional study with retrospective data collection at Point-G University Hospital over a period of 22 years. Our study population consisted of tetanus patients whose bacterial POEs were found upon admission. The variables analyzed were collected from complete and analyzable hospital records. The distribution of quantitative variables was described by the mean, standard deviation and extreme values. The expected significance threshold was set at $p < 0.05$. **Results:** We recorded 258 tetanus patients, representing 5% of hospitalizations. The POE was found in 217 cases (84.10%) with a sex ratio (M/F) of 9.85 and an average age of 35.94 ± 15.58 years. Unskilled laborers (32.7%), farmers (25.8%), pupils/students

(10.1%), traders (11.1%) and housewives (5.1%) were the predominant occupations, with no statistically significant difference in cases where POEs were not found (p = 0.63). The most common POEs were skin and mucosal injuries (65.4%), open fractures (10.6%), skin lesions (7.8%) and deep wounds (7.4%). The most significant anatomical sites were the pelvic limbs (62.2%), thoracic limbs (26.3%), head (5.5%) and uterus (2%). Generalized forms appeared to be more common in anatomical sites located on the pelvic and thoracic limbs, with no statistical difference as regards the origin of the clinical form (p = 0.45). The overall mortality rate was 42.2%. Specifically, 41.5% of deaths were observed in patients with bacterial portal of entry found (BPOEF) versus POEs not found (46.3%) with p = 0.77. **Conclusion:** Tetanus continues to be a reality despite the availability of effective prevention methods. The implementation of good practices in primary care for bacterial portals of entry would be a significant contribution to tetanus elimination strategies.

Keywords

Tetanus, Portal of Entry, Pelvic and Thoracic Limbs, Serotherapy, Vaccination, Bamako

1. Introduction

Tetanus is a neurological disease that was described in ancient times by Hippocrates [1]. It is a disease that can be prevented by proper vaccination. Tetanus is a medical emergency due to its severity and is still a rare disease in industrialized countries [2]. However, it remains a real public health problem in developing countries where vaccination coverage is lower [3] [4].

The global incidence of tetanus is estimated at 1 million cases per year [5] [6] with a mortality rate of 6 to 50% or even 72% depending on the authors and the level of equipment available in treatment units [7] [8]. Africa accounted for nearly 50% of tetanus cases, including 1038 cases in the DRC and 1822 cases in Uganda in 2010, making them the countries with the highest incidence [9]. At the Point-G University Hospital Centre in 2012, the frequency of hospital admissions for tetanus was 6.5% with a sex ratio of 5.26 [10]. In Côte d'Ivoire, it accounted for 6.3% of hospitalizations [11]. Globally, 14% of deaths in children under one month of age are attributable to neonatal tetanus [1].

Despite the progress made, hospital mortality remains high, at 46.6% in Bamako and 45% in Dakar [12].

The presence of a portal of entry (POE) remains an essential condition for the bacterium (*Clostridium tetani*) to enter the body, although it is not found in 15 to 25% of cases, depending on the authors [13] [14]. Various studies have concluded that there are a variety of portals of entry, including skin ulcers, abscesses, gangrene, burns, or after abdominal-pelvic surgery, childbirth or abortion, necrotic snake bites, and intramuscular injections [1] [10] [13] [14].

It would be worth looking into this diversity of POE both in number and severity. In fact, their severity and topography remain decisive in the progression of the disease. So, based on a collation of hospital data from Point-G, we carried out a study of POE identified in tetanic patients, their representativeness and established their tetanogenic profile.

2. Patients and Method

2.1. Study Setting and Location

Our study took place in the Infectious Diseases Department, which remains the main centre for the management of tetanus in Mali, and in the Internal Medicine Department, both located within the Point-G University Hospital Centre (CHU) in Bamako.

2.2. Type and Period of the Study

We conducted a cross-sectional study based on retrospective analysis of data on patients hospitalized for tetanus between January 2001 and December 2022, using data from the records of patients admitted for tetanus at the Point-G University Hospital Centre.

2.3. Study Population and Sampling

We focused on patients of all ages admitted to hospital with suspected tetanus and confirmed tetanus, in whom an active search for bacterial portal of entry was carried out and found.

Our study included patients confirmed to have tetanus, regardless of their HIV status, who were admitted during the study period, had a usable medical record, including information on POE, and were hospitalized at our study sites.

We used the following definitions for POEs: skin and mucosal wounds as any lesions non-bleeding or slightly bleeding caused by the point of impact of a sharp, cutting, stabbing or blunt object sometimes negligible and not considered by the victim. And skin lesions as any lesions occurring as a result of a road traffic accident, developed on an inflammatory basis and bleeding requiring treatment in a healthcare setting.

2.4. Course of the Study

We selected patient records based on the characteristics of the study population and eligibility criteria. The variables studied were collected from the records of the selected patients. The variables collected mainly concerned sociodemographic data and clinical variables taking into account the active search for the bacterial portal of entry, the profile of the lesions and the topographical sites of the lesions.

2.5. Data Entry and Analysis

The information was entered into a database using Epi Data software, Access, version 3.1. This database was cleaned and analyzed using SPSS software, version 12.0.

The calculation of frequencies enabled the description of qualitative variables. Pearson's chi-square test was used to compare these qualitative values.

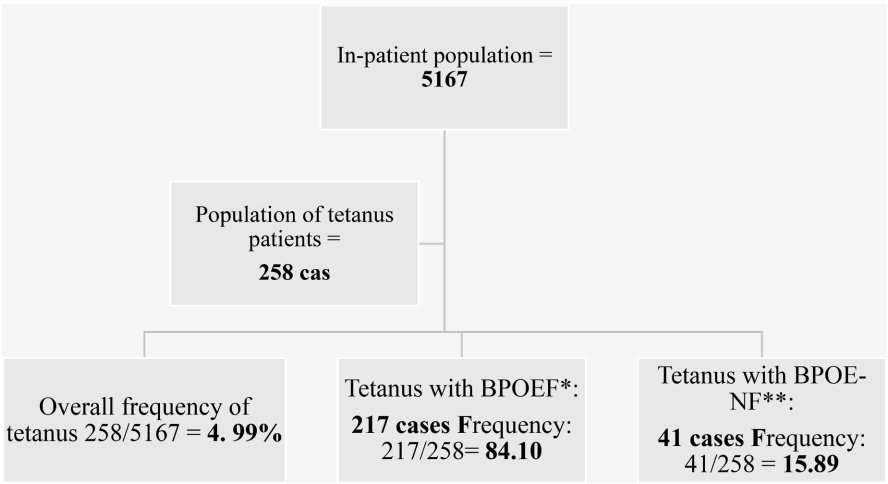
The expected significance threshold was set at $p < 0.05$. Pearson's chi-square test was used to verify the association with a significance threshold of 0.05.

2.6. Ethical Considerations

Prior to using the data, we obtained approval from the Point-G University Hospital Centre (UHC) authorities in accordance with the agreement between the UHC and our university. However, we were keen to guarantee the confidentiality and anonymity of the patients whose records were selected.

3. Results

The database analysis showed that tetanus accounted for 5% of hospitalizations. The portal of entry (POE) of *Clostridium tetani* was found on admission in 84.10% of subjects admitted and confirmed to have tetanus (Figure 1).



*Bacterial portal of entry found; **Bacterial portal of entry not found.

Figure 1. Distribution of tetanus patient flows.

Male subjects accounted for 90.3% of confirmed tetanus cases. The teratogenic bacterial portal of entry (BPOEF) was identified in 197 male tetanus patients versus 20 female cases. In the period immediately prior to admission, 2.8% and 4.1% of samples benefited from tetanus antitoxin therapy and tetanus vaccination, respectively (Table 1).

The residence of tetanus patients in urban areas was overrepresented among cases with BPOEF compared to peri-urban and rural residences, with no statistical difference ($p = 0.21$) (Table 1).

BPOEFs sites were mainly located on the pelvic (lower) limbs, accounting for 62.2% of POEs (Table 2). The profile of POEs was dominated by skin and mucosal injuries (65.4%) caused by sharp objects, open fractures (10.6%), skin lesions resulting from trauma and road traffic accidents (7.8%) and deep wounds (7.4%)

Table 1. General characteristics of tetanus patients.

Parameters	%	p
1. *Gender of tetanus patients*		
Male: 253	90.3	
Female: 25	9.7	
Sex-ratio (H/F): 9.32		
Bacterial POEs identified by gender		
Male: BPOEF	90.8	
Female: BPOEF	9.2	p = 0.76
2. *POE in tetanus patients who received serotherapy shortly after the onset of POE*		
BPOEF: 6 (2.8%)/Serotherapy unknown: 68 (31.3%)		
BPOE-NF: 1 (2.5%)/Serotherapy unknown: 20 (48.8%)		
3. *POE in tetanus patients who had recently received a tetanus vaccination*		
BPOEF: 9 (4.1%)/Unknown vaccination status: 72 (33.2%)		
BPOE-NF: 1(2.4%)/Unknown vaccination status: 20 (48.8%)		
4. *POE among tetanus patients according to their place of residence*		
Urban: BPOEF = 130 (59.9%)/BPOE-NF = 27 (65.9%)		
Peri-urban:BPOEF = 40 (18.4%)/BPOE-NF = 3 (7.3%)		p = 0.21
Rural: BPOEF = 47 (21.7%)/BPOE-NF = 11(26.8%)		
5. *Clinical course*		
Favourable: BPOEF = 122 (56.2%)/BPOE-NF = 19 (56.3%)		
Deaths: BPOEF = 90 (41.5%)/BPOE-NF = 19 (46.3%)		p = 0.77

Table 2. Distribution of patients according to the site of the bacterial portals of entry.

Site or location of the portal of entry	Number	Percentage
Lower limb	135	62.2
Upper limb	57	26.3
Head	12	5.5
Uterus	4	1.8
Male urogenital tract	1	0.4
Trunk	3	1.4
Buttocks	2	0.9
Oral cavity	2	0.9
ORL	1	0.5
Total	**217**	**100.0**

(Table 3). The occupations most affected by BPOEF were workers (71%), farmers (56%), traders and pupils/students (24% and 22% respectively) (Table 4), with no statistically significant difference (p = 0.63) between BPOEF and BPOE-NF in terms of patient occupations.

The average length of hospitalization for all tetanus patients was 5.136 ± 4.89 days [1 - 30]. The specific length of hospitalization for patients with BPOEF was

Table 3. Distribution of patients according to the bacterial portal of entry profile.

Type of portal of entry	Number	Percentage
Skin and mucous membrane injuries	142	65.4
Open fractures	23	10.6
Skin lesions	17	7.8
Deep wounds	16	7.4
Surgery	4	1.8
Intramuscular injections	4	1.8
Uterus	4	1.8
Burns	2	0.9
Dental surgery	2	0.9
Other*	3	1.4
Total	**217**	**100.0**

*: Tegumentary (1), Skin infection (1), Auditory (1).

Table 4. Distribution of patients according to occupation and presence of bacterial portal of entry.

Occupation	Portal of entry		Total (%)
	Found (%)	Not found (%)	
Worker	71 (32.7)	17 (41.5)	88 (34.1)
Farmer	56 (25.8)	12 (29.3)	68 (26.4)
Pupil/Student	22 (10.1)	5 (12.2)	27 (10.5)
Trader	24 (11.1)	1 (2.4)	25 (9.7)
Housewife	11 (5.1)	2 (4.9)	13 (5.0)
Child	8 (3.7)	2 (4.9)	10 (3.9)
Street vendor	5 (2.3)	1 (2.4)	6 (2.3)
Civil servant	4 (1.8)	0 (0)	4 (1.6)
Other*	5 (2.3)	1 (2.4)	6 (2.3)
Unknown	11 (5.1)	0 (0)	11 (4.3)
Total	**217 (84.1)**	**41 (15.9)**	**258 (100.0)**

*: Radio presenter (1); Artist (1); Retired security guard (1); Manager (1); Restaurateur (1); Building technician (1). Fisher's exact test = 6.557; df = 9; p = 0.639.

5.051 ± 4.67 days [1 - 30] (p = 0.48).

Generalized forms accounted for 95.4% of clinical forms. BPOEFs are mainly (94.8%) located on the pelvic limbs, followed by the thoracic limbs in generalized forms of tetanus, compared to localized forms of tetanus. BPOEFs found on the head, uterus, male genital tract, buttocks, within the oral cavity and ORL are found in subjects who have developed generalized tetanus (Table 5). There is no statistically significant difference in the origin of the clinical form (p = 0.45).

The clinical progression of tetanus patients was comparable in situations where BPOEFs were identified on admission compared to cases where POEs were not found (POE-NF) (Table 1), with no statistically significant difference (p = 0.21).

Table 5. Distribution of anatomical sites of bacterial portals of entry according to the clinical form of tetanus.

Site or location of the portal of entry	Tetanus		Total (%)
	Localized (%)	Generalized (%)	
Lower limb	7 (5.2)	128 (94.8)	135 (62.2)
Upper limb	2 (3.5)	55 (96.5)	57 (26.3)
head	0 (0)	12 (100)	12 (5.5)
Uterus	0 (0)	4 (100)	4 (1.8)
Male urogenital tract	0 (0)	1(100)	1(0.4)
Trunk	1 (33.3)	2 (66.7)	3 (1.4)
Buttocks	0 (0)	2 (100)	2 (0.9)
Oral cavity	0 (0)	2 (100)	2 (0.9)
ORL	0 (0)	1 (100)	1 (0.5)
Total	**10 (4.6)**	**207 (95.4)**	**217 (100.0)**

Fisher's exact test = 7.572; df = 7; p = 0.459.

4. Discussion

We conducted a descriptive and analytical study with a retrospective data collection focusing on bacterial portals of entry for *Clostridium tetani* in patients admitted to the Point-G University Hospital over a period of 22 years.

4.1. Constraints and Limitations of the Study

As with all retrospective studies, we encountered difficulties related to the completeness of the study variables. In some cases, the records were missing:

- notification of POE;
- information on the assessment of the Dakar or Mollaret prognostic score;
- information on the existence of preventive measures through the administration of serotherapy or tetanus toxoid.

Due to the originality of our work and the scarcity of studies specifically devoted to the POEs for *C. tetani* (BPOEF), our results in certain cases will be discussed

alongside work that has focused on tetanus in general.

However, despite the limitations associated with a retrospective study, the information obtained from our work is quite significant in terms of the information it provides.

4.2. Descriptive Results

Epidemiological aspects

During the study period, we recorded 258 cases of tetanus for a population of 5167 patients hospitalized at our study sites, representing an overall frequency of 5%.

In 2012, tetanus accounted for 6.5% of hospitalizations in the same hospital [9]. It represented 3% of admissions in Abidjan in 2004 and 6.3% of hospitalizations in 2010 [10] [15]. These results indicate the concern that tetanus could pose in hospitals.

The bacterial portal of entry for *C. tetani* (BPOEF) was not found in 41 patients, or 15.89%. However, those admitted with obvious POE (BPOEF) accounted for 217 cases, or a specific frequency of 84.10%. In practice, determining the tetanogenic bacterial portal of entry is not always straightforward, as confirmed by several studies. In Mali, an absence of POE was reported in 13.4% of cases [9]. The same observation was made in Côte d'Ivoire (22%) [15] and in India in 21% of cases [16]. These different results are close to ours, or 15.89%.

4.3. Socio-Demographic Aspects

We recorded a predominance of male subjects with an overall sex ratio of 9.32. In the same hospital, a male predominance was reported with a sex ratio (M/F) of 5.26 [9]. Tanon *et al.* noted a sex ratio (M/F) = 2.5 in Abidjan [15], and in the same city, a study specific to nosocomial tetanus reported male predominance with a sex ratio (M/F) = 6 [10]. Several studies confirm the higher frequency of tetanus in males [8]-[10].

The mean age of tetanus patients was 36.18 ± 15.65 years, with extremes ranging from 5 to 90 years. Minta *et al.* in Mali reported a mean age of 32.9 ± 15.9 years, with extremes ranging from 15 to 80 years in Bamako [9]. A Malian study on tetanus related to road traffic accidents (RTAs) showed a mean age of cases equal to 34 ± 8 years [21 - 65] years [17]. In 2010, Aba *et al.* reported that the mean age of patients with nosocomial tetanus was 36.2 years, ranging from 8 to 73 years [10]. The mean age recorded in Tanzania was 35.14 ± 14.82 years for men and 32.44 ± 11.22 years for women [8]. In all cases, our results are comparable to the majority of those found in the literature. In the African context, we note that tetanus particularly affects the younger age group, with a trend towards the masculinization of the disease.

4.4. At Clinical Level

The length of hospitalization can vary from a few hours to a few days. In our case,

the overall average length of admission for tetanus patients without specification of the POE was 5.13 ± 4.89 days after the onset of the first symptoms. Thus, the reported consultation lengths vary in the literature. The study from Côte d'Ivoire on the treatment of localized tetanus reported a consultation length of 5 days [18], while Minta *et al.* reported a consultation length of 5 days in 73% of cases, two weeks in 24.4% of cases, and more than two weeks in 2 cases [9]. A length of 2.8 ± 1.8 days for otogenic tetanus in Dakar [19]. In our series, the length of admission for PEBR cases was 5.051 ± 4.67 days. The lengths described above remain comparable despite some minor differences. The delay in consultation appears to be quite significant, which could affect the progression of the disease.

The most commonly reported and detected POEs profiles during interview and physical examination were injuries (65.4%), open fractures (10.6%), skin lesions (7.8%) and deep wounds (7.4%) (**Table 3**). The study on otitic POEs in Senegal revealed that it concerned 55 cases, or 2.4% of tetanus cases admitted [19]. Previous studies conducted at the Point-G University Hospital reported various POEs, including wounds (64.7%), open fractures (11%), scarification (3.4%), 3 cases per IM and 1 case during the following events (circumcision, ear piercing, surgical wound and post-abortion) [9]. The main POEs reported in Abidjan by Tanon and al. were open fractures (49.7%), intramuscular (IM) injections (18.2%), obstetric POEs (3.8%) and following traditional practices (1.6%) [15]. In Brazzaville, POEs were mainly IM-related orifices, accounting for 27.77% [20]. Surgical practices could serve as a vector for *C. tetani*. The main surgical POEs reported by a study in Côte d'Ivoire are: 3 open fractures, one (1) extensive burn, 4 voluntary terminations of pregnancy, 6 inguinal hernias, and 8 sutures on acute wounds [21]. In Tanzania, surgical POEs appears to be the most commonly reported type. It accounted for 4.83% of local surgical procedures (uvula removal = 1, circumcision = 1, tooth extraction = 1), 2 cases each of chronic otitis and cellulitis, and 1 case of voluntary termination of pregnancy (VTP). Acute injuries accounted for 87% of POEs cases [8]. Although rare, orbital POEs have been reported by some authors [22]. In some cases, the POE may appear to be a minor injury, such as finger pricks for blood glucose testing [1] [23]. We must not overlook intravenous (IV) drug injections in northern countries among IV drug users [1] [24].

Topographically, BPOEFs were mainly present on the pelvic limbs in 62.22% of cases, the thoracic limbs in 26.6% of cases, and the head in 5.5% of cases (**Table 2**).

This analysis shows that the POE profiles are variable and diverse (**Table 3**) depending on the mechanisms that caused them, as shown in our results and those of several authors [8] [9] [15] [19] [20]. Open fractures, skin lesions following road traffic accidents, injuries resulting from sharp or blunt objects, surgery (surgical procedures, obstetric procedures, burns), and IM as found in our study are reported by several authors [8] [9] [19] [20]. From 2013 to 2016, 36 cases of neonatal tetanus were reported in Mali [25]. We did not record any umbilical POE. This is due to the specific nature of our recruitment site, which is not suitable for

newborns.

4.5. Analytical Studies

Socio-demographic profile

BPOEFs were more prevalent among male tetanus patients, accounting for 90.8% of cases, with no statistically significant difference compared to POEs not found (p = 0.76). The specific sex ratio was 9.85 (**Table 1**). The predominance of males in tetanus cases is unanimously reported by all authors [1] [9] [10] [15]. BPOEFs are typically the result of trauma or impact points inherent in the risky behavior of male subjects in our context [17]. Female immunity is strengthened during antenatal consultations (ANC) and acquired through tetanus vaccination, a crucial public health intervention. The mean age of patients with BPOEF was 35.94 ± 15.58 years [5 - 76] years.

In light of the results of studies reported in the literature, a professional categorization of tetanus appears to emerge. Indeed, it most frequently affects individuals exercising a tetanus at-risk occupation or living in unfavorable socio-demographic conditions [15]. In Mali, for example, the most affected occupations were unskilled laborers (30.2%), farmers (21.8%), pupils/students (14.2%) and traders (9.2%) [9]. In Côte d'Ivoire, a study reported that the most affected occupations were as follows: 42% workers, 33% unemployed, 15% pupils/students and 5% agricultural workers [18]. In Tanzania, 51% were farmers, 21.6% were industrial workers, 5.8% were couriers, and 4.9% were domestic workers [8]. The professional activities recorded during obstetric tetanus in Dakar consisted mainly of unemployed individuals (66.6%), pupils/students (14.28%), domestic workers, and seamstresses (9.53% in each case) [26]. In our series, workers (71 cases), farmers (56 cases), pupils/students (22 cases) and traders (24 cases) were the most common occupations in the group of patients with BPOEF, with no statistically significant difference compared to patients with POEs not found (p = 0.63) (**Table 4**). There is a similarity between the occupational categories most frequently reported by various authors [8] [9] [21] [15] [18] and our study (**Table 4**). This predominance of workers, farmers and low-income populations can be explained by their frequent exposure to trauma and constant contact with soil (a reservoir of *C. tetani*) and their difficulty in accessing appropriate care.

Urban (59.9%) and rural (21.7%) areas were the main sources of tetanus cases with BPOEF, with no statistically significant difference (p = 0.21) compared to patients with POE not found (**Table 1**). A recent study on tetanus among RTAs revealed that the number of tetanus cases appeared to be higher as one approached urban areas (56% in urban areas, 28% in peri-urban areas and 16% in rural areas) [17]. However, it appeared that most patients with otogenic tetanus lived in the suburbs of Dakar (92.7%) [19]. In Abidjan, the majority lived in working-class neighborhoods with poor sanitation [15]. The high prevalence in urban areas is thought to be linked to injuries caused by increasingly heavy road traffic, which is responsible for the development of various portals of entry for *C. tetani*.

At clinical level

Tetanus vaccination remains the key to prevention, whether or not there has been exposure to tetanus risk. It was reported that only nine patients with BPOEF had recently received tetanus toxoid, with uncertainty as to whether the full course of doses had been completed (**Table 1**). In a population of 55 cases of otogenic tetanus, 10 patients were reported to have been vaccinated, with uncertainty regarding the completeness of the vaccination, 14 patients were not vaccinated, and 31 had no information available on their vaccination status [19]. This indicates a lack of interest or awareness, both professionally and within the community, of the benefits of vaccination.

BPOEFs are varied and located on different anatomical areas. It is common for POEs close to the brain to cause early or even generalized forms, given the short incubation and invasion period. Our work shows that generalized clinical forms appeared much more frequently in cases of POEs located on the pelvic limbs (94.8%), the thoracic limbs (96.5%), the head (100%), the uterus (100%), the male urogenital tract (100%), the oral cavity (100%) and the auditory system (100%) (**Table 5**). Chalya et al. observed a predominance of generalized forms (97.1%) and three cases of localized forms, with the majority of POEs located on the pelvic limbs (53.8%) and 5% in each of the cases on the upper limbs and head [8]. In Abidjan, cephalic locations of POEs accounted for 73% of generalized forms, while abdominal locations accounted for 50% of generalized forms (1 case) [18]. Regardless of anatomical location, there was no statistically significant difference in the genesis of clinical forms during our study ($p = 0.45$) (**Table 5**). The severity of the disease is assessed using several types of prognostic score, the most operational of which is the Dakar score, which takes into account parameters relating to incubation, invasion, POE, temperature and pulse. Another, the Mollaret score, takes into account more major clinical elements that will determine either a mild, acute generalized form or a severe form. The clinical outcome was unfavorable in the group of patients with POEs not found (POE-NF) compared to patients with BPOEF (46.3% versus 41.5%) without a statistically significant difference ($p = 0.77$) (**Table 1**). PEBNR and PEBR appear to be independent of the prognostic evolution, once the patient is admitted to the stage of severity of the disease in our series. During nosocomial tetanus, the mortality rate was 54.5% [10]. It was 9.1% in a population of tetanus patients with otogenic POE in Dakar [19]. Surgical POE was associated with a mortality rate of 45% in Abidjan [21]. Our results are comparable with the majority of studies targeting bacterial POEs [10] [21]. Early and correct wound management helps to clear *C. tetani* spores and prevent the development of spores within the wound into vegetative forms that produce tetanus toxin.

5. Conclusion

The search for the bacterial portal of entry for *C. tetani* is an essential step in the management of tetanus. Proper local management of the POE contributes to a favourable outcome of the disease. The predominance of skin and mucosal lesions

and open fractures located in various limbs is indicative of carelessness in road traffic and, in our context, often of professional negligence. Vaccination remains the main defence against tetanus.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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