

RESEARCH ARTICLE

Current Prognostic Factors of Tetanus in Abidjan: 2005-2014

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ABSTRACT

Objective: To describe the epidemiological, clinical and prognosis aspects of tetanus in patients hospitalized at the Infectious and Tropical Diseases Unit of Treichville Teaching Hospital.

Methods: A retrospective study of the medical records of all patients hospitalized between 2005 and 2014. The “Dakar prognosis score” was established on the basis of six parameters: incubation period, duration of invasion, site of entry, presence of paroxysms, body temperature and pulse rate. A logistic regression model was used to identify the factors associated with death.

Results: Overall, 455 cases of tetanus were included, with a predominance of males (86%). Most patients lived in Abidjan (77%). A very high proportion of cases were generalized tetanus (96%), and 137 patients (30%) died. The factors associated with death were age >60 years (aOR 2.76; 95% CI 1.07 to 9.91), being a labourer (aOR 2.83 95% CI 1.07-9.39), a severe Dakar prognostic score (aOR 5.76; 95% CI 2.26-14.72), no intrathecal serotherapy (aOR = 15.6; 95% CI 5.40- 44.84), no penicillin-therapy (aOR 2.33; 95% CI 1.11-4.87) and the presence of complications (aOR 8.53, 95% CI 4.83-15.09).

Conclusion: This study identifies a number of factors for a poor prognosis among patients with tetanus admitted to our hospital, indicating that measures to reduce morbidity and mortality due to tetanus should be strengthened and prevention improved in resource limited settings. The prognostic parameters in “the Dakar score” should therefore be adapted to the current epidemiological and clinical contexts in Côte d'Ivoire. *J Microbiol Infect Dis* 2017; 7(3):125-131

Keywords: Prognosis factors, tetanus Côte d'Ivoire, West-Africa

INTRODUCTION

Tetanus is a serious, accidental, non-contagious toxi-infection that does not confer immunity and is caused by *Clostridium tetani*, with a strong disparity in the world. Since the Dakar conference which established its prognosis criteria used in sub-Saharan Africa since 1975 [1], and despite the 1995 World Health Organization's (WHO) stated intention to eradicate tetanus in childbearing, it remains a severe endemic infectious disease, responsible for nearly one million deaths per year in developing countries [2].

In Côte d'Ivoire, the immunization schedule recommended for children consists of three vaccine injections at 6, 10 and 14 weeks of life. A vaccine booster dose is given at 16 months, at

6 and half years, at 11 and half years, and then every 10 years. For adolescent or adult subjects not vaccinated during childhood, the tetanus vaccine is recommended on the 1st day, and then 1 month and 6 months or 12 months later. A booster shot is given every 10 years. For women not vaccinated, the immunization schedule consists of a 1st dose of tetanus vaccine at the 1st visit regardless of age, followed by a 2nd dose one month after the 1st one. The booster shot is given six months after the last injection, the 2nd one is given one year after the last injection and the 3rd and last one is also given 1 year after the last injection.

Although the Expanded Program on Immunization (EPI) is the means by which these WHO initiatives are carried out, the booster shot program is not yet implemented for tetanus

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prevention in older age ranges (youngers, adults and elders) [3,4]. Moreover, recent African studies showed a trend towards increased incidence of tetanus in adults [4-8]. Hence the present study aimed at describing the current aspects of tetanus in patients admitted to the referral tetanus care unit, the Infectious and Tropical Diseases Unit (ITDU) at Treichville Teaching Hospital, Abidjan, over a period of ten years (2005-2014) while reporting the current features of poor prognosis [4,9,10].

METHODS

Study design and setting

A medical chart review was conducted at the ITDU, in Treichville Teaching Hospital, Abidjan, Côte d'Ivoire. That ITDU is the referral service for the management of tetanus cases in the country. Although since the creation of neonatology units in the various Teaching Hospitals of Côte d'Ivoire, cases of neonatal and infant tetanus are managed by medical pediatrics services, most cases of juvenile tetanus still attend ITDU [4]. It is also the referral service for the treatment and care of HIV/AIDS and illnesses with a high risk of epidemic and nosocomial infections (viral hemorrhagic fever, severe acute respiratory syndrome, bird flu, Ebola virus disease, AIDS etc.)

Study population

All patients with generalized or localized tetanus, admitted at ITDU from 1st January 2005 to 31st December 2014 were included.

Data collection

A standardized survey form was completed from patients' records and included Socio-demographic, clinical and treatment histories.

Diagnosis of tetanus

The diagnosis of tetanus was based on the presence of following clinical signs: (i) presence of trismus (difficulty of mouth opening) or permanent painful muscle contractions with or without paroxysms; (ii) no disorders of consciousness (coma, obtundation) [4-8]; (iii) point of entry such as skin injuries according to "the Dakar Prognosis Score" [1,4,5,7,10];

Statistical Analysis

Quantitative variables were described in terms of median and interquartile range. Categorical

variables were described in terms of numbers and percentage. Tetanus prevalence was estimated with its 95% confidence interval. The comparison of median was made using the Kruskal-Wallis test and that of qualitative variables using the Chi-square test or the Fisher's exact test according to theoretical numbers. A multivariate logistic regression model was used to identify factors associated with death. Data were analyzed using Stata 9.0 software.

RESULTS

Socio-demographic data

A total of 6988 patients were admitted to ITDU during the study period, including 467 (6.7%; 95 CI 6.1-7.3) cases of tetanus from which 12 were excluded because of incomplete data. Among the 455 cases of tetanus enrolled, 390 patients (85.7%) were male. Their median age was 41 years [IQR: 1-80] and the most affected age group was the ones between 15 and 60 years.

Patients were predominantly of Ivorian nationality (58.6%), and most of them were living in urban zone: Abidjan district (76.9%). The occupations most represented were liberal professions (small businesses at risk of skin excoriations: hairdressers, scrap merchants, masons, carpenters, cleaners etc.) (53.3%), followed by workers (14.1%) and the unemployed (13.9%). The majority of patients (93%) had no tetanus immunization coverage.

Clinical Findings

The main symptoms observed at admission were reported in Table 2. Muscle contractions (100.0%), trismus (92.7%) and paroxysms (80.2%) were the predominant symptoms. The incubation period was greater than or equal to 7 days in the majority of cases (73.1%) and the invasion period was less than 2 days in 66.3% of patients. A total of 435 patients had generalized tetanus and 20 patients had localized tetanus.

Main sites of entry

The sites of entry were known for 404 patients (88.8%). These were in the lower limbs in 304 cases (75.2%), on the face in 21 cases (5.2%), in the upper limbs 41 cases (10.2%) and finally on the head in 38 cases (9.4%).

Among patients whose sites of entry were found, those scored 1 according to "the Dakar

prognosis score" predominantly consisted of intramuscular injections (n=22; 4.8%), surgeries (n=13; 2.9%), fractures (n=8; 1.8%). The other sites of entry (scored 0) were the most observed in the study with 360 cases (79.1%) (Table 3).

Treatment history

Upon hospitalization, most of our tetanus patients received antibiotics, 429 cases (94.3%) because of over infected site of entry and sepsis in sub-Saharan Africa context. Among the treated patients, 388 received antibiotic monotherapy (85.3%) versus 41 cases which were treated with two antibiotics (9.0%). Penicillin G 100 000 IU/kg per day in continuous intravenous was the most prescribed in 382 cases (83.9%). It was replaced by metronidazole (500 mg three times intravenous) in 12 cases (2.6%) for allergic reaction to penicillin G. Patients with complications or over infection of the site of entry received a second-line amoxicillin/clavulanic acid combination therapy plus gentamycin in 164 cases (36%).

The daily treatment of the site of entry consisted in disinfection, cleaning and excision. Intrathecal serotherapy was performed with 1500 IU of heterologous antitetanus serum of equine origin combined with 25 mg of hydrocortisone hemisuccinate. Maintaining the hydro-electrolytic and caloric balance was done with continuous infusions of crystalloid solutions (hypertonic and isotonic glucoses, saline and Ringer's lactate). The sedation of contractions was based on intravenous infusions of diazepam at a dose of 1-2 mg/kg/day, sometimes combined with phenobarbital at a dose of 5-20 µg/kg in known drug-addicted patients.

Hospital stay ranged from 1 to 48 days depending on complications with a median of 10 days.

Evolution and complications

The 455 patients were divided into three groups according to "the Dakar prognosis score": 145 cases of Mild tetanus (score 0-1), 31.8%; 251 cases of moderate tetanus (score 2-3), 55.2% and 59 cases of severe tetanus (score 4-6), 13.0%.

Some complications were observed in 254 patients (55.8%). These were infectious complications characterized as severe sepsis

and infections associated with treatment in 100 cases (38.4%) and severe malaria in 22 cases (8.6%). Neurological complications were observed in 32 patients (12.5%), particularly subintractant paroxysms. As for respiratory complications, they included respiratory distress in 24 cases (9.4%) and pulmonary superinfection in 21 cases (8.2%). Finally, 10 cases of high blood pressure crisis were reported among cardiovascular complications (3.9%).

Patient outcomes

In the 455 patients, 318 were discharged alive from the hospital (69.9%). Among the alive ones, there were 296 cases of healing (93.1%) including 201 without sequels; 10 were referred to other services for additional care and 12 (2.6%) discharged themselves from the hospitalization unit against medical advice.

Factors associated with death or severity

The analysis of death-associated factors demonstrates that patients most at risk of dying were: (Table 4):

- Those over 60 years of age (aOR 2.76 : 95% CI 1.07-9.91),
- Workers and labour force (aOR=2.83, 95% CI 1.07-9.39),
- Those with a severe Dakar prognosis score (aOR=5.76, 95% CI 2.26-14.72),
- Those who did not received intrathecal injection (aOR=15.6, 95% CI 5.40-44.84),
- Those who did not received penicillin-therapy (aOR=2.33; 95% CI 1.11-4.87) and those with complication (aOR=8.53, 95% CI 4.83-15.09).

DISCUSSION

Tetanus remains an endemic disease in Abidjan with an average annual prevalence of 47 ± 10 cases, slightly above that reported by Aba et al. [5], but below those found by Tanon et al. [4] and Kakou et al. [7] in studies conducted more than 10 years ago in the same Unit [4, 5, 7].

This overall decrease in the prevalence of tetanus could be explained by the management of some cases of juvenile tetanus by paediatric services, whereas previously, tetanus cases were mostly referred to ITDU, on the one hand, and by proper awareness and tetanus

immunization coverage among women of childbearing age and infants as part of the EPI [2,3,9], on the other hand. However, there is still a need of vaccination in adults in several sub-Saharan Africa countries [3,5,8,11].

Table 1. The summarized characteristics of 455 patients with tetanus at admission in the ITDU.

Parameters	N=455 (%)
Age, range in years, n (%)	
≤14	57 (12.5)
15-60	360 (79.1)
≥ 61	38 (8.4)
Gender (M) n (%)	390 (85.7)
Residence, n (%)	
Urban	350 (76.9)
Rural area	105 (23.1)
Occupation, n (%)	
Student	52 (11.4)
Unemployed	61 (13.4)
Worker	52 (11.4)
Liberal	290 (63.8)
HIV Infection positivity, n (%)	22 (4.8)
"Dakar score", range, n (%)	
Mild	141 (31.0)
Moderate	246 (54.1)
Severe	59 (13.0)
Not specified	09 (1.9)
Antibiotherapy, n (%)	
One antibiotic	388 (85.3)
Two antibiotics	41 (9.0)
None received	26 (5.7)
Intrathecal serotherapy	
Done	407 (89.5)
Not done	48 (10.5)

Table 2. Main symptoms observed at admission (n=455).

Symptoms	No. of positives (%)
Trismus	422 (92.7)
Generalized Contraction	435 (95.6)
Localized Contraction	20 (4.4)
Paroxysm	365 (80.2)
Fever(>38.4 °C)	76 (16.7)
Pulse (≥120 /min)	34 (7.5)

Table 3. Frequency of main sites of entry (N= 455).

Site of entry	Number (%)
Site of entry scored 1	
Intramuscular injection	22 (4.8)
Surgery	13 (2.9)
Opened fracture	8 (1.8)
Uterus	1 (0.2)
Burn	0 (0.0)
Umbilicus	0 (0.0)
Sites of entry scored 0	360 (79.1)
Sites of entry not found	51 (11.2)

On socio demographical aspects, there was a male dominance of tetanus incident cases with a M/F sex ratio = 6, similar to that reported by Aba et al. [5] in Abidjan, but above those reported by Seydi et al. [12] in Dakar (Senegal) and Minta et al. [8] in Bamako (Mali) which were 4.3 and 2.41 respectively. This is evidence that the tetanus eradication policy through immunization for women of childbearing age, as advocated by WHO campaigns in all resource-limited countries, virtually works well.

The sites of entry were many, varied and dominated by the cutaneous ones, as in other African studies [6,9,12,13]. However, the proportions of the sites of entry scored 1 according to "the Dakar score" (intramuscular injections, umbilicus, burn, uterus, surgery and fracture) remain significant, with a grade always severe in our study; thus, health professionals' awareness must be raised when providing care in order to prevent or reduce these cases of iatrogenic tetanus [14-19]. The proportion of generalized tetanus cases in our study remains high (95.6%), as demonstrated in most studies conducted in Côte d'Ivoire, Mali, Senegal, and Congo [4,6,8,12,20].

As regards patient outcomes, 3.8% were discharged against the treating physicians' advice, more often for lack of financial resources, whereas Aba et al. recorded 10.4% [5]. This variation could be explained by better awareness-raising among patients' relatives by physicians, on the one hand, and the slow resumption of professional activities since the end of the post- electoral crisis in 2011 in Côte d'Ivoire, on the other hand.

The median duration of hospital stays in our study was 7 days [1 and 28 days], similar to that found in Mali and Senegal [6,8,12]. The in-hospital mortality rate related to tetanus was 30% over 10 years in our study. This is also similar to those of Aba et al. [5] (29.9%) and Tanon et al. [4] (32.0%) in the same service, but lower than that reported in Congo (37.50%) [16,20], whereas Seydi et al. [12] found only 22% in Senegal. The mortality rate was higher in the most active age group (20-55 years) with 71%, and predominantly greater among men (86%), more often due to the presence of complications or disease severity. Sometimes the lack of financial resources among some

patients led to insufficient treatment and care, which were responsible for early deaths [12].

The univariate and multivariate analysis of prognosis factors significantly associated with death revealed that age >60 years, high-risk workers' occupations, presence of complications especially respiratory distress and the lack of intrathecal serotherapy and antibiotherapy

(Penicillin-G) were significantly associated with death, apart from the poor prognosis features in the Dakar score [9, 18]. These results are similar to those of other studies in other countries. Indeed, a study conducted in Turkey in 1997 also showed that older age was associated with death among 88 adult patients with tetanus [21].

Table 4: Factors associated with death in patients with Tetanus admitted to ITDU from 2005 to 2014, Logistic regression model, univariate and multivariate analysis.

Parameters	Patients	Deaths	Univariate analysis			Multivariate analysis		
			OR	CI = 95%	P	aOR	CI = 95%	P
Age in years								
14	57	15 (26.3)	1.00			1.00		
15-60	360	99 (27.5)	1.06	0.56-2.00	0.85	1.12	0.40-3.13	0.83
>60	38	23 (60.5)	4.29	1.78-10.32	0.001	2.76	1.07-9.91	0.04
Sex								
Male	390	118 (30.3)	1.00	-	-			
Female	65	19 (29.3)	0.95	0.53-1.69	0.87			
Occupation								
Student	52	13 (25.0)	1.00	-	-	1.00	-	-
Unemployed	61	23 (37.7)	1.82	0.80- 4.10	0.15	1.34	0.43 – 4.18	0.25
Worker	52	26 (60)	3.00	1.31 – 6.88	0.01	2.83	1.07 – 9.39	0.048
Liberal	290	75 (25.9)	1.05	0.53 – 2.07	0.90	1.29	0.47 – 3.54	0.62
HIV status								
Non-infected	433	130 (30.2)						
Infected	22	7 (31.8)	1.09	0.43-2.73	0.86			
Dakar score								
Mild	141	22 (15.60)	1.00	-	-			
Moderate	246	68 (27.6)	2.07	1.21 – 3.52	0.008	1.77	0.91- 3.46	0.09
Severe	59	43 (72.9)	7.16	6.99-30.24	0.000	5.76	2.26 – 14.72	0.001
Not specified	09	04 (44.4)	4.32	1.08 – 17.39	0.039	0.78	0.12 – 5.12	0.80
Intrathecal therapy								
Done	407	97 (23.8)	1.00	-	-	1.00	-	-
Not done	48	40 (83.3)	16.00	7.23 – 35.30	0.000	15.6	5.40-44.84	0.001
Antibiotherapy								
Pen-G received	382	84 (21)	1.00	-	-	1.00	-	-
No Pen-G received	73	53 (72.6)	9.40	5.32 – 16.06	0.000	2.33	1.11 – 4.87	0.025
Complications								
No	291	38 (13.1)	1.00	-	-	1.00	-	-
Yes	164	99 (60.4)	10.14	6.38-16.11	0.001	8.53	4.83-15.09	0.001

Also, the administration of intrathecal serotherapy made it possible to considerably reduce (94%) mortality in our study. This practice, which aims to neutralize the circulating toxin in the nervous system that has not penetrated the neurons yet, demonstrated a reduction in mortality from 30% to 93% depending on the doses administered in the previous studies [22-25]. Thus, intrathecal serotherapy could be recommended in countries with no specific human tetanus immunoglobulin. Conversely, HIV positive status, male sex and liberal professions or crafts did not appear as pejorative features (p-value not significant). This study highlighted the need to conduct a multicentre study in the affected countries, in order to integrate new parameters in determining the real tetanus' prognosis score.

In our study, the majority of patients were not vaccinated". These results are similar to those reported in most of the Sub-Saharan Africa studies [4,5,8-13,19]. These results emphasize the importance of catch-up immunization or vaccination in adolescents or adults not vaccinated during childhood.

Finally, as any study with a retrospective component, ours has some limitations. Furthermore, some data were collected only based on the verbal reports of patients and/or their accompanying persons; this was particularly the case for the immunization status, because most of our hospitalized patients did not have vaccination records. In spite of these limitations noticed, the sample size and the long duration of our study allowed us to collect relevant data on the current aspects of tetanus and its treatment in Abidjan.

Tetanus remains an endemic disease with high in-hospital mortality in Côte d'Ivoire. Tetanus vaccine, although effective, is available free of charge only for women of childbearing age and children under 11 months of age, as part of the Ivorian EPI. This has tremendously reduced morbidity in this portion of the population. However, the latter as well as older populations remain the most vulnerable ones with an alarming death rate.

It therefore seems appropriate to revisit the prognosis parameters in "the Dakar score" so as

to adapt them to the current epidemiological and clinical contexts in resources limited settings.

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Competing interests: The authors declare no competing interest.

Ethics' aspects: Our clinical work has been done in context of thesis in Infectiology field. It has been approved by the department's head who is listed in the manuscript as the latest author (Professor Aka Rigobert Kakou). We had an oral consent of patients to be enrolled in the study but no submission was made to the country ethics committee. Patients' privacy was respected.

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REFERENCES

1. Vachon F. IVème international congress on tetanus (Dakar 6-11; 1975), Report. *Méd Mal Infect* 1975; 5,6: 310-11. 1975.
2. UNICEF, WHO. Sustainably eliminating maternal and neonatal tetanus: strategic plan 2012-2015. Available from: www.who.int/immunization/diseases/MNTEStrategicPlan_F.pdf.
3. Dalal S, Samuelson J, Reed J, Yakubu A, Ncube B, Baggaley R. Tetanus disease and deaths in men reveal need for vaccination. *Bull World Health Organ* 2016; 94 (8):613-21.
4. Tanon AK, Eholie SP, Coulibaly-Dacoury C, et al. [Morbidity and mortality of tetanus in the infectious and tropical diseases department in Abidjan 1985 - 1998]. *Bull Soc Pathol Exot* 2004; 97(4):283-287.
5. Aba T, Kra O, Ehui E, et al. [Clinical and developmental aspects of care-related tetanus in the reference service of the teaching hospital of Abidjan]. *Bull Soc Pathol Exot* 2011; 104(1):38-41.
6. Dao S, Oumar AA, Maiga I, Diarra M, Bougoudogo F. [Tetanus in a hospital setting in Bamako, Mali]. *Med Trop* 2009; 69(5):485-487.
7. Kakou AR, Eholie S, Ehui E, et al. [Localized tetanus in Abidjan: clinical and prognostic features (1976-1997)]. *Bull Soc Pathol Exot* 2001; 94(4):308-311.
8. Minta DK, Traore AM, Soucko AK, et al. [Mortality and morbidity of tetanus in the infectious diseases department, Point G teaching hospital, in Bamako, Mali (2004-2009)]. *Bull Soc Pathol Exot* 2012; 105(1):58-63.

9. Soumare M, Seydi M, Ndour CT, Ndour JD, Diop BM. [Epidemiology, clinical features and prognosis of juvenile tetanus in Dakar, Senegal]. *Bull Soc Pathol Exot* 2005; 98(5):371-373.
10. Sow PS, Seydi M, Diop BM, et al. Facteurs pronostiques du tétanos néonatal à Dakar. Prognosis factors for neonatal tetanus in Dakar. *Med Mal Infect* 2003; 33 (3):150-154.
11. Scobie HM, Patel M, Martin D, et al. Tetanus Immunity Gaps in Children 5-14 Years and Men ≥15 Years of Age Revealed by Integrated Disease Serosurveillance in Kenya, Tanzania, and Mozambique. *Am J Trop Med Hyg* 2017; 96(2):415-420.
12. Seydi M, Soumare M, Gbangba-ngai E, et al. [Current aspects of pediatric and adult tetanus in Dakar]. *Med Mal Infect*. 2005; 35(1):28-32.
13. Yeboue-Kouame BY, Bonny JS, Ahimon E, et al. Étude épidémiologique du tétanos à Abidjan et incidences professionnelles. *Archives des Maladies Professionnelles et de Médecine du Travail* 1999; 60 (2):132–135.
14. Aba YT, Kra O, Tanoh AC, et al. [Surgical tetanus in Abidjan, Cote d'Ivoire]. *Med Sante Trop* 2012; 22(3):279-282.
15. Adonis-Koffy LY, Tanon-Ano Bla MJ, N'Guessan R, Eboua TK, Adjaffi Sokolo AE, Timite-Konan AM. [Generalized tetanus with otitic portal of entry after using intra-auricular traditional remedies in a 2 old child]. *Bull Soc Pathol Exot* 2008; 101(4):301-302.
16. Boumandouki P, Kounkou RY, Teke-Bagamboula JN, Ekouele Mbaki H, Ndinga E. [Intramuscular injections of quinine and tetanus at the Centre Hospitalier Universitaire of Brazzaville, Congo]. *Bull Soc Pathol Exot* 2008; 101(4):298-300.
17. Ehui E, Kra O, Ouattara I, et al. [Generalized tetanus complicating a traditional medicine applied for snakebite]. *Bull Soc Pathol Exot* 2007; 100(3):184-185.
18. Ndour CT, Soumaré M, Diop BM, Touré AK, Badiane S. Tetanus in obstetric gateway in Dakar: epidemiological and prognostic aspects about 21 cases observed in the clinic of infectious diseases of the Dakar Teaching Hospital. *Med Mal Infect* 2002; 32:399-396.
19. Soumare M, Seydi M, Dia NM, et al. [Post-circumcision tetanus in Dakar, Senegal]. *Bull Soc Pathol Exot* 2008; 101(1):54-57.
20. Ribereau-Gayon R: Tetanus treatment in east African rural area (RD Congo-Zaire). Evaluation of a therapeutic protocol over 21 cases. *Med Afr Noire* 2000; 47(3):131-138.
21. Hosoglu S, Ayaz C, Faruk Geyik M, Yagmur Y, Faruk Kokoglu O. A continuing problem of tetanus in the southeast of Turkey. *Clin Microbiol Infect* 1997; 3(6):690-692.
22. Gallais H. [The value of intrathecal administration of antitetanus serum and corticoids in the treatment of manifest tetanus]. *Nouvelle Presse Med* 1977; 6(18):1571.
23. Kabura L, Ilibagiza D, Menten J, Van den Ende J. Intrathecal vs. intramuscular administration of human antitetanus immunoglobulin or equine tetanus antitoxin in the treatment of tetanus: a meta-analysis. *Trop Med Int health*. 2006; 11(7):1075-1081.
24. Miranda-Filho Dde B, Ximenes RA, Barone AA, Vaz VL, Vieira AG, Albuquerque VM. Randomised controlled trial of tetanus treatment with antitetanus immunoglobulin by the intrathecal or intramuscular route. *BMJ* 2004; 328(7440):615.
25. Wateba M, Diop S, Nichols S, et al. [Intrathecal therapy with 1 500 UI of antitetanic serum and 1.5 g of intravenous metronidazole: prognosis of tetanus in hospitalized patients in Togo]. *Sante* 2008;18(3):125-129.