

Complication of Tetanus: Report of 402 Cases at the Fann University Hospital Center of Dakar in Senegal

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Abstract

Objectives: Tetanus is a major health problem in Senegal. The objective of this study was to describe complications related to tetanus and to identify factors associated with their occurrence.

Materials and Methods: We conducted a descriptive and analytical retrospective study including patients hospitalized with tetanus at the Infectious Diseases Department of Fann National University Hospital in Dakar from 2009 to 2012. The diagnosis of tetanus was confirmed based on the presence of clinical signs and the occurrence complications was assessed. Data were collected from medical records. Multivariable logistic regression was used to evaluate potential risk factors for tetanus complications.

Results: We included 402 cases of tetanus. The mean age was 29 ± 21 years and the sex ratio (M/F) 3.06. Skin was the most frequent portal of entry (76%). Overall, 184 patients presented at least one complication (46%). Infectious (127 cases, 69%), cardiovascular (84 cases, 45%) and respiratory (79 cases, 43%) complications were the most common. In multivariable analyses, age > 40 years ($p < 0.001$), presence of co-morbidities ($p < 0.01$), Mollaret stage \geq II ($p = 0.02$) and Dakar score \geq 1 ($p < 0.001$) were factors associated with the occurrence of complications. Mortality was 21%. The circumstances of death were dominated by infections (71%), respiratory distress (45%) and laryngospasm (24%).

Conclusion: We observed high rates of complications and mortality among patients admitted with tetanus. The infection prevention and control in the intensive care unit, the improvement of life-support measures and diagnostic capacities will allow to significantly reduce morbidity and mortality related to tetanus complications.

Keywords: Tetanus; Complication; Dakar; Mortality

Introduction

Tetanus is a severe disease characterized by spasmodic contraction of voluntary muscles. This infection, caused by *Clostridium tetanus*, remains an important public health problem in developing countries, despite the availability of an effective vaccine. Even though neonatal tetanus has been eliminated in many countries [1], its incidence remains high in some resource-limited settings, particularly among children and young adults [2-4]. Absence of vaccination boosters and inadequate wound management by the health care workers partly explain the persistence of tetanus in several countries.

Studies conducted in African inpatient settings found a prevalence of tetanus ranging from 6 to 11% [2,4]. The case-fatality rate of tetanus generally lies between 20 and 60% [4-6]. Many studies have focused on factors associated with tetanus-related mortality. Advanced age, severity of disease at admission and presence of co-morbidities were identified as risk factors of death [4,5,7,8]. The occurrence of complications of tetanus, which are directly related to management practices, was also identified as prognostic factors [4,6,9]. Literature review has revealed that few studies had specifically addressed complications observed during this affection. The objective of this study was to describe the various complications occurring in patients with tetanus and to identify related risk factors.

Patients and Methods

Type of study

This is a descriptive and analytical retrospective study conducted at Infectious and Tropical Diseases Department (SMIT in french) of Fann

University Hospital in Dakar, Senegal. This is the national reference center for the management of tetanus.

Study population

All patients hospitalized with a diagnosis of tetanus at SMIT between January 1, 2009 and December 31, 2012 were included in this study. Neonatal tetanus cases (occurring within the first 28 days of life) were excluded. The diagnosis of tetanus was clinical and was based on the presence of epidemiological factors (portal of entry, lack of tetanus vaccination or incomplete vaccination) and clinical signs (lockjaw, dysphagia, contracture, tonic or tonic-clonic paroxysms).

Diagnostics criteria for complications

The diagnosis of infectious diseases was based on presence of clinical signs that appears during hospitalization in relation of nosocomial infections (fever or at most, bacteraemia or septic choc,

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diarrhea, urinary tract infection like hypogastric pain or burning of urination, respiratory infections like cough, purulent secretions...), biological abnormalities (non-specific inflammatory syndrome, isolation of germs in pathological fluids) and/or therapeutic criteria (clinical improvement after anti-infectious therapy). Respiratory mechanical complications were diagnosed based on presence of clinical signs (chest blockage, laryngospasm, respiratory failure). Nutritional abnormalities were diagnosed on dehydration and malnutrition signs. Diagnosis of cardiovascular complications (arrhythmias, blood pressure abnormalities, cardiac arrest, and phlebitis) was based on clinical signs and/or para clinical examinations (electrocardiogram, Doppler ultrasound). Diagnosis of iatrogenic complications related to the curative treatment of tetanus is based on the appearance of signs as coma, drug allergies, metabolic complications such abnormalities of sodium or potassium, overhydration.

Data collection

Epidemiological aspects (portal of entry, age, sex, other comorbidities: high blood pressure, diabetes, cancer, Sickle cell disease, asthma...), clinical data (Incubation, Period of onset, trismus, dysphagia, contracture, paroxysms, type of complication, date of complications), classification of tetanus [10]: Mollaret Stage (Table 1), Dakar Score prognosis (Table 2), and outcome (death, cure) were collected from medical records. A standardized data collection form was used.

Statistical analysis

The main epidemiological and clinical characteristics of the study

Stage I (Mild)	Period of onset: 4 to 5 days Trismus, sardonic facies No respiratory trouble No spasms No dysphagia
Stage II (Moderate)	Period of onset: 2 to 3 days Trismus, spinal stiffness Abdominal rigidity Respiratory troubles Dysphagia Spontaneous or induced tonic generalized spasms
Stage III (Severe)	Period of onset < 24 hours Generalized Contracture Respiratory disorders with chest blockage Severe Dysphagia Spontaneous tonic clonic generalized spasms

Table 1: Mollaret's classification of tetanus.

Prognostic Factors	Score 1	Score 0
Incubation period	< 7 days	≥ 7 days
Period of onset	< 48 h	≥ 48 h
Portal of entry	Umbilicus Burns Uterine Open fracture Surgical wound Intramuscular injection	All others
Spasms	Present	Absent
Fever	> 38,4°C (101.12 °F)	≤ 38,4°C (101.12 °F)
Tachycardia	Adult >120 beats/min Neonate > 150 beats/min	Adult < 120 beats/min Neonate < 150 beats/min

Table 2: Prognostic scoring systems in tetanus Dakar score

population as well as the distribution of tetanus complications were listed. We specified the average (\pm standard deviation) or the median (interquartile range) for quantitative variables after verification of the normality. Logistic regression was used to identify factors associated with the occurrence of tetanus complications. Odds ratios (OR) with 95% confidence intervals (CI) were presented. Univariable analyses were performed to explore associations between the presence of any tetanus complication and the following explanatory variables: age, sex, known portal of entry (Yes/No), the presence of other comorbidities (Yes/No), the Mollaret stage (I vs. III, I vs II) and Dakar score (0-6). All the factors associated with the occurrence of complications with a p value <0.20 were included in the multivariable analysis. The significance threshold was set at $p < 0.05$. The Epi Info software (Version 7.1.4) was used for statistical analysis.

Results

Description of the study population

During the period of study, 4336 patients were admitted to SMIT including 402 cases of tetanus representing a prevalence of 9% (95% CI: 8% - 10%). The mean age was 29 ± 21 years and patients aged less than 20 years (43%) were most represented (Table 3). There was a male predominance with a sex ratio (M/F) 3.06. The skin was the most common portal of entry (76%), secondary to an injury caused by a sharp or cutting object in 61% of cases. The acute generalized form of tetanus was predominant (99%). In the majority of cases, patients were admitted in stage II of Mollaret Classification (77%) and had a Dakar score ≥ 2 points (44%). The tetanus was associated with other

Characteristic	Number	Percentage (%)
Sex		
Male	303	75
Female	99	25
Age group		
1 month - 20 years	174	43
20 - 40 years	108	27
40 - 60 years	67	17
> 60 years	53	13
Co-morbidity		
No	44	11
Yes	358	89
Portal of entry		
Integumentary	306	76
Post-surgery	29	07
ENT*	18	05
Dental	14	04
Others**	26	06
unknown	9	02
Mollaret stage		
stage I	50	12
stage II	316	77
stage III	36	09
Dakar Score		
score 0 - 1	226	56
score 2 - 3	162	40
score 4 - 6	14	04
Complications		
Yes	184	46
No	218	54
Evolution		
Cure	319	79
Death	83	21

* Ear, Nose and Throat, ** intramuscular, obstetrical.

Table 3: Characteristics of 402 patients admitted for tetanus at the Infectious and tropical diseases department of Fann University Hospital center in Dakar-Senegal, from 2007 to 2011.

co-morbidities in 44 patients: high blood pressure (25 cases), diabetes (7 cases), asthma (5 cases), cancer (4 cases), Sickle cell disease (3 cases) and cerebrovascular accident (2 cases).

Description of complications

Among the 402 patients, 184 cases (46%) presented complications. More than half of patients (94 cases, 51%) developed at least two complications. Totally, 473 complications were observed. The average time between the date of hospitalization and the appearance of complications was 3.24 ± 5.03 days. Nearly all complications (90%) occurred during the first week of hospitalization. The most common complications were infectious (127 cases, 69%), cardiovascular (84 cases, 45%) and respiratory (79 cases, 43%) (Table 4). Infectious complications were dominated by pneumonia (80 cases, 63%), bacteremia (21 cases, 17%), and urinary tract infections (14 cases, 11%). Bacteriological isolation was done in one third of cases (44 cases, 34.6%): *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Staphylococcus* were the main pathogens isolated from clinical specimens. Cardiovascular complications were observed in 84 patients (45%); dysrhythmia (55 cases, 66%) hypertensive crisis (20 cases, 24%) and cardiac arrest (20 cases, 24%) being the most prevalent ones. They occurred at an average of 2.51 ± 3.09 days after the admission in the clinic. Mechanical respiratory complications occurred in 79 patients (43% of cases). They were dominated by laryngospasm (58%) and secondary apnea due to the blocking of thoracic muscles (38%). 18 of these patients required performing tracheotomy. The other complications were mainly metabolic or nutritional (32 cases, 17%) and iatrogenic coma due to sedative drugs overdose (16 cases, 8%).

Factors associated with the occurrence of complications and mortality

Overall, 83 patients (21%) patients died. All of them developed at least one complication. The circumstances of death were dominated by infections (59 cases, 71%), respiratory distress (38 cases, 45%) and laryngospasm (20 cases, 24%). In multivariable analysis, factors associated with the occurrence of any complication were age > 40 years ($p < 0.001$), the presence of other co-morbidities ($p < 0.01$), stage II and III of Mollaret classification ($p = 0,02$) and Dakar score ≥ 1 ($p < 0.001$). However, there was no association between complications and sex or the presence of an unknown portal of entry (Table 5).

Discussion

During tetanus infection, complications can occur at any stage of the clinical course. In our study, nearly half of the patients (184 cases, 46%) presented at least one complication. We found a high mortality rate (21%) and the predictors of tetanus complications were age, the presence of other co-morbidities, and the severity of clinical presentation. The complications were dominated by infectious complications, cardiovascular and respiratory. Similar complications have been reported in previous studies. In Nigeria, Chukwubike observed that half of the patients had essentially infectious and respiratory complications [11]. In India, Marulappa reported 47% complicated cases [12]. On the other hand, Manga in Senegal [5] and Tanon in Ivory Coast [13] reported a lower proportion of complicated cases with 18% and 17% respectively. However, the types of complications were identical, dominated by infections and respiratory diseases. In the intensive care unit, pulmonary infections are frequently observed and are mostly nosocomial. Among the 184 patients with a complication, two-thirds (69%) had an infection, pneumonia being the most frequent one. The study of Sbai in Morocco [14] found also 60%

Type of complication	Number	Percentage (%)
Infectious diseases (n=127)		
Pneumonia	80	63
Bacteremia	21	17
Urinary tract infections	14	11
Sepsis of unknown origin	46	36
Cardiovascular disease (n=84)		
Cardiac dysrhythmia	61	73
Hypertensive crisis	20	24
Cardiac arrest	20	24
Arterial hypotension	02	02
Thrombophlebitis	01	01
Respiratory disorders (n=79)		
Laryngospasm	46	58
Apnea	30	38
Atelectasis	03	04
Metabolic troubles (n=32)		
Dehydration	29	91
Denutrition	20	63
Electrolyte disorders*	19	59
Coma (n=16)	16	9
Others** (n=9)	9	5

* hyponatremia, hypokalemia, *** pressure ulcers, renal failure

Table 4: Distribution of 184 patients according to the type of complications (N = 184).

of pneumonia in tetanus patients.

In addition to lung infections, bacteremia was observed in 21 patients (17%) in our study. The frequent use of invasive devices such as venous or intra-arterial catheters, urinary catheter, and mechanical ventilation contribute to their occurrence. Tetanus affects both smooth muscles and striated muscles. The impairment of smooth muscle function explains bladder paresis and propensity to urinary tract infections and decreased chest expansion. Stasis of respiratory secretions favors infections of the respiratory system. Thus, the implementation of improved hygiene measures by health care staff and timely physiotherapy may reduce the occurrence of these complications.

Cardiovascular complications are relatively common during tetanus infection [15-17]. They are secondary to specific injuries of the autonomous nervous system by the tetanus toxin. Their consequence are the appearance of sympathetic and parasympathetic hyperactivity signs called dis-autonomic tetanus syndrome [18,19]. Among the 184 patients, 83 (45%) presented cardiovascular complications. Cardiac dysrhythmia, hypertension crisis and cardiac arrest were the main manifestations. This is in line with the results of a previous Senegalese study on cardiovascular events during tetanus which showed that the main abnormalities were dysrhythmia (80%), QT prolongation (76.7%) and ventricular hypertrophy (56, 7%) [20]. In a study from Brazil [17], Henriques Filho reported a high prevalence of supraventricular (55.2%) and ventricular (39.4%) arrhythmia. In our study, cardiovascular complications were probably underestimated because electrocardiogram was not performed systematically in all the patients.

Respiratory mechanical complications occur in severe tetanus cases and are often associated with poor prognosis. They are related to the contraction of the laryngeal muscle and to the blocking of the respiratory muscles. In our series, 79 patients presented respiratory complications. Laryngospasm and apnea were most frequently observed. In Nigeria, Chukwubike observed 11% of laryngospasm and 7% of respiratory distress [17]. Tanon observed that 8.6% of these patients had respiratory complications [13]. A respiratory intensive care combining intubation or tracheotomy and ventilation is required

Characteristic	OR crude [95%CI]	p-value	OR adjusted [95%CI]	p-value
Sex				
Male	1	0.39	-	
Female	0.82 [0.52 – 1.29]			
Age group (years)				
< 20	1	<0.0001	1	<0.001
20 – 40	0.87 [0.54 – 1.43]			
40 – 60	2.22 [1.25 – 3.95]			
> 60	4.91 [2.95 – 9.86]			
Co-morbidity				
No	1	<0.0001	1	<0.01
Yes	4.26 [2.09 – 8.69]			
Portal of entry				
Found	1	0.24	-	
Unknow	0.61 [0.26 – 1.40]			
Mollaret's Classification				
Stage I	1	<0.0001	1	0.02
Stage II	3.44 [1.66 – 7.11]			
Stage III	14.00 [4.91 – 39.91]			
Dakar score				
score 0	1	<0.0001	1	<0.001
score 1	3.03 [1.56 – 5.90]			
score 2	5.60 [2.81 – 11.17]			
score 3	9.26 [4.03 – 21.25]			
score 4	15.97 [3.93 – 64.95]			

Table 5: Predictors of tetanus complications at the infectious and tropical diseases department of Fann National University Hospital in Dakar-Senegal, from 2007 to 2011 (N =402).

for these situations. However, as in many resource-limited settings, we had only access to tracheotomy with spontaneous ventilation, which resulted in a sub-optimal management of those patients.

32 (17%) patients developed metabolic and nutritional complications, including mainly dehydration, malnutrition and electrolyte disorders. These complications are related to dysphagia. In our practice, patients with tetanus are not intubated and ventilated and therefore do not have a nasogastric tube to ensure proper nutrition and electrolyte rebalancing. All needs of the patient in water and electrolytes must be compensated in the treatment of tetanus otherwise electrolyte disturbances may appear. Hydro-electrolytic complications are also secondary to inadequate secretion of anti-diuretic hormone [16]. We rely solely glucose serums, which does not replace a balanced diet. The introduction of parenteral nutrition could improve the nutritional status of patients. However its implementation is difficult in our context due to its costs and the risk of thromboembolism, metabolic and infectious complications associated with this type of diet.

The reason of iatrogenic coma is due to sedative drugs overdose. In our practice, this complication is frequent in the elderly. However, before to retain these complication, it is necessary to eliminate certain differential diagnoses such as encephalitis, cerebro-vascular accidents.

In our series, mortality was 21%. Although this rate is high, it remains relatively lower than estimates found in other countries. In Mali, Dao observed a lethality of 38.9% [3]. Saltogluin Nigeria [8] and Marulappain India [11] reported 42.9% and 42.2% respectively. The difference of the management and the severity of the clinical presentation can explain the lower mortality found in our series in comparison to others. All tetanus patients are hospitalized in the same unit where they can receive round the clock a continuous and very close monitoring. Moreover, the lack of need for mechanical ventilation indirectly reduces the complications associated with this practice.

Circumstances relating to the death of our patients were dominated by infections, respiratory distress and laryngospasm. Chukwubike [12] observed the same causes of death: laryngospasm, respiratory failure and pulmonary inhalation. On the contrary, Sanya [21] in Nigeria reported sepsis and cardiac arrest. In our study, the severity of infection, the high prevalence of the sepsis of unknown origin (36%), financial inaccessibility or unavailable of antibiotics use in nosocomial infections can explain the fact that infections are the first causes of death. In our study, we show that the main predictors of tetanus complications were age > 40 years, presence of co-morbidities, stage of Mollaret equal to II or III and score of Dakar ≥ 1 . The same factors were associated with the risk of death and complications in previous studies. Age > 50 years and > 60 years were respectively reported by Sidhartha [5] and Sanya [21]. The association between presence of a co-morbidities and risk of death was reported by Manga [4] and Brian [22]. Many other authors [4,5,8] also reported the severity of the clinical forms with a high stage and score. The similarity between the predictors of death and those associated with complications confirm the key role of complications in the clinical course of patients with tetanus.

The main strength of our work is the inclusion of the majority of cases of tetanus registered in Senegal as Fann University Hospital is the national reference for tetanus management. Also, this is one of the first studies dedicated to tetanus complications in West Africa. However, we might have under-estimated the incidence of complications due to lack of means to confirm sepsis and cardiovascular complications.

Conclusion

Complications of tetanus disease were reported in close to one half of our patients. Age, the presence of other co-morbidities and severity of clinical presentation were associated with the occurrence of complications. The infection prevention and control in the intensive care unit, the improvement of life-support measures and diagnostic

capacities will allow to significantly reduce morbidity and mortality related to tetanus complications.

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