Publisher
MEDRESEARCH
www.medresearch.in

Pediatric Review - International Journal of Pediatric Research

2020 Volume 7 Number 2 February

E-ISSN:2349-3267
P-ISSN:2349-5499

Research Article

Infection

Clostridium tetani infection in pediatric intensive care unit of the CHU of Tamatave Madagascar

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DOI: https://doi.org/10.17511/ijpr.2020.i02.07

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Justification: Tetanus, fatal disease, still exists in Madagascar in spite of the vaccination sessions of mass, and attacks also the children. **Objective:** To describe the epidemiology, the clinical aspect, the treatments and the evolutions of infantile tetanus. **Patients and methods:** Retrospective study in the pediatric intensive care unit of the University Hospital of Tamatave, on the cases listed during four years (2013-2016). **Results:** Twenty-seven cases were recensed, with an average age of 10.8 years old and a sex ratio (M/W) equal to 6. Only forty-one percent were already vaccinated before the one year age. No child of more than 11 years-old profited from vaccine recall. The stain of the wound after the ablation of flea was the most frequent cause (76%). Tetanus was generalized in 80%, including 44.4% with respiratory disorder having required intubation. All the children presented hyperthermia above 38°C at the entry and 63% higher or equal to 40°C. Sedation by diazepam, used at all children, was used with an average amount of 4 mg/kg/day. The beta-lactamine antibiotics were used in 100% of the cases. The antitetanus serum was administered at 3000 IU/day. Nosocomial infections occurred in 61%. **Discussion and conclusion:** The vaccine recalls are still negligent in the old children, making these latter vulnerable. Mortality is especially due to superinfections and denutrition.

Keywords: Tetanus, Paediatric, Tamatave, Resuscitation

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How to Cite this Article

Ratsimbazafy ABA, Andrianarivelo AM, Rakotomahefa M, Rakotoarivony ST, Rakotoarisoa H, Rasolonjatovo JC. Clostridium tetani infection in pediatric intensive care unit of the CHU of Tamatave Madagascar. Pediatric Rev Int J Pediatr Res. 2020;7(2):87-92. Available From https://pediatrics.medresearch.in/index.php/ijpr/article/view/564

To Browse

Manuscript Received	Review Round 1	Review Round 2	Review Round 3	Accepted
2020-01-20	2020-02-01	2020-02-06		2020-02-11

Conflict of Interest	Funding	Ethical Approval	Plagiarism X-checker	Note
No	Nil	Yes	7%	

Introduction

Tetanus is an infectious, non-contagious disease caused by *Clostridium tetani*, also known as Nicolaier's bacillus. It is a ubiquitous anaerobic telluric bacillus that produces toxins: tetanolysin and tetanospasmin. Tetanospasmine is a potent neurotropic exotoxin and once it reaches the anterior horns of the spinal cord and cerebellum, it causes an increase in muscle tone.

Tetanus is a fatal but completely preventable disease through vaccination and the administration of anti-tetanus serum as post-exposure prophylaxis [1]. In developed countries, this condition has become increasingly rare. The number of confirmed cases of tetanus identified since 2006 has ranged from 49 to 167 per year, with a downward trend. In 2014, the total incidence reported in the European Union was 0.01 cases per 100,000 inhabitants [2].

In Madagascar, tetanus is still prevalent despite the efforts of the state-supported by its partners, particularly in mass vaccination campaigns. The tetanus vaccination coverage rate was 73% in 2009 [3]. Efforts and the program to combat this disease are concentrated on the fight against neonatal tetanus and on prophylaxis for pregnant women, which fall within the scope of the Expanded Program on Immunization (EPI). In recent years, several Malagasy researchers have been interested in monitoring the epidemiological trend of neonatal tetanus [4].

Moreover, few studies have focused on the evaluation of juvenile tetanus, even though this disease does not spare children. It is in this context that the current study carried out this study whose objectives were to describe the epidemiological profile, clinical manifestations, treatments and evolution of infantile tetanus in the pediatric resuscitation unit of the University Hospital Centre of Tamatave (UHCT).

Patients and Methods

Study framework: The present study took place in the university hospital of Analankinina, a reference hospital of the first resort located in the city of Tamatave, in the eastern region of Madagascar. A city whose population has been estimated at 300, 813 inhabitants in 2014. Our service receives children aged 0 to 15 years old coming from all the districts of the eastern part of Madagascar.

Study types: This is a retrospective and descriptive study of children in the Paediatric Resuscitation Unit of the University Hospital for Tetanus in Tamatave.

Period and duration of study: The present study runs from January 1, 2013, to December 31, 2016, that is for a period of four years.

Data collection and analysis: The recruitment of these patients is carried out in an exhaustive manner on all patients of both genders, aged between 1 month and 15 years, admitted to the tetanus department. For this study, it can be used as a pre-established collection form. These data are collected from hospitalization registers and medical observations, as well as the results of paraclinical examinations, carried out. The data were entered and evaluated by using Microsoft Excel 2016 software. The data are expressed in terms of the number of staff (n), percentage (%).

Inclusion criteria: The present study includes all children of both genders, aged between 1 month and 15 years, admitted to the pediatric intensive care unit from January 1st, 2013 to December 31st, 2016 for tetanus or other reasons but subsequently diagnosed at discharge as tetanus and having complete data on the variables selected in the study.

Exclusion criteria: The excluded criteria from the present study were all children diagnosed with tetanus for whom data were incomplete.

Ethical considerations- This study was carried out after authorization from the Head of the Paediatric Resuscitation Department and the Head of the Hospital, who gave their agreement and authorization for this research to be carried out. The current study has guaranteed the confidentiality of our data by expressly omitting names from the survey questionnaires. The current study has collected and processed the data in absolute anonymity.

Results

During these three years, 27 cases of childhood tetanus were collected from 1026 inpatients in pediatric intensive care units, representing a hospital prevalence of 2.6%.

The ages of the children ranged from 7 to 14 years old, with an average of 10.8 years old (Figure 1). Male predominance was noted with a sex ratio of 6.

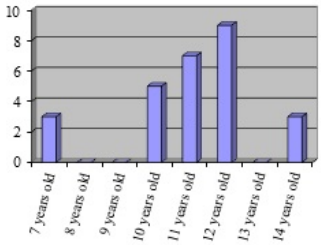

Fig-1: Distribution of patients according to the age.

In terms of immunization status, the notion of tetanus vaccine third dose before the age of 1 year was reported in only 41% of cases. None of the children over 11 years of age received a tenth-year booster vaccination. Wound staining after chewing flea removal was the most common cause (76%) (Table 1).

Table-1: Entrance ways of infantile tetanus

Entrance ways	n	%
Wound after flea extraction	21	77,8
Traditional Circumcision	2	7,4
The wound of the foot by fishbone	1	3,7
Superinfected skin of the lower limbs	1	3,7
Wound after burn	1	3,7
Unidentified entrance ways	1	3,7

Tetanus was generalized from the outset in 81.5% of cases, of which 44.4% had respiratory distress due to glottic spasm and/or diaphragmatic contracture. All of these cases were treated with long-term manual ventilation after intubation with diazepam and/or pancuronium. Isolated trismus was observed in 18.5% of cases (Table 2).

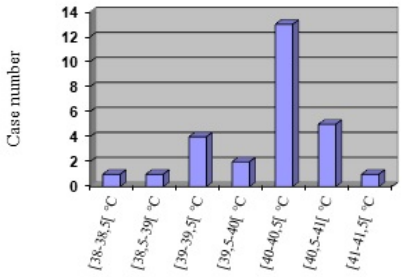

Fig-2: Distribution of patients according to the temperature at admission.

Table-2: Clinical signs of infantile tetanus

Clinical signs	n	%
Generalized contracture	22	81,5
- with respiratory distress	12	44
- without respiratory distress	10	37
Trismus	5	18,5
Photophobia	21	77,8
Phonophobia	23	85,2

All the children had hyperthermia above 38°C at admission and 70.4% of the cases had a very high fever with a temperature of 40°C or above (Figure 2).

All children were sedated with diazepam at an average dose of 4 mg/kg/day (0.25-6 mg/kg/day). All children received beta-lactamine (Penicillin G, 3rd generation cephalosporin). Serum anti-tetanus toxoid (SAT) was administered at the alternate dose of 1500 to 6000 IU/day. Nutritional management was impossible in 27% of cases. Nosocomial infections occurred in 29.6% (8 cases) including pneumonitis in 5 cases, urinary tract infection in 2 cases, and skin infection in the form of superinfected bedsore in 1 case. One case of thromboembolism with fatal pulmonary embolism was observed (3.7%). Hospitalization ranged from 5 to 25 days with a mean of 12.7 days. Moderate malnutrition was noted on admission in 13 children (48.1%). For seven children (25.9%), this malnutrition became severe during hospitalization. Mortality mainly due to superinfections and undernutrition was 22.2% (6 cases).

Discussion

Advantages, limitations, and constraints of the study: One of the benefits of this retrospective study is that it allows for the accumulation of data. The present study, due to its retrospective nature, had some limitations and constraints, notably the incompleteness of medical records, especially the unknown vaccination status and outings without medical approval, which did not allow us to have an exhaustive idea of the evolution. Despite these shortcomings, this study provided a first epidemiological, clinical and evolutionary overview of childhood tetanus in the eastern part of Madagascar.

Epidemiology

Hospital frequency: During the present study period, tetanus cases represented 2.60% of children hospitalized in the pediatric intensive care unit. From an epidemiological point of view, it should be noted that in developing countries there was a lack of technical means and epidemiological data due to the insufficient budget allocated to research, which has a negative impact on the publication of tetanus.

As a result, very little work has been done on tetanus [5].

In Madagascar, few studies are devoted to infant tetanus, where surveillance is concentrated on maternal and neonatal tetanus as in African countries [6].

This study shows that morbidity related to childhood tetanus accounts for 2.6% of all hospitalized tetanus cases. In Dakar Soumaré M. reported a prevalence twice as high (5.3%) as that of the present study [7], while an even higher prevalence was found in Conakry Guinea, reaching 8.28% [8]. Although this prevalence was lower than that found in Dakar, it is not reassuring because our hospital data does not reflect the reality on the ground because of the underestimation of this figure. Thus, as in all developing countries, many cases occur outside the health system and are not reported [2].

Tetanus is most prevalent in unimmunized or unboosted vaccine recipients [9]. It is the only vaccine-preventable and non-contagious disease. In the series studied by Sbai H, none of the patients were vaccinated [10]. Tetanus was preceded by unbooster vaccination in 2.64% of cases in the series studied by Patel JC [9]. Soumaré M. and his team in Dakar reported that none of these patients had been properly vaccinated against tetanus [7]. In our series, only 41% of cases were vaccinated before the age of one year, and none of the children over 11 years of age received a tenth-grade booster. In children, 39.2% of non-neonatal tetanus cases occur before the age of 10 years old [9]. In our series, three cases were recorded under 10 years of age (11.1%). This can be explained by the fact that the tetanus vaccination coverage rate before the age of 1 year in Madagascar is 73% [3].

Entrance door: According to some authors, the portal of entry remains identifiable in 89% of cases and not found in 11%, dominated by cutaneous wounds in 46.3%, operative wounds in 22.2%, open fractures in 3.7% and abscesses in 3.7% [11]. In Senegal, the study by Attinsounon CA and al reported that the portal of entry was dominated mainly by the integument, reaching 82.1% of cases [12]. This figure was not far from our series, wound staining after chewing flea removal was the most frequent cause (21 cases, 77.8%). This frequency can be explained by the tropism of chewing fleas always in the toes, an area exposed to the ground and objects possibly infested by *Clostridium tetani* as described in Africa [13].

Clinic: The clinical expression of tetanus is highly variable, ranging from crude, localized and generalized forms, making diagnosis sometimes difficult. In our series, trismus was observed in only 18.5% of cases (5 cases), hyperthermia was the constant sign (in 100%), followed by phonophobia (in 23 cases, 85.2%), then generalized contractures (in 22 cases, 81.5%) and photophobia (in 21 cases, 77.8%). In the Weng WC study in Taiwan, the incubation period was 8±5 days [14]. In the Weng WC study in Taiwan, the incubation period was 8±5 days [14], sometimes even allowing for local healing of the entrance door. The onset is progressive and marked by non-specific symptoms. The state phase is manifested by trismus (78%), generalized contractures with opistothonos posture, a glottic and/or diaphragmatic spasm that can be life-threatening (57%), and finally neuro-vegetative disorders [14,15]. In a study conducted by Aba YT and al in Côte d'Ivoire, on 273 cases of tetanus, and a study in Senegal showed that tetanus was immediately generalized in all patients on admission [[16,17].

Treatment: Treatment consists of assisted or controlled ventilation via tracheostomy or intubation under curare (pancuronium), myorelaxation and sedation (diazepam, phenobarbital, chlorpromazine), immediate anti-tetanus serotherapy as soon as the diagnosis is suspected, antibiotic therapy against Clostridium and anaerobes (penicillin G, metronidazole), vaccination according to vaccination status, sterilization of the entrance door (curettage and antiseptic lavage), parenteral nutrition, fluid, and electrolyte balance, and management of complications [10,18,19]. The dose of tetanus serum (TSS) to be prescribed in children ranges from 1500 IU to 3000 IU [20]. A single intrathecal injection of 1500 IU combined with intravenous metronidazole reduces mortality [21]. Prevention consists of updating tetanus vaccinations, especially in at-risk individuals, and injecting TTS in the event of a soiled wound [14,18]. Apart from one dose on the first day of hospitalization, booster shots should be given at discharge and every 10 years [19,22].

In our observation, diazepam sedation, used in all children, was used at an average dose of 4 mg/kg/day. Beta-lactams were used in 100% of cases. Tetanus serum was administered at a dose of 1500 to 6000 IU/day. Nutritional management was impossible in seven children (25.9%) due to the impossibility of insertion of the gastric tube at the

Risk of glottic spasm and was limited only to the administration of crystalloids.

Evolution: Depending on the early diagnosis and treatment, the evolution can be good (18%), fatal (60-82%), sequelae, or full of serious complications, such as nosocomial infections (respiratory in 60% and urinary in 20%), thromboembolism (10%), cardiovascular dysautonomia, pressure ulcers (30%), and decompensation of a pre-existing defect [10,18].

In our series, nosocomial pneumonitis occurred in 29.6% (8 cases), urinary tract infections in 2 cases (7.4%), superinfected bedsores in 1 case (3.7%), and thromboembolism in 1 case (3.7%). The aggravation of malnutrition in the 7 cases was mainly due to swallowing problems, while a feeding tube stimulated a glottic spasm in them and became impossible.

The duration of hospitalization is long and heavy, on average 19 days ranging from 5 to 42 days, which is generally reported in the literature [10,18], whereas, in our series, hospitalization lasted on average 12.7 days (5 to 25 days).

Mortality: In our work, mortality was 22.2%, while some authors such as Barry MC and al and Sbai H and al recorded high mortality of 60% and 80%. Hounkpè PC and al in their study showed that the determining factors for poor prognosis are mainly the length of hospitalization, but gender did not influence the prognosis [23].

Conclusion

Three main points emerge from this study.

Clinically: as trismus is not constant during a *Clostridium tetani* infection, any hyperthermia in children must be checked for a recent wound soiled by the soil, and the tetanus vaccination status must be checked.

Given the seriousness of this disease and the heavy burden of management, it is essential to prevent this serious and fatal disease in children, so the Expanded Programme on Immunization must also target older children over ten years of age. The improvement of case management in the present study center requires the supply of a complete parenteral feeding kit and equipment for the technical platform.

What does the study add to the existing knowledge?

Finally, the present study, although limited to a small sample and of monocentric type, has provided an overview of childhood tetanus in the eastern part of Madagascar. This work opens the way for a more extensive, prospective, multi-center study of tetanus in children, in order to avoid bias due to lack of data and to obtain a database that reflects the current reality of childhood tetanus in Madagascar.

Author's contribution

All the authors contributed equally in the conduct, study design, statistical analysis and manuscript preparation.

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