Le Infezioni in Medicina, n. 1, 93-102, 2023
doi: 10.53854/liim-3101-13

Tetanus secondary to oral and odontogenic infections: a case report and systematic literature review

Edinson Dante Meregildo-Rodriguez[1], Martha Genara Asmat-Rubio[2], Gustavo Adolfo Vásquez-Tirado[2]

[1]Universidad César Vallejo, Escuela de Medicina, Trujillo, Peru;
[2]Universidad Privada Antenor Orrego, Escuela de Medicina, Trujillo, Peru

Article received 11 July 2022, accepted 31 December 2022

SUMMARY

Objectives: Tetanus is a potentially lethal infection and remains a priority public health problem in countries with low vaccination coverage. We aim to synthesize the evidence on the clinical-epidemiologic characteristics of oral (odontogenic) tetanus.
Methods: We report a case of oral tetanus. Furthermore, we collected eligible articles about oral tetanus published to date. We performed a systematic review with an exhaustive search of the literature published up to June 30, 2022, in Medline (PubMed), Google Scholar, Scopus, EMBASE, Web of Science, and ScienceDirect.
Results: We analyzed 19 studies that enrolled 26 cases of oral tetanus. The mean age was 51.60 ± 21.95 (range 10-77) years. The frequency and lethality of odontogenic tetanus were higher in males than females. More than 60% of cases occurred in North America. Almost three-quarters of cases were associated with a dental procedure - mainly dental extraction - meanwhile, tooth decay accounted for 23% of cases. The median incubation period was 8.0 (IQR 10.0) days. The time between trismus and death was 4.25±1.89 (range 3-7) days. *Clostridium tetani* was isolated in only 11.54% of cases. Administration of anti-tetanus immunoglobulin alone or combined with anti-tetanus toxoid was reported in at least 42% of cases, and antibiotics in 32% of cases. Patients required tracheostomy and mechanical ventilation in 12% and 8% of cases, respectively. The mean hospital stay was 18.38±14.97 (range 4-53) days. The lethality of odontogenic tetanus was (30.77%).
Conclusion: Since the diagnosis of tetanus is merely clinical, it is crucial to have a high index of suspicion to diagnose this disease correctly. Although odontogenic tetanus is rare, it is potentially life-threatening.

Keywords: Tetanus, tooth extraction, oral health, risk factors, systematic review.

INTRODUCTION

In developed countries, tetanus is extremely rare due to well-implemented immunization programs, though it still carries a mortality of some 13% [1, 2]. However, in resource-limited countries, tetanus remains common and is a significant cause of mortality. Tetanus is estimated to be responsible for about 100,000 cases and 38,000 deaths globally in 2017 [3, 4]. Furthermore, although most tetanus cases originate in developing countries, most reports occur in rich countries. Underreporting in developing countries explains this apparent paradox [5, 6].

The diagnosis of tetanus is merely clinical. Consequently, it is crucial to have a high index of suspicion [1]. Besides, tetanus cases without a typical or evident point of entry can represent an even more significant diagnostic challenge, so clinical suspicion is the key to diagnosis [4-6].

Here, we report the case of an older man with no history of recent immunizations, whose only known injury was a previous dental procedure and poor oral hygiene. We also carried out a systematic review aiming to synthesize the evidence

Corresponding author
Edinson Dante Meregildo-Rodriguez
E-mail: edmeregildo@ucvvirtual.edu.pe

regarding the clinical-epidemiological characteristics of odontogenic tetanus.

CASE REPORT

We describe the clinical case of a 74-year-old male, married and working as a driver of a cargo motorcycle. The last vaccines he received were during his childhood. He had been taking antihypertensive drugs for nine years. He denied taking illicit substances. He had undergone a tooth extraction three weeks before admission to the emergency department (ED). He argued that the dentist did not give him post-extraction instructions or any antibiotic prescription.

Eight days before admission, he began with numbness in the mandibular region, a limitation in opening the oral cavity, and difficulty ingesting liquid and solid food. In addition, he reported burning back pain of moderate intensity. He consulted a private doctor who prescribed him analgesics. Six days before admission, back pain intensified. He went to a neurologist, who ordered sodium valproate 500 mg PO every 8 hours and diagnostic tests. Due to imaging findings of maxillary sinusitis, he consulted an oto-rhino-laryngologist who prescribed antibiotics. After that, intermittent painful muscle spasms appeared in the mandibular region and back, and stiffness in the lower limbs prevented him from walking. Muscle stiffness became generalized, making it impossible for him to walk, open his mouth, and articulate words. The spasms became more frequent, intense, and painful two days before admission. He returned to the neurologist, who referred him to our hospital. He was admitted to the ED of the "Hospital Regional Lambayeque" on February 12, 2020.

The clinical examination revealed a diaphoretic patient in poor general condition, complaining of generalized pain, but ventilating spontaneously, ABP 140/80 mmHg, HR 100 bpm, RR 18 rpm, temperature 36.7°C, and oxygen saturation of 97% on room air. Moist warm skin with no lesions. Trismus made impossible to explore the oral cavity. No adenopathies. Respiratory, cardiovascular, abdomen, and genitourinary systems without any relevant alterations. The patient was awake and oriented, with preserved superior brain functions. There were generalized hypertonia, hyperreflexia,

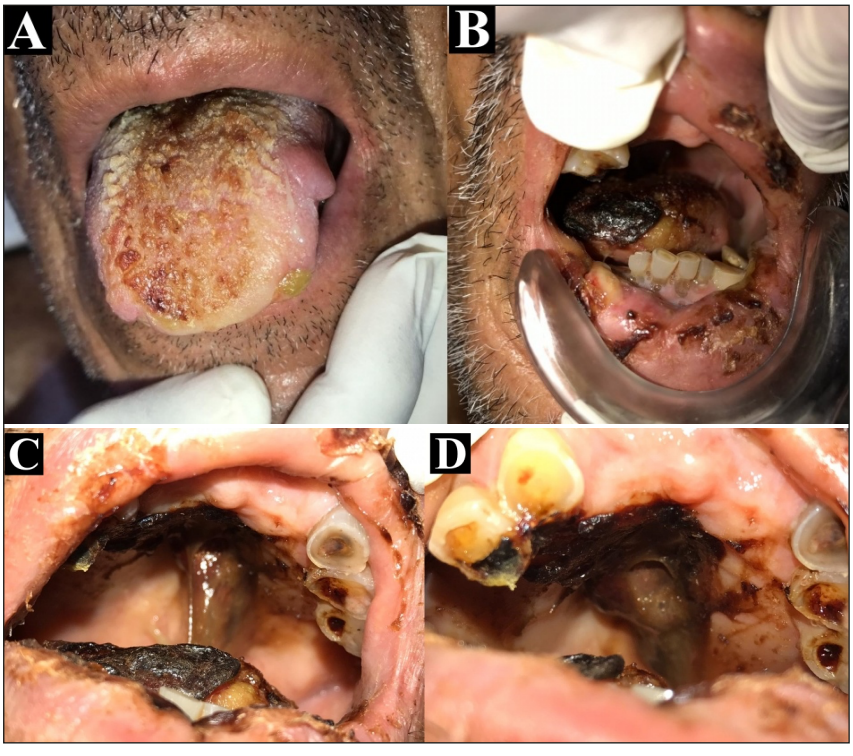

Figure 1 - Oral cavity examination on the third day of admission. Limitation for full mouth opening (A). Dry oral mucosa with crusting on the dorsum of the tongue and soft and hard palate (A-D). Decayed, worn teeth and edentulism (B-D).

and muscle spasms, but no meningeal and Babinski's signs. The initial diagnosis was "cryptogenic" tetanus. ED physicians indicated metronidazole intravenously, anti-tetanus toxoid, and anti-tetanus immunoglobulin. In addition, they prescribed analgesia with tramadol and monitoring in shock trauma.

Total CPK was 3,930 IU/L (reference range 24-195) and CPK-MB 50.8 IU/L (reference range 0-25); CBC, serum electrolytes, biochemistry, and arterial blood gases were normal. Serologies for HIV, syphilis, hepatitis B, and C were negative. An electroencephalogram (taken before admission) showed movement artifacts, frontal muscle contraction, and no paroxysmal activity. Non-contrast enhanced CT and MRI of the brain (also taken before admission) showed atrophic changes and bilateral maxillary sinusitis. The chest X-ray was normal.

Two days after admission, due to the persistence of muscle spasms, baclofen 5 mg PO every 8 hours, diazepam 5 mg IV every 6 hours, and feeding by a nasogastric tube were prescribed. Subsequently, diazepam was changed to midazolam infusion 5 mg/h IV, with which the spasms and trismus subsided considerably, facilitating the examination of the oral cavity. Examination of the oral cavity showed lacerations in the dry oral mucosa with crust formation on the dorsum of the tongue and generalized dental erosion (Figure 1). Six days after admission, he was transferred to a hospitalization ward. Two days later, tramadol and midazolam were discontinued. The final diagnosis was tetanus of odontogenic origin, and he was dis-

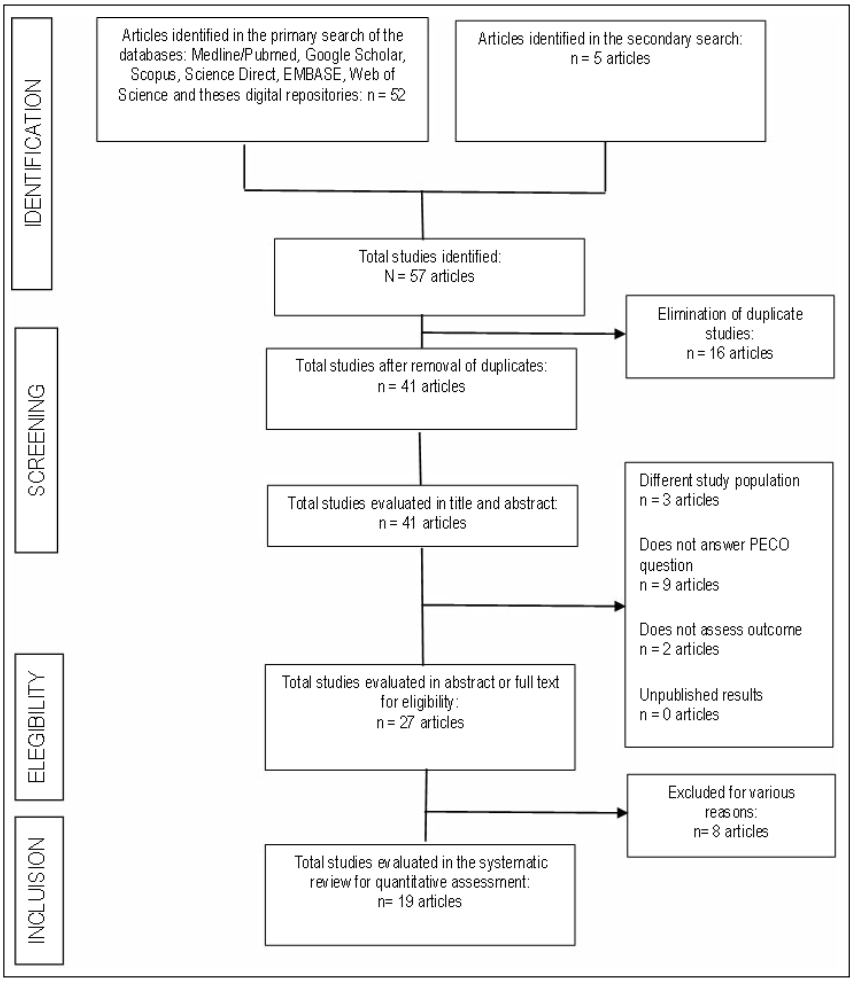

Figure 2 - Flow chart of the selection process of the primary studies included.

charged on February 26, 2020. The patient was seen for the last time one month after discharge with good clinical evolution.
To publish this case, we previously obtained informed consent from the patient and approval from the Ethics and Research Committee of the "Hospital Regional Lambayeque".

MATERIALS AND METHODS

Systematic review
To prepare this systematic review, we followed the PRISMA and AMSTAR 2 guidelines [7, 8]. In addition, we searched Medline (PubMed), Google Scholar, Scopus, EMBASE, Web of Science, and Science Direct for relevant articles up to June 30, 2022. We searched the electronic database using both controlled vocabularies (MeSH or Emtree) and free terms following the PECO methodology (population: patients of any age; exposure: tooth extraction OR dental procedure OR tooth decay; comparator: no tooth extraction OR no dental procedure OR no tooth decay; outcome: tetanus). We registered the protocol in PROSPERO (CRD42022340574) and detailed the search strategy in Supplementary Materials. Figure 2 shows the study selection process.
We included articles in full text or abstract. There were no language or year of publication restrictions. Once we established the review protocol, we distributed electronic copies to the authors. We used Rayyan™ software for the peer-review process. Two blind reviewers evaluated the papers and resolved their discrepancies by consensus or consultation with a third reviewer. All included studies were case reports and case series. In addition, we searched for more primary studies among references of retrieved studies and relevant reviews. We also included our clinical case in this case series. Finally, we extracted the most pertinent information of each included study, *i.e.,* author, year and country of publication, clinic-epidemiological characteristics of the patients, the point of entry of *Clostridium tetani*, treatment, culture for *C. tetani*, incubation time, time of evolution from the onset of trismus to death, hospital stay, and clinical outcome (discharge or death).

RESULTS

We describe the characteristics of the included studies in Table 1, and we summarize the results of the analysis of the cases in Table 2. In addition, we detail in Supplementary Materials the excluded papers and the exclusion reasons. We identified 19 studies that enrolled 26 patients with oral tetanus. The mean age was 51.60±21.95 (range: 10-77) years. The frequency and lethality of odontogenic tetanus were higher in males than females. More than 60% of cases occurred in North America, followed by Europe (15.38%), Asia (11.54%), Africa (7.69%), and South America (3.84%).
In most cases, the authors did not report the patient's occupation. Almost three-quarters of cases were related to a dental procedure (mainly dental extraction); tooth decay accounted for 23% of cases. The incubation period was as follows: mean 21.08±47.94 (range 2-180) days and median 8.00 (IQR 10.0) days. The interval between trismus and

Table 1 - General characteristics of the included studies.

Study, year	*Country*	*Main features*	*Origin*	*Treatment*	*Culture for C. Tetani*	*Time(days)*	*Hospital stay (days)*	*Outcome*
Lucket [41], 1910	USA	N = 1. Female, 10 y. IS: NR. Occupation: NR.	Canine and premolar tooth decay.	NR	Positive	IP 4 d. Trismus to death 7 d.	NR	Death
Graffagnino [11], 1924	USA	N = 1. Sex, age: NR. IS: NR. Occupation: NR.	NR	NR	NR	NR	NR	NR
Maranon [12], 1924	Spain	N=1. Female, 60 y. IS: NR. Occupation: NR.	Molar extraction.	NR	NR	NR	NR	NR
Jugel [42], 1925	Germany	N =1. Male, 32 y. IS: NR. Occupation: NR.	Premolar extraction.	NR	Positive	IP 7 d. Trismus to death 3 d.	NR	Death

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Study, year	*Country*	*Main features*	*Origin*	*Treatment*	*Culture for C. Tetani*	*Time(days)*	*Hospital stay (days)*	*Outcome*
Bettsack [43], 1926	Germany	N = 1. Sex and age: NR. IS: NR. Occupation: NR.	Decayed molar.	NR	NR	NR	NR	NR
Graves [44], 1930	USA	N = 4. Sex and age: NR. IS: NR. Occupation: NR.	Tooth extraction in 3 cases.	NR	NR	NR	NR	Death in 1/4
Vinnard [26], 1945	USA	N = 5. Sex and age: NR. IS: NR. Occupation: NR.	Tooth extraction.	NR	NR	NR	NR	Death in 3/5
Griswold [27], 1949	USA	N = 1. Male, 60 y. IS: NR. Occupation: NR.	Tooth extraction.	IG, ATB	NR	IP 9 d.	13	Discharge.
Robinson [4], 1957	USA	N = 1. Male, 67 y. IS: NR. Occupation: NR.	Molar tooth decay.	IG, toxoid, ATB	Positive	IP 11 d.	17	Discharge.
Treadway [28], 1967	USA	N = 1. Female, 71 y. IS: not vaccinated. Clerical worker.	Incisor extraction.	IG, toxoid	NR	IP 8 d.	NR	Discharge.
Cone [19], 1973	USA	N = 1. Female, 59 y. IS: NR. Occupation: NR.	Curettage and scraping of teeth.	IG, ATB, TQT	Negative	IP 14 d.	53	Discharge.
Babajews [45], 1985	UK	N = 1. Female, 71 y. IS: NR. Occupation: NR.	Tongue laceration due to carious tooth.	IG, ATB, MV, TQT.	NR	IP 3 d.	21	Discharge.
Igarashi [46], 2001	Japan	N = 1. Female, 77 y. IS: not vaccinated. Occupation: NR.	Tooth extraction.	NR	NR	PI 6 d.	NR	NR
Darraj [21], 2016	Canada	N = 1. Male, 32 y. IS: no booster dose. Mechanic.	Caries and molar fracture.	IG, ATB.	Negative	IP 14 d.	NR	Discharge.
Bassey [9], 2018	Nigeria	N = 1. Male, 70 y. IS: NR. Farmer.	Tooth extraction.	IG	NR	IP 2 d. Trismus to death 3 d.	3	Death
Ulfa [36], 2019	Indonesia	N = 1. Male, 42 y. IS: "incomplete". Occupation: NR.	Teeth decay.	IG, ATB.	NR	NR	16	Discharge.
Ajayi [24], 2019	Nigeria	N = 1. Female, 22 y. IS: no booster dose. Occupation: NR.	Tooth extraction.	IG, toxoid, ATB.	NR	IP 180 d.	8	Discharge.
Beviskar [47], 2020	India	N = 1. Male, 27 y. IS: NR. Worker at a utensil shop	Dental treatment for premolar caries.	IG, toxoid, ATB, MV, TQT.	NR	IP 3 d. Trismus to death 4 d.	4	Death.
Meregildo-Rodriguez 2022	Peru	N = 1. Male, 74 y. IS: no booster dose. Cargo motorcycle driver	Tooth extraction.	IG, ATB.	NR	IP 13 d.	15	Discharge.

NR: no reference; IP: incubation period; IS: immunization status; IG: anti-tetanic immunoglobulin; ATB: antibiotics; MV: mechanical ventilation; TQT: tracheostomy.

Table 2 - Summary of included cases.

Total cases (n)	*26*
Age (years)	51.60 ± 21.95 (range 10-77)
Gender	
Male	8 (30.77%)
Female	7 (26.92%)
NR	11 (42.30%)
Continent of origin	
North America	16 (61.54%)
Europa	4 (15.38%)
Asia	3 (11.54%)
Africa	2 (7.69%)
South America	1 (3.84%)
Immunization status	
Not vaccinated / incompletely vaccinated	6 (23.08%)
NR	20 (76.92%)
Occupation	
Clerical worker	1 (3.85%)
Mechanic	1 (3.85%)
Farmer	1 (3.85%)
Worker at a utensil shop	1 (3.85%)
Cargo motorcycle driver	1 (3.85%)
NR	21 (80.77%)
Origin of infection	
Tooth extraction	17 (65.38%)
Tooth decay	5 (19.23%)
Other dental procedure	2 (7.69%)
Tongue lesion due to caries	1 (3.85%)
NR	1 (3.85%)
*Treatment**	
IG ± Toxoid	11 (42.31%)
MV	2 (7.69%)
TQT	3 (11.54%)
ATB	9 (34.62%)
NR	15 (57.69%)
Culture for C. Tetani	
Positive	3 (11.54%)
Negative	2 (7.69%)
NR	21 (80.77%)
Incubation period (days)	Mean: 21.08 ± 47.94 (range 2-180) Median: 8.00 (RIC 10.0)
Time between trismus and death (days)	4.25 ± 1.89 (range 3-7)
Hospital stay (days)	
Total	Mean 16.67 ± 14.91 (range 3-53)
In survivors	Mean 20.43 ± 14.90 (range 8-53)
In non-survivors	Mean 3.50 ± 0.78 (range 3-4)
Outcome	
Discharge	14 (53.85%)
Death	8 (30.77%)
NR	4 (15.38%)

NR: no reference; IP: incubation period; IS: immunization status; IG: anti-tetanic immunoglobulin; ATB: antibiotics; MV: mechanical ventilation; TQT: tracheostomy.

death was 4.25±1.89 (range 3-7) days. *C. tetani* was isolated in only 11.54% of cases. Studies reported using anti-tetanus immunoglobulin alone or combined with anti-tetanus toxoid in at least 42% of cases and antibiotics in 32% of cases. Patients required tracheostomy and mechanical ventilation in 12% and 8% of cases, respectively. The hospital stay was as follows: total 16.67±14.91 (range 3-53) days, in survivors 20.43±14.90 (range 8-53), and in non-survivors 3.50±0.78 (range 3-4). The lethality of odontogenic tetanus was 30.77%.

DISCUSSION

This study is the first systematic review of the clinical-epidemiological characteristics of tetanus secondary to oral and odontogenic infections. We compiled all cases of odontogenic tetanus regardless of the patient's age. In addition, we present a clinical case of an elderly patient without a recent history of immunizations who had tetanus after a dental procedure. This clinical case is also the first report of odontogenic tetanus in Peru.

The portal of entry of *C. tetani* is deep penetrating wounds, compound fractures, gunshot injuries, and surgical intervention [5, 9]. But in a few cases, the organism can enter through superficial skin injuries, snakebites, and scorpion stings [9]. In this study, 73% of oral tetanus cases were related to a dental procedure, and tooth decay accounted for 23% of cases. Odontogenic tetanus has been reported after tooth decay, tooth extraction, root canal therapy, periodontal abscess, and oral soft tissue trauma. Sometimes, an odontogenic cause cannot be ruled out when there is no obvious point of entry [9, 10]. It is estimated that up to 2% of tetanus cases were due to a previous tooth extraction [11]. In 7% of tetanus cases, no evident portal of entry is found [12].

Odontogenic tetanus is very rare. Since 1910 about 30 cases have been reported in the world. Graffagnino and Davidson estimated that a tooth was the portal of entry in only one of 627 cases of tetanus seen in a hospital in New Orleans, USA [13]. In cases associated with tooth extraction, as in our patient, it is likely that the clostridium was previously present in the oral cavity and then reached the bloodstream through the extraction wound [14]. The most widely accepted mechanism is that tetanospasmin is intra-axonally transported to the motor nuclei of the spinal cord's cranial nerves or ventral horns [15]. However, Abel and Chalion argued that tetanospasmin is absorbed into the bloodstream through the lymphatics and is then transported to the central nervous system (CNS) [16].

It is important to remember that tetanus vaccination does not generate long-term immunity and requires a booster dose every ten years. Our study confirmed that almost all cases of tetanus worldwide occur due to a lack of primary immunization or subsequent booster doses [1, 4]. In all tetanus cases in which we were able to retrieve the immunization status, 100% of patients had not been vaccinated or received a booster dose. In this review, only 11.54% of the reported cases came from poor or developing countries, despite tetanus being endemic in these countries. Since, in many of them, the notification of this disease is not mandatory, the under-reporting of cases in these countries explains this apparent discordance [4, 17, 18].

In the present review, the frequency and lethality of odontogenic tetanus were higher in men than women. A similar trend has been reported for tetanus of non-odontogenic origin [19, 20]. The occupations varied, although the studies did not mention it in most cases. Although the incidence of non-odontogenic tetanus is frequently related to certain risky occupations and increases after natural disasters such as earthquakes and tsunamis, particularly in emerging countries, in this review, we did not find a pattern concerning the occupation [17, 19-22].

In the present study, culture samples (from wound swabs from the socket, the extracted tooth, and periapical tissue) for *C. tetani* were only reported in 19.23% of cases, being positive in three of five of these patients. There are some important considerations regarding these cultures:

1) the mere presence of this clostridium in a wound is not sufficient to cause tetanus;
2) the failure to isolate it from the oral cavity may not be considered to contradict the oral portal of entry, since *C. tetani* is isolated from less than a third of the suspected portal of entry in proven cases of non-odontogenic tetanus;
3) a negative culture for *C. tetani* should not be used to rule out the diagnosis of tetanus, especially when the patient's clinical history and the clinical picture is suggestive of tetanus [6, 21, 23]. Therefore, the diagnosis of tetanus - and the portal of entry - is entirely clinical and

does not require bacteriological isolation [1, 10, 24, 25].

The incubation period (IP) in tetanus is usually seven days, although it can last several days or even several months [24]. In our study, due to an extreme value reported by Ajayi et al., it is more appropriate to consider the median IP, 7.5 days (IQR 10.5 days) [26]. Sometimes, we cannot specify the exact moment of the infection initiation. Injuries on the head and neck are no more dangerous than those on other body regions, where, interestingly, the time of disease onset is not determined by the proximity of the portal of entry to the CNS. By contrast, tetanus severity depends upon of depth of the penetrating wounds, the amount of tetanus toxin that reaches the CNS, the IP, and the onset time - interval between the first symptoms and the first spasm -. The shorter the IP and the onset time, the more severe the clinical features of tetanus [6, 22, 27].

The diagnosis of tetanus can be challenging when there are no apparent external injuries. In three reports, some of the patients with tetanus were initially diagnosed with hysteria [28-30]. It is worth noting that several doctors evaluated our patient (clinical case) before admission to our hospital without an adequate diagnosis. Given the high lethality, the relevance of early diagnosis is obvious. A delay in treatment can be fatal [20, 22, 31-35]. According to our results, the lethality of odontogenic tetanus was 30.77%. Lethality for non-odontogenic, non-neonatal tetanus is highly variable depending upon the availability of modern supportive care, ranging from 5 to 50% or even more [31-37].

Tetanus can mimic other conditions with similar early symptoms. For example, some drugs and infections, such as meningitis, can cause stiffness in the neck and jaw muscles. Furthermore, pericoronitis, deep neck infections, and traumatic injuries to maxillofacial structures can cause trismus [5, 6, 29]. Although such affections might be the primary cause of trismus, they could disguise superposed tetanus in some cases, especially in underlying compound mandibular fractures or facial lacerations [6, 30, 38].

In our study, the interval between trismus and death was relatively short (4.25±1.89 days), which is concordant with other studies [22, 39]. Trismus is tetanus's most common premonitory symptom, followed by dysphagia and cervical stiffness [6, 9, 40]. Other occasional initial symptoms include restlessness, irritability, limb stiffness, persistent headache, chills, and fever [6, 40]. As the disease progresses, persistent and generalized muscle spasms may occur, and the back muscles become stiff. Muscle spasms can be so intense as to produce opisthotonos or even fractures of long bones and vertebral bodies [10]. In addition, the facial muscles can be affected, giving the so-called sardonic smile (*risus sardonicus*). Painful tetanic spasms can be precipitated by relatively mild stimuli such as noise or movements. Laryngeal and respiratory muscle spasms may cause cyanosis, suffocation, and seizures. Although respiratory obstruction is the eventual cause of death, on other occasions, the cause of death can be attributed to exhaustion or dysautonomia. Our patient did not present a sardonic smile, opisthotonos, or seizures, but he does have trismus, rigidity, and generalized muscle spasms [38].

Regarding treatment, in this series, anti-tetanus immunoglobulin alone or combined with anti-tetanus toxoid was administered in 42.31% of cases. In addition, antibiotics, tracheostomy, and mechanical ventilation were indicated in 32%, 12%, and 8% of cases. But, in most patients, the authors did not report the administered treatment. Although the purpose of this study is not to review in-depth the treatment of tetanus, it is essential to note that the USA Centers for Disease Control and Prevention (CDC) recommends a single dose of 500 units of anti-tetanus immunoglobulin. Nonetheless, the previously recommended dose range was 3000-6000 units [41-42].

Our findings are consistent with other studies performed in developing countries. For example, in our study, the mean duration of hospital stay among surviving patients was 20.43±14.90 (range 8-53) days, and among non-surviving patients was 3.50±0.78 (range 3-4) days. Anuradha S. in India reported that the mean duration of hospital stay in the patients who recovered from tetanus was 17.7±9.8 days (range 2-56 days), while the mean interval from admission to death in the patients who expired was 5.7±4.8 days (1-23 days) [31]. Similarly, Joshi S et al. found that overall hospital stay was 20.1 days, and Chukwubike OA et al. in Nigeria found that the mean duration of hospitalization for patients who survived was 20.8±7.2 days, compared to 7.0±8.8 days for patients who died (p=0.000) [32, 33]. However, longer and short-

er lengths of hospital stay than our results have been described in different latitudes [34, 35].
In this systematic review, we found some limitations:

1) several studies did not report all the variables of interest;
2) there likely exists information bias due to publication bias of studies that report favorable outcomes. That is, there may exist cases of fatal odontogenic tetanus that have not been published.

In conclusion, tetanus of odontogenic origin is very rare. However, clinical suspicion and knowledge of the disease among doctors and dental practitioners are crucial for timely diagnosis and correct treatment. Although this systematic review does not entertain a novel disease or therapy, it serves as a reminder that this presentation can be a diagnostic challenge.

Conflict of interest
None to declare.

External grants and funding
None to declare.

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Search strategy

1. MEDLINE VIA PUBMED		*Results*	*Date*
#1	"Tetanus" [Mesh]	9,724	14/June/2022
#2	"Mouth" [Mesh]	311,848	
#3	"Tooth Extraction" [Mesh]	21,029	
#4	#1 AND #2 AND #3	12	

2. GOOGLE SCHOLAR		*Results*	*Date*
#1	"Tetanus"	576,000	14/June/2022
#3	"Tooth Extraction" OR "Teeth Extraction"	16,200	
#4	#1 AND #2 AND #3	1,010	
#5	All in Title AND keyword AND abstract: "tetanus" AND ("Tooth Extraction" OR "Teeth Extraction")	64	

3. SCOPUS		*Results*	*Date*
#1	TITLE-ABS-KEY ("tetanus")	2 102	15/June/2022
#2	TITLE-ABS-KEY ("Tooth Extraction" OR "Teeth Extraction")	6 301	
#3	#1 AND #2	24	

4. EMBASE		*Results*	*Date*
#1	'Tetanus'/exp	20,667	15/June/2022
#2	'Tooth Extraction'/exp OR 'Teeth Extraction'/exp	36 642	
#3	#1 AND #2	23	

5. WEB OF SCIENCE		*Results*	*Date*
#1	"Tetanus"	16,209	15/June/2022
#2	"Tooth Extraction" OR "Teeth Extraction"	5,098	
#3	#1 AND #2	2	

6. SCIENCE DIRECT		*Results*	*Date*
#1	"Tetanus"	62,239	15/June/2022
#2	"Tooth Extraction" OR "Teeth Extraction"	77,541	
#3	#1 AND #2	232	
#4	#3 Refine by: Article type: Review articles, Research articles, Case reports.	81	
#5	#4 Refine by: Access type: Open access & Open archive	13	

List of excluded studies

Author	*Year*	*Title*	*Journal*	*Reason for exclusion*
Tramuset M et al.	1952	Tetanus and wisdom tooth.	*Revue Stomatol.*	No full text available. Article in Undetermined language.
Anzouan-Kacou et al.	2015	Post-dental extraction tetanus. About an observation.	*Odontostomatol Trop.*	No full text available. Article in French.
Rheinwald U.	1950	Tetanus infection of dental wounds.	*Osterr Z Stomatol.*	No full text available. Article in German.
Richter KJ et al.	1971	Tetanus after dental procedures: review of literature and report of case.	*J Oral Surg.*	No full text available.
Slepchenko MA et al.	1983	A case of generalized tetanus following tooth extraction.	*Voen Med Zh.*	No full text available. Article in Russian.
Rendu R et al.	1948	Dysphagic tetanus and dyspnea of dental origin.	*Lyon Med.*	No full text available.
Costa G.	1956	A case of tetanus infection after a dental extraction	*Clin. Odontoiat.*	No full text available.
Switzer JL	1974	The differential diagnosis of acute reflex trismus and tetanus, after exodontia	*Am Pract Dig Treat.*	No full text available.