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Outcome and Associated Factors among Adult Tetanus Patients Admitted to Jimma University Medical Center: A Retrospective Study

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Authors' contributions

This work was carried out in collaboration among all authors. All the authors played a key role in carrying out the study to a fruitful outcome. Ethical approval, implementation of the research, and data collection were done by the authors ET, MM, RM and VVB. Study design, data analysis, and interpretation with proof reading were done by the author DL. Author DL also contributed in conceptualization of the research, revisions of the article and final approval of the version to be published.

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ABSTRACT

Background: Although, tetanus is a vaccine preventable disease mortality remains high. And despite the establishment of intensive care unit in Jimma University Medical Center the overall mortality reaches up to 40%. This study will question why the outcome of patients has not improved despite the improvement in the setup of ICU and tries to come up with possible associated factors that prognosticated the outcome.

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Objective: The objective of this study will be to assess the outcome and factors associated with adult tetanus patients treated at JUMC, ICU from 1st Nov 2019 to 31st March 2021.

Methodology: A retrospective cross-sectional study was conducted at JUMC on admitted patients with the diagnosis of tetanus. The study recruited all admitted patients from 1st Nov 2019 to 31st March 2021 at medical and surgical ICU. A structured checklist will be developed and the relevant information from the patients' card will be entered in the structured checklist. Outcome will be defined as a binary variable (death, survival) independent variables will be examined for possible association with the dependent variable. Descriptive statistics like means, frequency and tabulations will be used.

Conclusion: Tetanus has high case fatality rate. Prevention of tetanus could have minimized the mortality. Delayed health care seeking by patients had determinant role for management outcome.

Keywords: CDC: centers for disease control and Prevention; EPI: extended program of Immunization; TAT: Tetanus Anti Toxoid; NGT: Nasogastric Tube.

1. INTRODUCTION

Tetanus is a common nerve system disease that is diagnosed clinically (with supportive laboratory confirmation of the presence of C. tetani), and case definitions are frequently employed to help with clinical and epidemiologic assessments [1]. According to the Centers for Disease Control and Prevention (CDC), probable tetanus is "an acute disease characterized by muscle spasms or hypertonia in the absent [2].

Trismus (lockjaw), muscle soreness and stiffness, back pain, and difficulty swallowing are the most typical early symptoms. Muscle spasm develops as the condition progresses. The discomfort of a generalized muscular spasm can be excruciating. The laryngeal muscles are frequently implicated early in the process, or even in isolation. Because full airway obstruction may occur, this is a life-threatening situation. Breathing failure occurs when the respiratory muscles spasm. Respiratory failure is the most prevalent cause of mortality in tetanus patients who do not have access to a ventilator [3].

During the second week of severe tetanus, autonomic disruption is at its peak, and death from cardiovascular events becomes the leading cause of death. Blood pressure is typically labile, with rapid swings from high to low and tachycardia. It is also possible to get bradycardia and heart block. GI stasis, sweating, and increased tracheal secretions are all signs of autonomic involvement and acute (often highoutput) renal failure [4-5,6].

The clinical manifestations of tetanus occur only after tetanus toxin has reached presynaptic inhibitory nerves. Once these effects become apparent, there may be little that can be done to affect disease progression. Because recovery necessitates the creation of new axonal nerve terminals, the effects of tetanus toxin are long-lasting. Clinical tetanus lasts four to six weeks on average.

In underdeveloped countries, case-fatality rates remain high and have not altered appreciably over the last several decades. A total of 3043 adult African patients died in 27 investigations, with a fatality rate of 43% (95% CI 37 to 50 percent). The high fatality rate likely reflects the fact that mechanical ventilation is often not available in African medical facilities. Longer incubation periods were associated with lower fatality rates [5]. Which is best done in the intensive care unit under the supervision of an anesthesiologist or critical care specialist who is trained in the management of the disease's consequences, particularly early and vigorous airway control, treatment goals include halting toxin generation, neutralising unbound toxin, airway management, muscle spasm control, and management of dysautonomia, general supportive management.

To try to deactivate any circulating tetanus toxin and prevent its uptake into the nervous system, antitoxin should be given early. Human tetanus immune globulin (TIG) and equine antitoxin are the two options. TIG is the preferred preparation because it is less prone to cause anaphylactic responses. A single IM dose (3000-5000 IU) is given, with a portion injected around the wound. Equine-derived antitoxin is available widely and is used in low-income countries; after hypersensitivity testing, 10,000-20,000 U is administered IM as a single dose or as divided doses. Some evidence indicates that intrathecal TIG of inhibits disease administration progression and leads to a better outcome. The

results of relevant studies have been supported by a meta-analysis of trials involving both adults and neonates, with TIG doses of 50–1500 IU administered intrathecally.

Spasms are controlled by heavy sedation with Chlorpromazine benzodiazepines. and phenobarbital are commonly used worldwide, and IV magnesium sulfate has been used as a muscle relaxant. A significant problem with all these treatments is that the doses necessary to control spasms also cause respiratory depression: thus, in resource-limited settings without mechanical ventilators. controlling spasms while maintaining adequate ventilation is problematic, and respiratory failure is a common cause of death. In locations with ventilation equipment, severe spasms are best controlled with a combination of sedatives or magnesium and relatively short-acting, cardio vascularly inert, nondepolarizing neuromuscular blocking agents that allow titration against spasm intensity. Infusions of propofol also have been used successfully to control spasms and provide sedation.

It is important to establish a secure airway early in severe tetanus. Ideally, patients should be nursed in calm, quiet environments because light and noise can trigger spasms. Tracheal secretions are increased in tetanus, and dysphagia due to pharyngeal involvement combined with hyperactivity of laryngeal muscles makes endotracheal intubation difficult. Patients may need ventilator support for several weeks. Thus tracheostomy is the usual method of securing the airway in severe tetanus. Nonpharmacological management includes regular chest physiotherapy which includes breathing exercises, chest mobilization and suction of excessive secretions to help prevent respiratory complications [7,8].

Cardiovascular instability in severe tetanus is notoriously difficult to treat. Rapid fluctuations in blood pressure and heart rate can occur. Shortacting drugs that allow rapid titration are preferred: particular care should be taken when longer-acting β antagonists are administered, as their use has been associated with hypotensive cardiac arrest. Complications arising from treatment are common and include thrombophlebitis associated with diazepam injection, ventilator associated pneumonia, central-line infections. and septicemia. Prophylaxis against deep-vein thrombosis and thromboembolism is commonplace in several centers [9-13].

Tetanus recovery can take 4–6 weeks. Because tetanus toxin is present, patients must receive a full main course of immunization is poorly immunogenic and the immune response following natural infection is inadequate [14].

1.1 Significance of the Study

There are only limited studies done on tetanus in our country especially in higher institutions. So this study will provide base line for further studies especially in Jimma University Medical Center and in general for the national higher institutions to assess tetanus patterns, mortality and prognostic factors in our set up where there is limited facility. It can also give research directions to conduct studies in the vaccine coverage and in other high risk groups like reproductive age women and pediatric age groups.

This study can provide latest information in showing the gaps in the management and types of interventions that can be provided that would have altered the outcome of the patient. It can provide evidence to support any particular therapeutic intervention in tetanus.

It will necessitates the attention of policy makers and health education providers to create awareness in the respective society in disease prevention and in creating early health seeking behavior in individuals to the health institutions prior to the advancement of the disease.

2. MATERIALS AND METHODS

2.1 Study Area and Period

The study will be conducted in ICU department of JUMC, Oromia region, southwest Ethiopia. Jimma University Medical Center is located in Jimma town, 354km, south west of Addis Ababa. It is one of the biggest referral hospitals in Oromia region. Besides it is one of the teaching hospitals for medical students in the country. It is responsible for more than 15-20 million people with very wide catchment area which is 17,500 km².

The study period will be conducted from 1st Nov 2019 to 31st March 2021.

2.2 Study Design

Retrospective cross sectional study.

2.3 Source Population

Tetanus patients admitted to Jimma University Medical Center.

2.4 Study Population

Total coverage of all clinical record of tetanus patients admitted to Jimma University Medical Center from 1st Nov 2019 to 31st March 2021.

2.5 Variables

The following information will be collected from a recorded card by using structured questionnaire.

2.5.1 Dependent variables

• Outcome of patients (Dead or Survived)

2.5.2 Independent variables

- Age
- Sex
- Occupation
- Trismus
- Risus sardonicus
- Dysphagia
- Spasm and rigidity
- Fever at presentation
- Respiratory failure (aspiration pneumonia, lung abscess)
- Element of Management Protocol
- o Oxygen
- o Suction
- o Tracheostomy
- o Muscle relaxant
- o Antibiotic
- o Tetanus Antitoxoid
- Wound debridement

2.6 Data Collection Tools and Procedures

A structured checklist will be developed in English language to extract relevant information about patients' socio demographic characteristics, complaints, clinical picture diagnosis and outcome of the treatment.

The relevant information from the patients' card will be entered in the structured checklist.

3. RESULTS AND DISCUSSION

3.1 Data Analysis

Data will be checked, cleared and feed into SPSS (version 22.0) software for statistical analysis. The association of independent variables with patient outcome (dead or survived) will be investigated by using bivariate logistic regression. All independent variables with p-value ≤ 0.25 in the bivariate logistic analysis will be fitted into multiple logistic regressions to identify associated factors in the final model. The degree of association will be interpreted by using ORs with 95% CI and P ≤ 0.05 will be considered as statistically significant.

Out of 24 cases planned to be included in the study, only 18 cards were available making the coverage of 75 percent. The rest 6 were not available in the card room. But few data was registered in ICU log book. The result is summarized as below.

3.2 Age and Sex Distribution

The youngest is 21 years and the oldest is 80 yrs. 10 cases (41.67%) were in the age of 21 to 30 years, 7 cases(29.17%) were in the range of 31 to 40 years, 7 cases(29.17%) were in the range of > 40 years. Mortality is lowest (14.29%) among age between 31-40 years and highest (50.00%) among cases with age between 21 to 30 years. (Table 2, Graph 2).

Twenty- three cases (95.83%) were male and one case (4.17%) was female making male to female ratio of 23:1. 60.87 percent of males and the single case admitted female is dead (Table 3, Graph 3).

3.3 Occupational Distribution

Among cards identified only 10 of them hold the information for occupation and all of them were farmers.

3.4 Portal of Entry

Table 5 shows the incidence of various modes of infection & their relative mortality. The commonest portal of entry was traumatic abrasion accounting for 45.80%, followed by penetrating trauma (41.67%). There was a single case following tooth extraction (4.17%), traditional practices (4.17%). No pregnancy

related maternal infection was identified. Portal of entry was not identified for 4.17% of cases. All tetanus cases following traditional practices and tooth extraction, chronic wounds, 50 percent of tetanus cases following penetrating trauma and 36.35% of cases following traumatic abrasion were dead. Of those whose portal of entry was not identified, all percent were died. But the difference in mortality between different nature of infections were not statistically significant (p>0.05).

Lower limb was the commonest site of entry accounting for 33.33% of the total followed by those whose site of entry was not identified accounting for 27.78% of the total. Lower limb as the site entry, mortality was 58.33% and 25 percent for each of trunk and head and neck. There was no death following upper limb injury while 20% of deaths occur following unknown site of entry. However, the difference in mortality for different site of entry was not statically significant with p>0.05 (Table 6, Graph 6).

3.5 Clinical Features

Trismus was present in 33 cases (91.67%), Dysphagia in 25 cases (69.44%), and Generalized spasm and neck stiffness each in 15 cases (41.67%). All cases were diagnosed based on clinical grounds.

Incubation period was determined in days in 27 cases; there were 7 cases with incubation period of less than 7 days, 13 cases with 7-14 days and 7 cases above 14 days. 28.57% of those with incubation of <7 days, 30.77% of those of with 7-14 days and 57.14% of those with >14 days were died.

Period of on set was also determined in 27 cases. There were 20 cases with period of onset less than 24 hours, between 24 and 48 hours in 5 cases and greater than 48 hours in 2 cases. 35% of those with period of onset of <24 hrs, 40% of those with period of onset of 24-48hrs, and 50% of those with period of onset of >48 hrs were died. However, the difference in mortality rate with this classification of period of onset was not statistically significant with P value>0.05 like incubation period (Table 6, Graph 6).

Generalized spasm was present in 69.44percent of cases and 48 percent of these cases died. All of those who had no generalized spasm at admission were not died. With P-value<0.05, the difference in case fatality rate with presence or absence of generalized spasm at presentation was statistically significant (Table 6, Graph 6).

As shown on Table 6, Graph 6, 26 patients had fever at admission and 34.61percent of this case died. Only 33.33 percent of those who had no fever died. For four cases (11.11%) of whom 25% were died, the presence or absence of fever was not recorded. And this difference in mortality was not statistically significant (p>0.05).

3.6 Management of Patients in the Hospital

Patients were admitted to both tetanus room and ICU. Out of 36 cases, 20 were admitted to tetanus room and treated conservatively. Treatment included antibiotic, toxin neutralization, wound debridement and muscle relaxant.

the rest 16 patients were admitted in ICU and were treated by muscle relaxant with intubations by Endotrachial tube to administer oxygen, by mechanical ventilation plus conservative treatment. Tracheotomy was done only for 2 of these patients to decrease dead space.

From 30 adult cases; all except one were given crystalline penicillin. 20 cases were given 4-12 million IU IV in 4-6 divided doses per 24 hours and 45 percent of these died, 9 cases were given 12-18 million IU IV in 6 divided doses per 24 hour and 22.22 percent of these died. This difference in mortality between low and higher doses of crystalline penicillin was not statistically significant with P-Value >0.05 (Table 8, Graph 8).

Some cases were treated by combination of muscle relaxants with oxygen and some were treated conservatively with chlorpromazine and diazepam alternating every three hours with optimal dose. All adult cases were given diazepam 40 mg over 24 hours in 4 divided dose and chlorpromazine 100 mg over 24 hours alternating with diazepam. Children were given diazepam 12-40 mg in 4 divided doses per 24 hours alternating with chlorpromazine.

Spasm was controlled in 58.33percent of cases and all survived, spasm was not controlled in 13.89% of cases and they died of respiratory spasm subsequently. In 27.78 percent of cases the condition of the patients were not recorded. TAT was given to all cases except two who couldn't afford to buy. Adult were given 10,000IU IM while children were given 1,500-10,0001UIM. 18 cases had accessible wound but wound debridement was done only for 66.67% of these cases. 66.67% of those who had no wound debridement were died.

The difference in mortality between those who had and those who had not wound debridement was not statistically significant (p>0.05) (Table 7, Graph 7).

Tracheostomy was done for 12 patients of those admitted in ICU to supply oxygen with high degree of respiratory spasm. Also suctioning of the trachea was done. If it was done properly, it decreases mortality significantly.

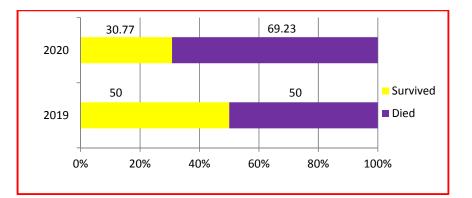
Concerning supportive treatment, oxygen was given for those who need ventilator support in ICU, suctioning of trachea was done for those who had tracheostomy and tracheal secretion. Out of 16 patients those admitted in ICU, 10 cases (62.2%) were died due to improper treatment.

3.7 Outcome

- The overall case fatality rate was 62.50%. The average period of hospitalization was 10 days (range, 1 - 35 days) for those who dies, 6 cases(53.3%) of the total death occurred in the first six days of hospitalization.
- 9 cases were survived and the average period of hospitalization was 28 days, (range,11 - 47 days). Over all the average period of hospitalization was 12 days, the range being 1-78 days.
- In majority of the cases the cause of death was not recorded (53.85%). Of those with recorded cause of death respiratory spasm was found to be the commonest cause accounting for 30.77%. One case died of respiratory failure (aspiration pneumonia, Lung abscess) and one case died of sepsis.

Table 1. Showing survival and deaths of tetanus cases by year of admission to JUMC

Year	Out come									
		Survived		Died	Total					
	No.	%	No.	%	No.	%				
2019	5	50.00	6	50.00	11	45.83				
2020	4	30.77	9	69.23	13	54.17				
Total	9	37.5	15	62.5	24	100.00				

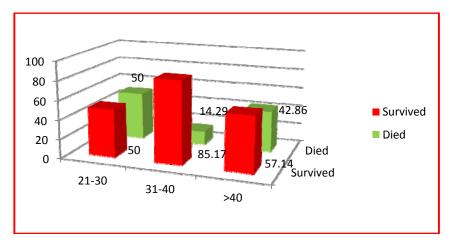


Graph 1. Showing survival and deaths of tetanus cases by year of admission to JUM

Table 2. Age by incidence and outcome of	tetanus	cases in JUMC
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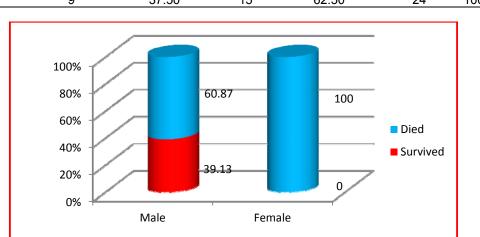
Year			Ou	Itcome		
	Survived		Died		Тс	otal
	No.	%	No.	%	No.	%
21-30	5	50.00	5	50.00	10	41.67
31-40	6	85.71	1	14.29	7	29.17
>40	4	57.14	3	42.86	7	29.17
Total	9	37.50	15	62.50	24	100.00

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Graph 2. Age by incidence and outcome of tetanus cases in JUMC

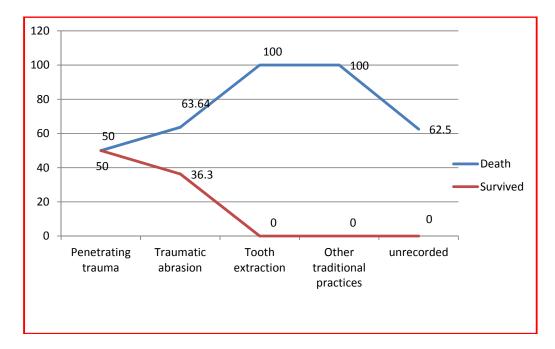
Sex	Outcome							
	Survived		Died		Total			
	No.	%	No.	%	No.	%		
Male	9	39.13	14	60.87	23	95.83		
Female	0	0	1	100	1	4.15		
Total	9	37.50	15	62.50	24	100		



Graph 3. Sex, by Incidence and outcome of tetanus cases in JUMC

Mode of infection	Outcome							
		Death		Survived		Total		
Penetrating trauma	5	50.00	5	50.00	10	41.67		
Traumatic abrasion	7	63.64	4	36.3	11	45.83		
Tooth extraction	1	100	0	0	1	4.17		
Other traditional practices	1	100	0	0	1	4.17		
unrecorded	1	100	0	0	1	4.17		
Total	15	62.5	9	37.5	24	100		

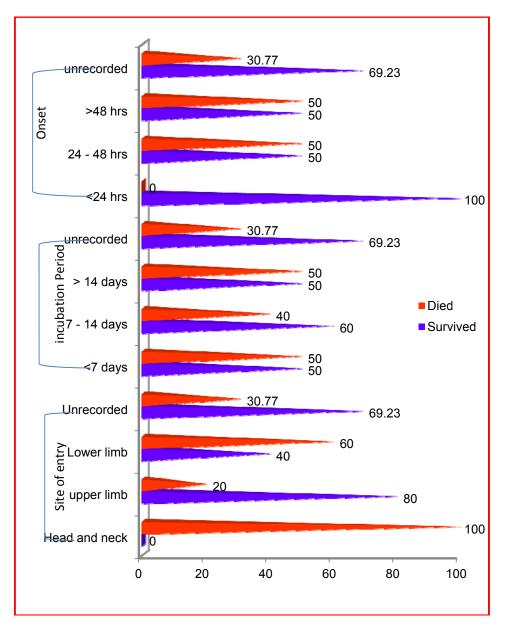
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Graph 4. Mode of infection by outcome of tetanus cases in JUMC

Variables			0	utcome		
	Survived		Died	Died		
	No.	%	No.	%	No.	%
Site of Entry						
Head and neck	0	0	1	100	1	4.17
upper limb	4	80	1	20	5	20.83
Lower limb	2	40	3	60	5	20.83
Unrecorded	9	69.23	4	30.77	13	54
Total	15	62.5	9	37.5	24	100
Incubation Period						
<7 days	2	50.00	2	50.00	4	16.67
7 - 14 days	3	60.00	2	40.00	5	20.83
> 14 days	1	50.00	1	50.00	2	8.33
unrecorded	9	69.23	4	30.77	13	54.17
Total	15	62.5	9	37.50	24	100.00
Onset						
<24 hrs	1	100.00	0	0	1	4.17
24 - 48 hrs	1	50.00	1	50.00	2	8.33
>48 hrs	4	50.00	4	50.00	8	33.33
unrecorded	9	69.23	4	30.77	13	54.17
Total	15	62.50	9	37.50	24	100

Table 5. Selected variables by outcome of tetanus cases in JUMC



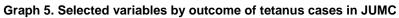
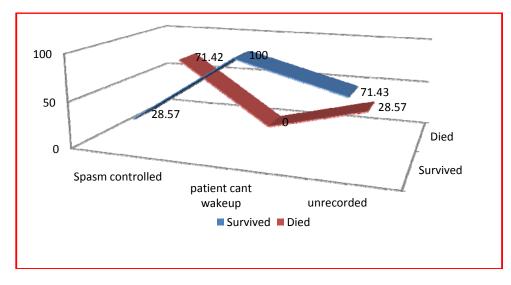


Table 6. Condition of tetanus cases in Jimma Hospital after initiation of muscle relaxants with
optimal dose JUMC

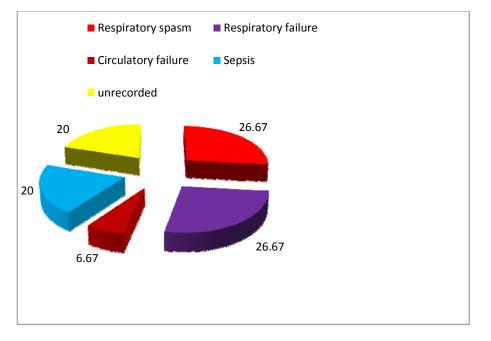
Condition	Outcome							
	Survi	ved	Die	d	Tot	al		
	No.	%	No.	%	No.	%		
Spasm controlled	2	28.57	5	71.42	7	29.17		
patient cant wakeup	3	100.00	0	0	3	12.50		
unrecorded	10	71.43	4	28.57	14	58.33		
Total	15	62.50	9	37.50	24	100		

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Graph 6. Condition of tetanus cases in Jimma Hospital after initiation of muscle relaxants with optimal dose JUMC

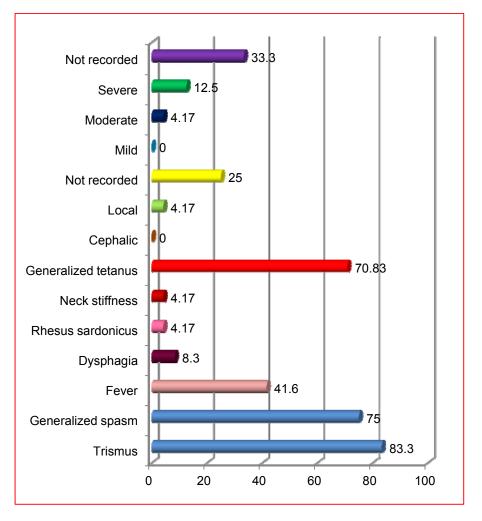
Causes of death	Number	percent
Respiratory spasm	4	26.67
Respiratory failure (aspiration pneumonia, lung abscess)	4	26.67
Circulatory failure	1	6.67
Sepsis	3	20.00
unrecorded	3	20.00
Total	15	100



Graph 7. Cause of death among tetanus patients admitted to JUMC

Clinical Manifestation at admission	Yes No. (%)
Trismus	20 (83.3)
Generalized spasm	18 (75.0)
Fever	10 (41.6)
Dysphagia	2 (8.3)
Rhesus sardonicus	1 (4.17)
Neck stiffness	1 (4.17)
Clinical Form	
Generalized tetanus	17 (70.83)
Cephalic	0
Local	1 (4.17)
Not recorded	6 (25)
Severity	
Mild	0
Moderate	1 (4.17)
Severe	3 (12.5)
Not recorded	8 (333)

Table 8. Showing tetanus cases by common clinical manifestation, clinical form and severity, JUMC



Graph 8. Clinical manifestation at admission

The overall mortality in this study was 62.5% which was 40.0% and 38.0% in previous two consecutive studies done at JUMC [15]. There are, however, inherent differences between these two studies like sample size. Mortality within age groups peaks at age 21-30 and stabilizes thereafter while respective overall proportions of survivals and deaths both showed decreasing tendency after age of 20 years.

Male were predominantly affected accounting for 95.83 percent of the total. Male to female ratio was 23:1. This could be due to their greater exposure to tetanus prone injuries. And TAT vaccination is the main component of ante natal care and reproductive health programs which made this variation higher.

Modes/portal of entry can be viewed as different labels for the same underlying phenomena. Site has prognostic importance in this study, similar to the previous study at JUSH [15]. The within site risk of mortality tended to rise as location moves up towards head and neck. Sites located on lower limbs were commonest and mildest while those on head and neck were less common and severe. The importance of site is also reflected in the fact that cases with unrecorded sites had 30.77% mortality and 100% in the previous study [15-16].

Period of onset had predictive significance in this investigation, as it had in a prior study done at the same institution [15]. As the period of onset became shorter, mortality within groups of duration of onset tended to grow. However, the onset period may be dictated by the location. In other words, the site can shorten or lengthen the duration of onset, and it (period of onset) may not be dependent on time but rather on the site/order of presentation.

The fact that 12 (50.0 percent) of cases had generalized spasm on admission and that 6(50.00 percent) of those with generalized spasm died while 1(11.1 percent) of those with no generalized spasm died shows need for understanding of the course of the disease, for localized and cephalic forms can also progress to generalized form similar to previous study at JUMC [15].

Patients admitted to ICU contributed for all deaths and 6 (53.3%) of all deaths occurred within the first six days of hospitalization. Both the patient's condition at admission and the

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quality of service after admission determine patient's fate.

There was some indication that presence of fever was related with high probability of death. This may be due to systemic infection, or some locus of infection which if not identified might have led to complications and subsequent death [15,17]. However, the majority of the patients in this study are unable to provide data.

4. CONCLUSION

Tetanus has high case fatality rate. Prevention of tetanus could have minimized the mortality. Delayed health care seeking by patients had determinant role for management outcome. Quality of care at ICU was suboptimal. This indicates the importance of prevention and proper management. Asphyxia from respiratory spasm is the commonest cause of death. As most of deaths occurred in the first six days of hospitalization, basic life supports like, oxygen supply through the appropriate method, frequent suctioning and NGT insertion for feeding could have reduced mortality if done in proper time by well-trained person.

CONSENT

Written and Oral informed consent was obtained from all individual participants included in the present study.

ETHICAL APPROVAL

Ethical clearance was obtained from Institute of Health Sciences, Jimma University through a letter of permission prior to the initiation of data collection. The Ethical code: JU/Int.Med./066/2019.

DATA AND MATERIALS AVAILABILITY

All data associated with this study are present in the paper.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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