



“CLINICAL AND BIOCHEMICAL STUDY OF TETANUS”

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ABSTRACT

Tetanus is a medical condition characterized by a prolonged contraction of skeletal muscle fibers. Tetanospasmin is a neurotoxin which causes the symptoms of tetanus. It is a neurotoxin produced by gram positive bacterium *Clostridium tetani*. Infection starts with wound contamination and steadily progresses causing muscle spasms known as “lock jaw”. Under the present study, all cases of tetanus admitted under the Department of Medicine of Goa Medical College from July 2008 to October 2010 were studied and analyzed. Following admission, a detailed history of the patients was taken, the patients were then thoroughly examined and clinical findings noted. At admission, all patients received tetanus toxoid injection and 3000 IU of tetanus immunoglobulin. Appropriate treatment was given to patients who developed complications. At the end of the study, it was concluded that tetanus is more common in the rural areas, in younger males. Incubation period and period of onset are reliable indicators of severity of tetanus and prognosis. Grading of tetanus is very helpful in predicting the prognosis of tetanus and injection of intrathecal TIG probably influences the course of disease favorably.

KEY WORDS: Tetanus, tetanolysin, tetanospasmin, lockjaw, toxoid



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INTRODUCTION

About four to five decades ago the three "T's" typhoid, tuberculosis and tetanus were a problem which had remained unsolved. But with the passage of time typhoid and tuberculosis have been successfully dealt with. However a specific cure for tetanus is still a long way off, although mortality figures are on the decline. Tetanus has remained a deadly killer since the days of Hippocrates. To quote the words of Hippocrates¹, "Those who are attacked by the disease die within four days or if, they pass through these they recover". Recent advance have however changed this gloomy concept of the disease. The effect of the menace varies from one country to another. Though rare in the affluent countries it is still rampant in India and is one of the major causes of death especially in rural India. Illiteracy, poverty, ignorance regarding immunization programme, unhygienic habits have contributed to its spread in India. Tetanospasmodic epitomizes the disease². Being a disease of antiquity literature on tetanus is vast and confusing with contradictory reports on various aspects of the disease. In the present study an attempt is made to find out the prognostic importance of various parameters like age, incubation period, period of onset, grade of tetanus, and intrathecal tetanus immunoglobulin. The bacteriological cause of tetanus is a disease caused by infection with clostridium tetanii³. The genus clostridium to which this organism belongs contains Gram positive anaerobic spore forming bacilli. This genus includes a number of species that produce powerful toxins and are dangerous pathogens for men and animals e. g. Clostridium Welchii, Clostridium Tetanii etc. Also included under this genus are a number of species which are non-pathogenic eg. Clostridium Sporogenes^{1,4}. Morphologically, Clostridium tetanii is a Gram positive actively motile slender bacillus 4-8 u x 0.5 u in size, though there may be considerable variations in size. The bacilli can occur singly or in chains. Young cultures are strongly positive but older cultures may be Gram negative or even Gram variable. The spores are spherical in shape placed at terminal and giving the characteristic "drum stick" appearance. In some bacilli

spores may be oval or sub-terminal. Occasionally they may be present at both the ends giving "dumb bell appearance"^{1,4}.

Biochemical reactions of Clostridium Tetanii exhibit the following biochemical reactions:-

- (a) Mild proteolytic activity with gelatin liquification.
- (b) Indole is formed.
- (c) No saccharolytic property, hence sugars are not fermented⁵.

Resistance: The vegetative forms are as susceptible to adverse factors as any other bacteria and are readily killed by antiseptics or heat. It is the spores that are more resistant to antiseptics and heat with the result they can survive for many years. They are killed slowly on prolonged exposure to sunlight provided abundant air is available. Water at 100° c for 1 hour is sufficient to kill the spores. Autoclaving at 121° c requires only 20 minutes. Spores being resistant to antiseptics are not killed by 5% phenol, 5% Lysol or 0.1% mercuric chloride. Most efficient chemicals used to kill the spores are 1% aqueous iodine solution, 10 volumes of hydrogen peroxide and 2% gluteraldehyde at pH of 7.5 - 8.5.

The clinical manifestations of clostridium tetanii infection are the result of release of toxins tetanolysin and tetanospasmin⁶.

MECHANISM OF ACTION

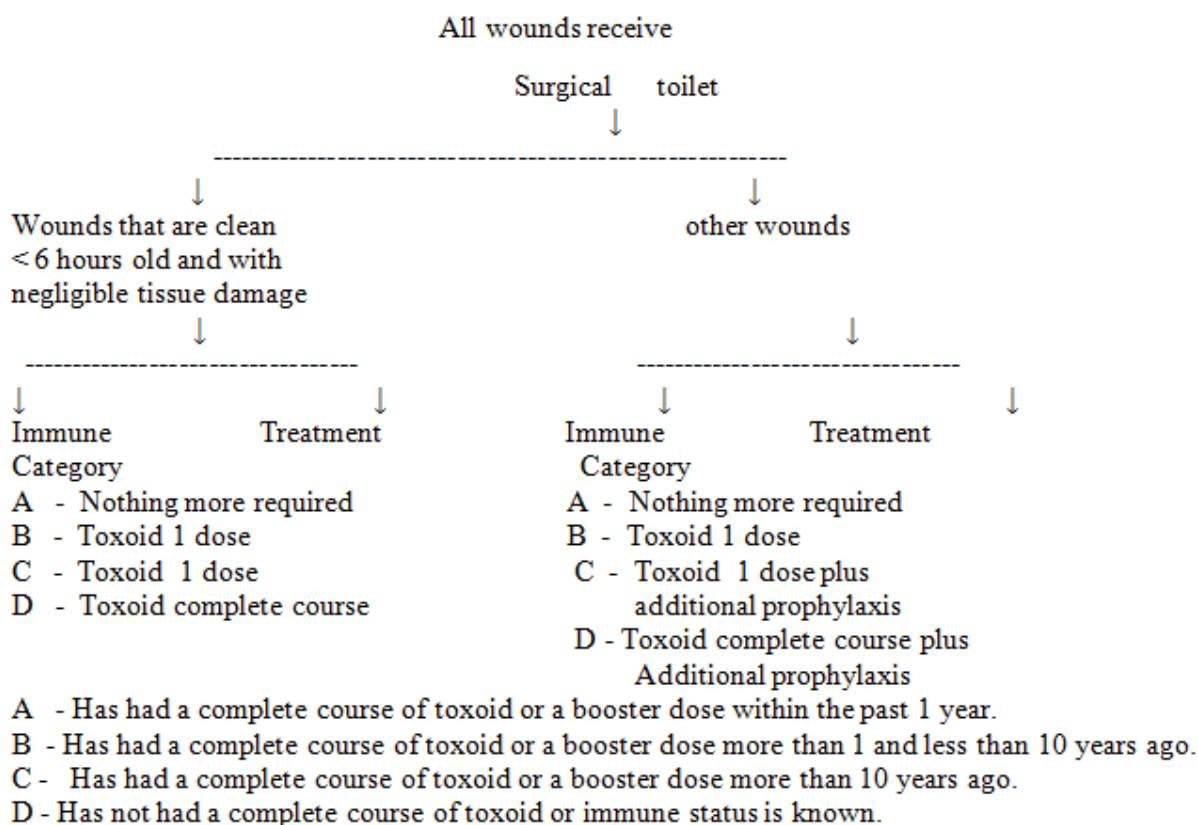
The toxin liberated travels along the axis cylinder of the peripheral nerves and is avidly fixed by gangliosides of the grey matter of the nervous tissue. Initially polysynaptic reflexes are affected though monosynaptic reflexes may also be affected in the later stages. The toxin released acts at the presynaptic level and specifically blocks the synaptic inhibition of the cord from higher centers, presumably at inhibitory terminals that use glycine and GABA as neurotransmitter. With the abolition of the inhibitory effect, uncontrolled spread of impulses initiated anywhere into the central nervous system occurs resulting in muscle rigidity and spasms due to the simultaneous contraction of both agonists and antagonists in the face of absent reciprocal inhibition, spasm pattern being established by the most powerful muscle acting at a given joint. The toxin that

has once bound to nerve tissue cannot be neutralized by neutralized by anti-toxin. It is eventually inactivated by some unknown mechanisms as the patients recovering from tetanus show no residual neurological defects^{7,8}.

COURSE

Once tetanus occurs the manifestations increase in severity over 2-4 days and then stabilize over the next 5-7 days. After about ten days spasms decrease in frequency and disappear by two weeks. Most survivors recover completely without any residual deficit.

Complications: In mild or moderately severe cases, managed by sedation only. Complication are few and provided spasms are adequately controlled, the patient makes an uninterrupted during or after a spasm, and this may lead to collapse of lung lobules and pneumonias. On the other hand a patient with severe tetanus is liable to suffer from several dangerous complications. These are seen mainly in patient's curarized and on artificial ventilation; in other words, in patients kept alive long enough for these complications to develop. The complications may be cardiovascular, hyperpyrexia, neurological, metabolic or renal failure⁹.



METHODS AND MATERIALS

In the present series all cases of tetanus admitted under the Department of Medicine of Goa Medical College from July 2008 to October 2010 were studied and analyzed. Following admission a detailed history of the patients was taken with special mention of age, nature of injury, incubation period, period of onset, presenting complaints and previous immunization status of the patient. The

patients were then thoroughly examined and clinical findings noted. This helped to assess the severity of tetanus. At admission all the patients were given tetanus toxoid injection and 3000 IU of tetanus immunoglobulin at different sites. In the last 20 patients 250 IU of intrathecal tetanus immunoglobulin was given to alternate patients irrespective of the severity of tetanus. All the patients were given 8 lakh

units of procaine penicillin for a period of 7 days. In case of patients who developed respiratory tract infection, urinary tract infection, etc. appropriate antibiotics were added. Methocrobamol was used for muscle relaxation. Diazepam 10 mg, Chlorpromazine 50 mg and Promethazine 25 mg were used IM at 2-6 hourly interval alternately to sedate the patients. In the patients who had severe rigidity or frequent spasms drugs were given more frequently and if not, the interval was increased such that the patient was well sedated but retained the ability to respond to oral commands. In the patients who had thick secretions interfering with adequate and free flow of air in the airways or spasms persisting despite adequate sedation, tracheotomy was undertaken followed by curarisation using tubocurarine and ventilator support. Complications such as urinary tract infection, respiratory tract infection, etc. were adequately taken care of. Nutrition was maintained by feeding through the Ryle's tube. As the patients improved the ventilator support, sedation and muscle relaxants were gradually

tapered and stopped. At discharge the patients were advised to complete their immunization. The data thus obtained was tabulated and the patients were graded using the following criteria:-¹⁰

Criteria No. 1 :- Lockjaw

Criteria No. 2 :- Spasms

Criteria No. 3 :- Incubation period of less than equal to 7 days.

Criteria No. 4 :- Period of onset of less than equal to 48 hours.

Criteria No. 5 :- Axillary Temperature of 99 F or more or rectal temperature of 100 F or more on admission or within 24 hours of admission.

Grade V : - All five criteria present.

Grade IV : - Any four criteria present.

Grade III : - Any three criteria present.

Grade II : - Any two criteria present.

Grade I : - Any one criteria present.

The importance of various factors like age, sex, and incubation period, period of onset, fever and grading of tetanus in prognosis of patients with tetanus was analyzed.

RESULTS

Table 1
Mortality of patients of tetanus

Total Cases	Died	Recovered
34	14 (41.17%)	20 (58.82%)

In the present study 34 cases were analyzed of which 14 died and 20 recovered with a mortality of 41.17%.

Table 2
Incidence of cases in males and females.

Total No.	Males	Females
34	25 (73.52%)	9 (26.47%)

Out of the 34 patients analyzed in the study 25 were males and 9 were females. The incidence was higher in males compared to females.

Table 3
Incidence and mortality in relation to age.

Age	Total	Died	Recovered
10-20 years	4 (11.76%)	0 (0%)	4 (100%)
21-30 years	2 (5.88%)	0 (0%)	2 (100%)
31-40 years	9 (26.47%)	4 (44.44%)	5 (55.55%)
41-50 years	6 (17.64%)	3 (50%)	3 (50%)
> 50 years	13 (38.23%)	7 (53.84%)	6 (46.15%)

The above table analyses incidence of tetanus in various age groups and the prognostic importance of age. Out of the 34 cases under study, 4 patients were in the age group between 10-20 years of which all 4 recovered mortality being 0%; 2 patients were between 21-30 years with a mortality of 0%; 9 patients were between 31-40 years with a mortality of 44.44%; 6 patients were between 41-50 years with a mortality of 50% and the remaining 13 patients were above 50 years of age and had a mortality of 53.84% which is the highest compared to other age groups.

Table 4
Nature of injury.

Nature of injury	Total	Died	Recovered
Abrasions	10	3(30%)	7 (70%)
Puncture	14	7 (50%)	7 (50%)
Burns	1	1 (100%)	0 (0%)
Unknown	5	2 (40%)	3 (60%)
Others	4	1 25%)	3 (75%)

In the present study of 34 patients history of injury could be obtained in 29 patients only. Of the 10 patients who had abrasions 3 died with a mortality of 30%. One patient who had burns on the anterior abdominal wall succumbed to the injury. In the group of 14 patients who had puncture wounds 7 died, mortality being 50% while in those patients with otorrhoea, incised wounds and lacerated wounds the mortality was 25%, least of the lot.

Table 5
Incubation period

Incubation period	Total	Died	Recovered
0-7 days	11	6 (54.54%)	5 (45.45%)
8-14 days	9	3 (33.33%)	6 (66.66%)
15-21 days	2	1 (50%)	1 (50%)
> 21 days	7	2 (28.57%)	5 (71.42%)
Unknown	5	2 (40%)	3 (60%)

Table 5 analyses the prognostic importance of incubation period. In the present study 11 patients had an incubation period of less than or equal to 7 days of which 6 died, mortality=54.54%. As the incubation period increased the mortality dropped and in the 7 patients who had an incubation period of greater than 21 days the mortality was only 28.57%.

Table 6
Period of onset.

Period of onset	Total	Died	Recovered
< 24 hours	4	3 (75%)	1 (25%)
25-48 hours	3	2 (66.66%)	1 (33.33%)
49-72 hours	3	2 (66.66%)	1 (33.33%)
73-96 hours	4	1 (25%)	3 (75%)
> 4 days	3	0 (0%)	3 (100%)

In the present series period of onset could be measured in only 17 patients of which 4 patients had a period of onset of less than 24 hours, 3 patients between 25-48 hours, 3 between 49-54 hours and 3 greater than 4 days. Analysis of the above table shows that the mortality was highest in patients who had a period onset of less than 24 hours and prognosis improved with increase in period of onset.

Table 7
Importance of fever in prognosis

	Total	Died	Recovered
FEVER AT ADMISSION OR WITHIN 24 HRS	6	6 (100%)	0 (0%)
FEVER AFTER 24 HRS TILL DATE OF DISCHARGE/EXPIRY	7	3 (42.85%)	4 (57.14%)
AFEBRILE DURING HOSPITAL STAY	21	5 (23.80%)	16 (76.19%)

Table 7 analyses the prognostic importance of fever in tetanus. In the present study 6 patients had fever at admission and all of them died mortality being 100%. Out of the 7 patients who were febrile 3 died mortality being 42.85%. On the other hand mortality in patients who were afebrile throughout their hospital stay was only 23.80%.

Table 8
Presenting complaint

Total No.	TRI SMUS	NO TRISMUS
34	28 (82.35%)	6 (17.64%)

The above table shows that out of 34 patients under study only 28 cases i.e. 82.35% presented with trismus and in the remaining 6 i.e. 17.64% the presenting complaints were other than trismus.

Table 9
Importance of grading in prognosis

	TOTAL	Died	Recovered
Grade I	9	2 (22.22%)	7 (77.77%)
Grade II	9	2 (22.22%)	7 (77.77%)
Grade III	8	5 (62.50%)	3 (37.50%)
Grade IV	1	1 (100%)	0 (0%)
Grade V	2	2 (100%)	0 (0%)

In the present series of 34 patients only 29 patients could be graded. It will be evident from the above table that those belonging to Grade IV and Grade V were the most severe of the lot and carried a high mortality of 100%. Cases in Grade I and Grade II were of mild severity with a mortality of 22.22% each while Grade III was moderately severe with mortality of 62.50%.

Table 10
Incidence in urban and rural population

Total	Urban	Rural
34	12 (35.29%)	22 (64.70%)

In the present series of 34 patients 12 patients were from urban areas and the majority i.e. 22 patients were from rural areas.

Table 11
Intrathecal TIG

PATIENTS GIVEN INTRATHECAL TIG			PATIENTS NOT GIVEN INTRATHECAL TIG	
	Total	MORTALITY	Total	Mortality
Grade I	3	0%	6	33.33%
Grade II	1	0%	8	25%
Grade III	3	0%	5	100%
Grade IV	1	100%	0	-
Grade V	1	100%	1	100%

In the present series 250 IU of tetanus immunoglobulin was given to alternate patients out of the last 20 irrespective of the severity of tetanus. In Grade I group out of 9 patients all 3 patients who were given TIG recovered while in the 6 patients who were not given TIG only 4 recovered mortality being 33.33%. In Grade II group mortality in patients who received TIG

was 0% whereas in those who were not given TIG it was 25%. In Grade III group mortality in the two sub groups were 0% and 100% respectively. Only one patient in the series belonged to Grade IV and despite giving intrathecal TIG patient expired. In Grade V group mortality was 100% in both the groups

patient. However they consisted of only one patient each.

DISCUSSION

Out of the 34 patients under study 14 patients died whereas 20 patients recovered with a mortality of 41.17%. This is in keeping with the standard mortality rates in our country. In the present series as shown in table 2 of the total number of patients studied 25 were males whereas 9 were females. The lower incidence in females compared to the males is probably explained by the fact that as children and by occupation females are less likely to get severe or infected wounds and when they do they keep them clean. In a study conducted by cole, of the 43 cases under study 38 were males and only 5 females. Table 3 shows the prognostic importance of age in tetanus. From the table it can be seen that the best prognosis was noted in patient's up to the age of 30 who had a mortality of 0%. This can be explained by assuming that the patients below 30 years of age have a higher resistance. As age increases immunity decreases, the body is unable to mount an intense immune response against the offending agent and hence mortality is higher¹¹. In tetanus good physique is likely to count a great deal. Cardiovascular degeneration certainly militates strongly against recovery. Chronic bronchitis and emphysema are also dangerous, because these, when combined with tonic rigidity of the muscles of the chest, make breathing difficult and predispose to pneumonia. These factors also probably explain the high death rate over the age of 50 years, for most of the patients in this age group are bad subjects in these respects. In all patients recurrent diseases particularly of the lungs or the heart are of serious significance and the risk of pneumonia must always be borne in mind, particularly in patients requiring curarisation and ventilation. The high incidence in the younger age group can be attributed to the fact that these people lead a comparatively active life and there consequently is an increased risk of infection through injuries etc. than in the other age group¹ From the analysis of Table 11 it can be seen that in Grade I, II and III mortality was less (0%) in the sub group that received

intrathecal TIG when compared to those who didn't. On the other hand in Grade V patient's mortality was the same irrespective of whether intrathecal TIG was given or not. In Grade IV because there was only one patient comparison cannot be made. From the above analysis it appears that in tetanus of mild and moderate severity injection of intrathecal TIG favorably influences the course of the disease. Grade IV and V do not seem to benefit much. However despite these results no definite conclusions can be drawn. A larger study with age matched control will have to be conducted to authentically state that TIG intrathecally is beneficial¹³.

CONCLUSION

1. Tetanus is more common in the rural areas.
2. Incidence of tetanus is more in the males as compared to the females.
3. Though tetanus is more common in younger patients mortality increases with increasing age.
4. Incubation period is one of the factors affecting prognosis. Shorter the incubation period worse the prognosis.
5. Period of onset is a reliable indicator of severity of tetanus and prognosis. Prognosis improves with increasing period of onset.
6. Patients who are febrile fare worse as compared to those who are afebrile during period of hospitalization; and in patients who develop fever at admission or within 24 hours the mortality is very high.
7. Grading of tetanus is very helpful in predicting the prognosis of tetanus. In Grade I and II the disease is mild and prognosis good as compared to Grade IV and V where the disease is severe and mortality high.
8. Injection of intrathecal TIG probably influences the course of disease favorably.
9. In conclusion it can be said that though the mortality, due to tetanus is on the decline, it is still considerable, (41.17%) in present series and in the absence of a specific cure prevention is of utmost

importance. Educating the people and immunization will help a long way in

control of the disease.

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