

## Evidence of Frequency of Autonomic Dysfunction in Patients presenting with Tetanus in Urban and Rural population. Experience at Tertiary Care Hospital of Sind

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### Abstract

**Objective:** To determine the frequency of autonomic dysfunction in patients presenting with tetanus. **Design:** Descriptive cross sectional study **Patients and Methods:** This study was conducted in department of Neurology, Jinnah Postgraduate Medical Centre, Karachi. Total 105 patients of both genders, age 20-60 years, having diagnosed of tetanus since at least 5 days were consecutively selected. Comatose patient or with history of drug reaction, sepsis, encephalitis/ meningitis, epilepsy or electrolytes imbalance were excluded. Mean  $\pm$  SD, frequencies & percentages were calculated. Chi-square was applied with a P value  $\leq$ 0.05 taken as significant. **Results:** Frequency of autonomic dysfunction among patients of tetanus was 37.14% (n = 39). The stratification analysis showed that frequency of autonomic dysfunction was significantly (P value= 0.027) more in younger, rural living (P value 0.030) & those with a longer history of tetanus (P value = 0.001). **Conclusion:** One out of every three tetanus patients was affected. Younger age, rural patients & late presenters had higher incidence of autonomic dysfunction. **Keywords:** Tetanus, Autonomic dysfunction, Frequency.

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### INTRODUCTION:

Tetanus is brought about by disease of Clostridium tetani, a gram-positive, spore-shaping commit anaerobic coccus. Its spores are found in soil, dust, and the nutritious tracts of different creatures. Spores enter the human body through tainted/sullied wounds.<sup>1</sup> Clostridium tetani produces tetanus toxin (a neurotoxin) which is the second most noxious substance known, being outperformed in strength just by botulinum poison; the human deadly portion of tetanus toxin is assessed to be

10-6 mg/kg and is the reason for all indications of tetanus. Tetanus is described by muscle unbending nature and difficult muscle spasm. Lockjaw is otherwise called tetanus, which is an intense, spastic loss of motion of the masseter muscles.<sup>2, 3</sup>

The malady can influence any age gathering and have higher case-casualty rates (up to 80%) even where present-day concentrated consideration is available.<sup>4,</sup>

<sup>5</sup> The evaluated mortality because of tetanus overall is 1,000,000 passing for

each time of which about 80% passing happen in only 12 tropical Asian and African countries.<sup>6</sup> A. Tetanus might be either summed up, which is increasingly normal or restricted. The hatching time frame ordinarily is 2-14 days; however it might be the length of months after the injury. In generalized tetanus, trismus (masseter muscle spasm or lock-jaw) is the introducing manifestation in about a portion of cases. Migraine, anxiety, and fractiousness are early side effects, frequently followed by solidness, trouble biting, dysphagia, and neck muscle spasm<sup>7</sup>. The cynical grin of tetanus (risus sardonius) results from unmanageable spasm of facial and buccal muscles. At the point when the loss of motion stretches out to stomach, lumbar, hip, and thigh muscles, the patient may expect a curved stance of outrageous hyperextension of the body, opisthotonos, with the head and the heels bowed in reverse and the body bowed forward with just the rear of the head and the heels contacting the supporting surface. The laryngeal and respiratory muscle spasm can prompt aviation route check and suffocation. Since tetanus toxin doesn't influence tangible nerves or cortical capacity, the patient sadly remains conscious.<sup>8</sup>

For the most part in the second week stretch of lockjaw the poison arrives at the brainstem (due to the more slow intra axonal vehicle to the parallel horn cells) and prompts autonomic brokenness and paroxysmal increments in thoughtful action, with basal catecholamine levels rising ten-fold.<sup>9</sup> This outcomes in serious hyper-strain and tachycardia may exchange with significant hypotension, bradycardia, or intermittent heart failure and pyrexia, with a hyperkinetic flow, low/ordinary fundamental vascular obstruction, and typical right and left sided cardiovascular filling pressures.<sup>10</sup> Different highlights incorporate over the top salivation and perspiring (may lead to dehydration), gastric stasis, ileus, loose bowels, and high output renal failure may likewise be identified with the autonomic disturbance.<sup>11</sup> A remote report recommended that about in any event 33% (32%) of lockjaw patients might be

influenced with autonomic neuropathy.<sup>12</sup> Autonomic instability is the primary driver of death in patients who are not given ventilatory support.<sup>13</sup> Contrasted with 15% passing happening lockjaw patients without autonomic dysfunction; the demise rate was 48% in lockjaw patients with autonomic dysfunction (p value= 0.002). Magnesium sulfate or morphine is utilized to treat the autonomic dysfunction in lockjaw patients.<sup>14</sup>

All vital functions of the human body like cardiovascular framework, temperature regulation, respiration and so forth are directed via the autonomic nervous system. It tends to be influenced in tetanus due to tetanus toxin may arrive at the brainstem. Because of unhygienic practices tetanus is very basic in our nation. In spite of that the occurrence of ANS association in tetanus patients in local settings was not found with the exception of just one study discovered which was led very nearly 10 years back. The present study with this solid method of reasoning has estimated the extent of the burden of autonomic dysfunction in tetanus patients. The after effects of this study prescribe for preemptive administration of autonomic dysfunctions in tetanus to diminish mortality and morbidity.

#### **MATERIAL & METHOD:**

This cross-sectional study was led from March 2015 to September 2015 at the department of Neurology, Jinnah Postgraduate medical Center, Karachi. Full history, clinical assessment, and research facility examinations (Complete Blood Count, Erythrocyte Sedimentation Rate, Urea Creatinine, and Electrolytes levels, Liver Capacity Tests, Blood Glucose Levels) were done. All out 105 patients of the two sexes, age 20-60 years, have analyzed tetanus since in any event 5 days from the emergency of the neurology were sequentially chosen. Torpid patient (Glasgow Trance state Scale < 7) or with a history of medication response, sepsis, encephalitis/meningitis, epilepsy, electrolytes imbalance (hyponatremia, hypercalcemia, hypoglycemia), patients taking corticosteroids, and patients with a history of injury because of a fall (analyzed through previous history and as of now accessible CT scan) were excluded

from the study. Informed consent was taken from the patients, and looked into an ethical board the institution. sample size was determined by taking evaluated predominance of autonomic dysfunction in tetanus patients at the rate of 32%, 12 bound of error 9%, and level of significance 95% and utilizing WHO's sample size calculator; the determined example size was 104 ~ 105.

Nonprobability sequential testing method was applied to collect the samples. The information was collected on an endorsed poll with respect to segment factors like name, age, gender, habitation, and span of illness. Blood pressure and pulse were estimated consistently and two perusing at 4 hours interim was recorded soon as the patient is shifted in the ward (patient in resting state-not in tetanic spasm). Primary outcome variables were presence of autonomic dysfunction (Yes/No) in tetanus patients. Patients were given the convention treatment for tetanus according to guidelines. The data entry and analysis were done through SPSS-19. Mean  $\pm$  SD were communicated for nonstop factors like age, term of illness, pulse, and blood pressure. frequency and rates were communicating for gender, habitation (rural, or urban) and presence of autonomic dysfunction (Yes/No-the result variable). The impact alteration of the result variable (recurrence of autonomic dysfunction) due to age, gender and length of the malady were dissected by delineation of these factors followed by utilization of the chi-Square test with a P value  $<0.05$  taken as significant. Selection criteria were strictly followed to control for the potential confounders.

## RESULTS:

During study period, consecutive 105 patients presented with tetanus were included in this study to assess the autonomic dysfunction among them. The results on these patients are as under.

Mean age  $\pm$  SD was  $32.70 \pm 9.22$  years. Ages of these patients ranged from 20-59 years. Duration of disease ranged from 05

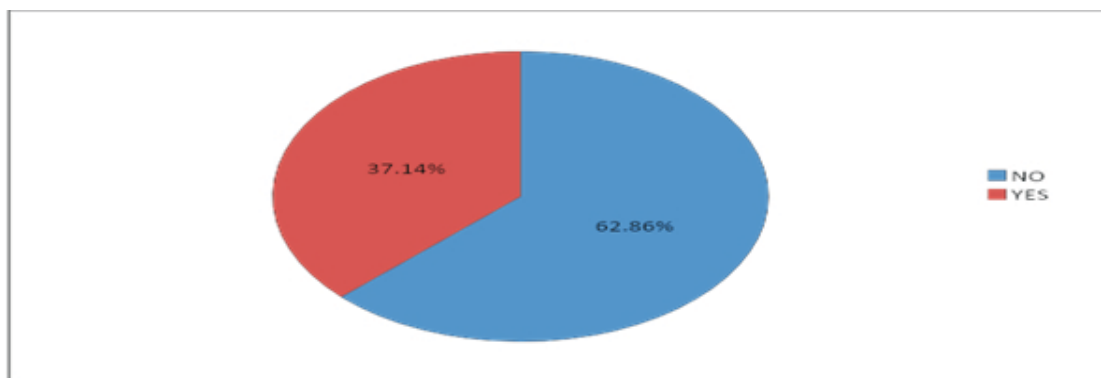
to 12 days with mean  $\pm$  SD duration of  $7.39 \pm 1.83$  days. Mean  $\pm$  SD pulse rate was  $98.97 \pm 24.31$  beats per minute and ranged between 40 minimum & 140 maximum beats per minute. Mean  $\pm$  SD systolic/ diastolic blood pressure recorded was  $147/98 \pm 28/10$  mmHg with a range of 100/70 to 210/115 mmHg.

It was observed that majority of patients (81.90%, n=86) were of 20-40 years of age while other 18.10%, n=19) were of age group of 41-60 years. Slightly less than two thirds (60.95%; n= 62) were males patients. Table 1 shows that only one third patients belonged to urban areas (35.2%; n= 37). Fifty nine percent (n= 62) patients had history of tetanus infection since 5-7 days; other 35.24% (n= 37) had history of 8-10 days while those having a longer history i-e; of 11 or more days were only 5.71% [n= 6].

Principle outcome of this study was frequency of autonomic dysfunction among patients of tetanus which was detected among 37.14% (n = 39) patients (Figure 1). In this study the stratification analysis showed that frequency of autonomic dysfunction was significantly (P value = 0.027) more in patients of younger age i-e; [20-40 years]. It was also noted that frequency of autonomic dysfunction was almost similar among the two genders; however the finding was not significant (P value = 0.546). Longer the duration of disease, higher was the frequency of autonomic dysfunction among tetanus patients [25.8% with 5-7 days; increasing to 45.9% with 8-10 days & further upto 100% with duration of  $> 11$  days]. The finding was statistically very significant (P value = 0.001, Table 2). Effect of residence on frequency of autonomic dysfunctions among tetanus patients was also high [i-e; 41.2% among rural compared to 29.7% among urban patients]. However; the finding was not significant (P value 0.030, Table 3).

**Table 1:** Residence of patients (n= 105)

Residence	Frequency	Percentage
Urban	37	35.2
Rural	68	64.8
Total	105	100



**Figure 1:** Frequency of autonomic dysfunctions among patients presenting with Tetanus. (n=105)

**Table 2:** Effect of duration of disease on frequency of autonomic dysfunctions among patients presenting with Tetanus

Duration of disease	Autonomic Dysfunctions		Total	Chi-Square Test & P value
	Yes	No		
5-7 Days	16	46	62	Chi-Square= 14.795
	25.8%	74.2%	100%	
8-10 Days	17	20	37	df= 2
	45.9%	54.1%	100%	
> 11 Days	6	0	6	P value= 0.001
	100%	0%	100%	
Total	39	66	105	
	37.1%	62.9%	100%	

**Table 3:** Effect of residence on frequency of autonomic dysfunctions among patients presenting with Tetanus.

Residence	Autonomic Dysfunctions		Total	Chi-Square Test & P value
	Yes	No		
Urban	11	26	37	Chi-Square= 1.345
	29.7%	70.3%	100%	
Rural	28	40	68	df= 1
	41.2%	58.8%	100%	
Total	39	66	105	P value = 0.172
	37.1%	62.9%	100%	

**DISCUSSION:**

One of exceptionally ancient depicted irresistible condition of tetanus is an intense, frequently deadly illness caused by the exotoxins produced by *Clostridium tetani*. Satisfactory immunization programs can effectively anticipate the disease. The tetanus immunization is part of immunization program (EPI) in Pakistan since eighties. The illness in any case remains common around the world & Pakistan isn't distinctive from other developing countries.<sup>4-7</sup> In spite of the fact that overwhelmingly an infection of developing nations, the management of tetanus remains a challenge to critical care specialists in developed countries. Its presentation could be a clinical triad of inflexibility, muscle spasms, and in the event that extreme, autonomic dysfunction, which shows as tachycardia and hypertension; bradycardia, hypotension, and cardiac arrest may happen<sup>4, 6, 10, 15, 16</sup>

As advanced intensive care prevents death from acute respiratory failure, autonomic dysfunction has ended up the foremost life- debilitating complication of exceptionally severe tetanus, which remains a challenge for most physicians.<sup>17, 15, 18, 19</sup>

The current study was conducted to evaluate the burden of autonomic dysfunction among the patients which show to the neurology ward with history and presentation of acute tetanus infection. The current study found that 39 out of 105 (37.14%) patients had clinical findings of autonomic dysfunction. This appears to be a high rate of complication of tetanus in case we compare with the developed nations. However; the data from developing countries appears that the rate of autonomic dysfunction among tetanus patients is similar as found within the current study. Autonomic dysfunction rates are between 10-20% among developed whereas it ranges from 30-45% among developing nations.<sup>6, 9, 11, 15, 20</sup>

In our patients the foremost common clinical findings among tetanus patients having autonomic dysfunctions were tachycardia and hypertension; bradycardia, hypotension & respiratory instability which required ventilation support. Other modern studies too reported the mimicking clinical pictures. Autonomic dysfunction presenting as severe hypertension and tachycardia with relative hypotension and bradycardia, is

classified as enduring from exceptionally severe tetanus.<sup>7-11, 14, 19, 21</sup> In current arrangement of patients there was much variety in blood weight & beat readings taken at diverse times. Recorded systolic BP was as low as 100 mmHg & as high as 210 mmHg with a mean value of 147 mmHg. Variety in diastolic pressure appeared that was as low as 70 mmHg & as high as 128 mmHg with a mean value of 98 mmHg. Variety in pulse was too found to be exceptional and ranged between 70 to 134 bpm & a cruel of 100 bpm. Patients taken in this study were of age 20-60 years; whereas 20- 40 years age group patients being more in number. The stratified analysis altogether (P value = 0.027) revealed that this group was too influenced more with autonomic dysfunctions compared to elder patients of 41-60 years.

Studies have found that elder age patients are more influenced with tetanus whereas other studies found higher recurrence of tetanus in younger patients.<sup>7,9,10,14,19,24</sup>

It is conceivable that this distinction of age between different studies is due to the contrast of region (developed/ developing) as well as the distinction of utilized selection criteria of the study. But it is curiously to note that most of all studies found that autonomic dysfunction is more common in younger patients which mimics the findings of this study.<sup>7, 10, 19, 20</sup>

Tetanus in children is greatly uncommon, which may be the reason why physicians may ignore their potential chance in children with injury.<sup>7, 11-15, 22, 23, 24</sup>

In any case; taking information from children was past the scope of this study. This study suggests that this contrast of age ought to be encouraging evaluated in future studies with a bigger sample and wider age criteria.

On the other hand the study noted that male gender was more influenced with tetanus however autonomic dysfunction almost similarly influenced both genders with as it were miniature distinction of recurrence; in any case the finding was not significant (P value = 0.546). Other studies have reported comparable drift of autonomic dysfunction among both genders.<sup>7, 8, 11, 14, 19,</sup>

The current study too assessed the difference of residence which was not archived by past studies as well as the impact of length of tetanus infection on the recurrence of autonomic dysfunction. Appropriately; it came to our knowledge that rural zone patients develop more

autonomic dysfunction as compared to urban region. This may be due to the reason that patients from rural regions have low hygiene practices, negligible preventive and primary care facilities, no information of tetanus infection additionally they show exceptionally late to the tertiary care setup. This point can moreover be affirmed from the reality in current consider the late presenters had higher recurrence of autonomic dysfunction than those who comes to clinic with a shorter history. Afterward presenters and rural region patients had extreme infection also. There is no standard treatment for severe tetanus with autonomic dysfunction, and most publications are as case reports or little arrangement. Analgesics, narcotics, hostile to convulsants and muscle relaxants are at first utilized, but autonomic dysfunction is refractory to medications. 7, 11-15, 22, 23, 24

The current study was brief study with smaller sample size; the reason being the constrained time and financial resources. Be that as it may; it can be fairly expressed that the study has highlighted a very vital issue of tetanus patients who are either misdiagnosed or analyzed of late when they have developed genuine tetanus. The physicians at tertiary hospitals will be sensitized with significance examination & early support of the autonomic functions

#### CONCLUSION:

Tetanus is related with much morbidity and additionally with possible lethal infectious illness. Developing nations have a burden of infectious illnesses and tetanus is one of these. Progressing clinical research like this study conducted in JPMC is obligatory to get it the flow of the illness and complications. In current study the size of recurrence of autonomic dysfunction among tetanus patients was measured. One out of each three tetanus patients was influenced. Younger age, rural patients & late presenters had higher frequency of autonomic dysfunction.

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