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Head and Neck Symptoms as Predictors of Outcome in Tetanus Patients

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ABSTRACT

Objective: This study aims to investigate which, if any head and neck symptoms (trismus, dysphagia, alterations in speech or facial movements, and dyspnea) might be good predictors of outcomes (mortality, tracheostomy, discharged, decannulated) and prognosis of tetanus patients.

Methods:

Design: Retrospective Cohort Study

Setting: Tertiary National University Hospital

Patients: Seventy-three (73) pediatric and adult patients diagnosed with tetanus and admitted at the emergency room of the Philippine General Hospital between January 1, 2013 and December 31, 2017. Demographic characteristics, incubation periods, periods of onset, routes of entry, head and neck symptoms, stage, and outcomes were retrieved from medical records and analyzed.

Results: Of the 73 patients included, 53 (73%) were adults, while the remaining 20 (27%) were pediatric. The three most common head and neck symptoms were trismus (48; 66%), neck pain/ rigidity (35; 48%), and dysphagia to solids (31; 42%). Results of multivariate logistic regression analysis showed that only trismus (OR = 3.742, p = .015) and neck pain/ rigidity (OR = 4.135, p = .015) were significant predictors of decannulation. No dependent variable/symptoms had a significant effect in predicting discharge and mortality.

Conclusion: Clinically diagnosed tetanus can be easily recognized and immediately treated. Most of the early complaints are head and neck symptoms that can help in early diagnosis and treatment resulting in better prognosis. In particular, trismus and neck pain/rigidity may predict the outcome of decannulation after early tracheotomy, but not of discharge and mortality.

Keywords: *tetanus; head and neck symptoms; outcome; predictors of outcome; trismus; neck pain/ rigidity; tracheotomy*

Tetanus remains a persistent global health problem despite its inclusion in the Expanded Program on Immunization (EPI) by the World Health Organization. Its high morbidity and mortality especially in developing countries is unjustified by its preventable nature and course. One million cases are reported annually with a case fatality ratio ranging from 6% to

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72% depending on the availability of a well-equipped intensive care unit.[1] The diagnosis of tetanus is clinical, and the primary complaints and history are important in determining the course of the disease.[2] Most of these early complaints and presenting symptoms (trismus, dysphagia, alterations in speech or facial movements, and dyspnea) concern the head and neck region, making otolaryngologic evaluation indispensable.[3] However, there is lack of local protocols that focuses on the prognosis and outcome of tetanus in association with head and neck symptoms.

The Cole staging system is currently used in determining prognosis.[4] Existing severity scores such as Philips, Dakar and Tetanus severity score (TSS) are utilized as predictors of outcome.[5] Only the Dakar score includes spasm as one of its variables; none have taken into account head and neck symptoms as prognostic parameters despite their being the most common early presentation. Although preventable through immunization, this disease remains an important threat worldwide. If not recognized early, it may progress to disability and worse, death.

This study aims to investigate which, if any head and neck symptoms (trismus, dysphagia, alterations in speech or facial movements, and dyspnea) might be good predictors of outcomes (mortality, tracheostomy, discharged, decannulated) and prognosis of tetanus patients.

METHODS

This retrospective cohort study included all pediatric and adult patients diagnosed with tetanus and admitted at the emergency room of the Philippine General Hospital between January 1, 2013 and December 31, 2017. The patient lists were retrieved from the yearly census of the departments of neurosciences, pediatrics and otorhinolaryngology. This study was approved by the University of the Philippines Manila Research Ethics Board (UPMREB 2018-391-01). Informed consent was waived by the board.

All in-patient and out-patient records of identified patients were considered for inclusion and retrieved from the hospital records section. Patients that were diagnosed with tetanus at the out-patient department but not subsequently admitted and those with incomplete records were excluded.

Data was collected as specified in the Case Report Form. Only head and neck symptoms (trismus, dysphagia, alterations in speech or facial movements, and dyspnea) were considered, and all other symptoms like abdominal rigidity, fever, generalized rigidity or stiffening were not included. Outcomes of the disease listed included: mortality, tracheostomy, discharged, decannulated.

Deidentified data was tabulated, encoded, and summarized into frequencies/rates (mortality, case fatality rate) and percentages using the MS Excel for Mac v.15.13.3 (Microsoft Corp. 2015, Redmond, WA, USA). Multivariate logistic regression analysis was performed using Stata 14 (Stata Corp. 2015, College Station, TX, USA) to determine the predictors of the three dependent variables. A stepwise selection approach was applied in model building. The independent variables were the presence or absence of trismus, dysphagia to solids, dysphagia to liquids, dysarthria, Chvostek sign, dyspnea, and neck pain/rigidity, while the dependent variables were discharge, mortality, and decannulation. A p-value of less than or equal to .05 was considered statistically significant.

RESULTS

A total of 78 patients from all age groups and genders who were clinically diagnosed with tetanus between January 1, 2013 and December 31, 2017 were included in the initial list. Five were subsequently excluded; two males with incomplete records and three (1 female, 2 males) who were only seen in the out-patient department but not admitted to the emergency room. A total of 73 patients were finally included in this study. Their ages ranged from 3 to 79 years old, with 53 (73%) adults and 20 (27%) pediatric. There were 50 (68%) males and 23 (32%) females.

The three most common head and neck symptoms were trismus (48; 66%), neck pain/rigidity (35; 48%) and dysphagia to solids (31; 42%). The incubation period ranged from 1 to 30 days, while the period of onset was one to nine days. The specific route or source of disease in the majority were wounds or burns (47; 64%), followed by dental caries (15; 21%) and animal bites (11; 15%). Of the 73 patients, only 19 (26%) had a history of immunization for tetanus, although there was no mention if a complete dose or booster was administered. Sixty seven patients (92%) already presented with moderate to severe disease: 23 (32%) were Stage II and 44 (60%) were already Stage III. Only six patients (8%) were diagnosed as Stage I. All patients, despite the severity of the disease, underwent tracheostomy. Of these, 35 (48%) were decannulated, 59 (81%) were discharged from the hospital, while 14 (19%) expired in hospital.

Thirty four out of fifty males (68%) presented with wound/burns possibly sustained during work (occupational accidents). Majority of patients had incubation periods of less than 7 days (45/73; 62%) and 58% of those patients had severe disease (Stage III). Sixty two percent (31/50) of those with period of onset of less than 3 days had Stage III disease. Sixty one percent (33/54) of those who did not receive any vaccination for tetanus were staged III tetanus patients. More severe cases of tetanus or those stage III patients (22/37 patients; 59%) stayed longer than 26 days in the hospital. Twenty-seven percent (12/45) of those patients with incubation periods of less than 7 days expired

and 18% (9/50) of those patients with periods of onset of less than 3 days expired. Causes of death were sepsis and cardiopulmonary complications. The case fatality rate increased with age from 18% for those < 40 years old, to 20% for those 40 to 59 years old, and 22% for those > 60 years old.

Predictors versus outcomes for multivariate logistic regression analysis are presented in *Table 1*. Chvostek sign was omitted in all analysis due to collinearity. The remaining independent variables were not found to be significant predictors of discharge and mortality (*Table 2* and *3*, respectively). On the other hand, results of the analysis showed that only trismus (OR = 3.742, p = .015) and neck pain/ rigidity (OR = 4.135, p = .015) were significant predictors of decannulation *(Table 4)*. The final model used was:

Decannulation = 0.151 + 2.93 (Trismus) + 3.43 (Neck pain/rigidity)

Table 1. Predictors vs Outcome for Multivariate Logistic Regression Analysis

	TRACHEOSTOMY N (%)		DISCHARGED N (%)		MORTALITY N (%)		DECANNULATED N (%)	
	Y	N	Y	N	Y	N	Y	N
Trismus								
With opening	9 (100)	0	5 (56)	4 (44)	4 (44)	5 (56)	0	9 (100)
Slight opening	48 (100)	0	40 (83)	8 (14)	8 (14)	40 (83)	27 (56)	21 (44)
No opening	16 (100)	0	14 (88)	2 (12)	2 (12)	14 (88)	8 (50)	8 (50)
Dysphagia to solid								
Yes	31 (100)	0	27 (87)	4 (13)	4 (13)	27 (87)	14 (45)	17 (55)
No	42 (100)	0	32 (76)	10 (24)	10 (24)	32 (76)	21 (50)	21 (50)
Dysphagia to liquid								
Yes	29 (100)	0	25 (86)	4 (14)	4 (14)	25 (86)	15 (52)	14 (48)
No	44 (100)	0	34 (77)	10 (23)	10 (23)	34 (77)	20 (45)	24 (55)
Dysarthria								
Yes	18 (100)	0	17 (94)	1 (6)	1 (6)	17 (94)	8 (44)	10 (56)
No	55 (100)	0	42 (76)	13 (24)	13 (24)	42 (76)	27 (49)	28 (51)
Chvostek								
Yes	0	0	0	0	0	0	0	0
No	0	0	0	0	0	0	0	0
Dyspnea								
Yes	20 (100)	0	15 (75)	5 (25)	5 (25)	15 (75)	8 (40)	12 (60)
No	53 (100)	0	44 (83)	9 (17)	9 (17)	44 (83)	27 (51)	26 (49)
Neck pain/ rigidity								
Yes	35 (100)	0	27 (77)	8 (23)	8 (23)	27 (77)	21 (60)	Í14 (40)
No	38 (100)	0	32 (84)	6 (16)	6 (16)	32 (84)	14 (37)	24 (63)

Table 2. Multivariate logistic regression analysis for outcome DISCHARGE

	ODDS RATIO	95% CONFIDENCE INTERVAL	Coefficient Estimate	STD Error	p Value
Trismus	1.957483	.6242783 - 6.137872	.6716595	.5830814	.249
Dysphagia to solid	1.057708	.0711268 - 15.72889	.0561042	1.377268	.968
Dysphagia to liquid	1.322432	.0936691 - 18.67025	.2794724	1.350769	.836
Dysarthria	4.041451	.4082257 - 40.01053	1.396604	1.169684	.232
Dyspnea	0.71226	.1877907 - 2.701488	-.3393123	.6801732	.618
Neck pain/rigidity	0.6248123	.1797529 - 2.171817	-.470304	.6356587	.459

Table 3. Multivariate logistic regression analysis for outcome MORTALITY

	ODDS RATIO	95% CONFIDENCE INTERVAL	Coefficient Estimate	STD Error	p Value
Trismus	.5108601	.1629229 - 1.60185	-.6716595	.5830814	.249
Dysphagia to solid	.9454406	.0635773 - 14.05939	-.0561042	1.377268	.968
Dysphagia to liquid	.7561826	.0535611 - 10.67588	-.2794724	1.350769	.836
Dysarthria	.2474359	.0249934 - 2.449625	-1.396604	1.169684	.232
Dyspnea	1.403982	.3701664 - 5.325077	.3393123	.6801732	.618
Neck pain/rigidity	1.600481	.4604439 - 5.563193	.470304	.6356587	.459

Table 4. Multivariate logistic regression analysis for outcome DECANNULATION

	ODDS RATIO	95% CONFIDENCE INTERVAL	Coefficient Estimate	STD Error	p Value
Trismus	3.74158	1.291081 - 10.84318	1.319508	.5428817	.015
Dysphagia to solid	.2944081	.0272301 - 3.183099	-1.222789	1.214637	.314
Dysphagia to liquid	3.833531	.3719673 - 39.50874	1.343786	1.190193	.259
Dysarthria	.5039372	.133073 - 1.908372	-.6853035	.6793768	.313
Dyspnea	.569629	.1620717 - 2.00206	-.56277	.6413111	.380
Neck pain/rigidity	4.135222	1.320891 - 12.94585	1.419541	.5822732	.015

DISCUSSION

Our present study found that trismus, neck pain/rigidity, and dysphagia to solids were the most common head and neck symptoms. Trismus is a common initial symptom in tetanus that may be unilateral early in the course of disease, but usually progresses to bilateral involvement.[5] Similar to our findings, other head and neck symptoms that present as the chief complaint aside from trismus are stiffness of the neck and dysphagia.[3,6] Our findings suggest that tetanus patients with trismus or neck pain/rigidity are more likely to be decannulated. Thus, patients presenting with either of these head and neck symptoms that undergo immediate tracheostomy and management may have a higher chance of resolution of symptoms and decannulation. Although

the decannulation time was not recorded in the study, future research may include this variable for further comparison and analysis.

As Mukherjee highlighted, the efficacy of tracheostomy in the treatment of tetanus cannot be overemphasized.[7] He also stated that the sooner tracheostomy is done, the better for the patient.[7] Fasunla recommended that patients diagnosed as Stage II must undergo tracheostomy sooner for better chances of survival, and that tetanus patients in general must not be allowed to reach Stage III before the procedure is commenced, since prognosis becomes poor.[8] The reason for this is if tracheostomy was not initiated earlier, these patients would have died of asphyxia or cardiorespiratory failure.[8] This correlates well with our findings that most of our patients (92%) already had Stage II and III or moderate to severe disease, which is mostly determined by the severity of the trismus. The decision for tracheostomy is made right away when trismus is observed. If trismus becomes more severe, the feasibility of orotracheal intubation for temporary airway protection becomes more difficult, hence tracheostomy is administered as a definitive airway protection measure. The key component is early detection of symptoms, specifically trismus and neck pain/rigidity, for immediate initiation of intervention to attain a favorable prognosis and outcome. Referring to Cole Staging, it is noted that even during Stage I, there is already trismus of mild severity, which raises the suspicion of tetanus. Thus, the importance of trismus as a symptom cannot be overemphasized in tetanus infection. Its presence leads to early detection and management to achieve a good outcome, survival, and in our case, decannulation. Aydin *et al.* found a direct correlation between the clinical stage and the requirement of tracheostomy.[3] Sun *et al.* stated that the mainstays of treatment were early ventilatory support and tracheostomy.[9] Orotracheal intubation may be an initial intervention, but to ensure long term ventilatory support, tracheostomy may be performed early.[10] Although some did not advocate routine tracheostomy in tetanus cases, there were still those who considered it a lifesaving procedure, especially in moderate and severe stages.[2,8] Smith and Drew emphasized that all tetanus patients should at least be considered candidates for tracheostomy.[2] As part of the course of the disease, laryngeal and respiratory muscle spasm may ensue without prior notice and cause sudden death. Early tracheostomy is preferred over endotracheal intubation because the latter can provoke laryngospasm and thus exacerbate airway distress.[11] Other reasons for tracheostomy include difficulty in intubation and reintubation in patients with severe hypertonic state, and prolonged intubation and mechanical ventilator support of more than 7 days in adults and greater than 30-60 days in pediatric patients.[8] A study by Espinosa and Vinco looked into the relationship between the timing of tracheostomy and outcomes of tetanus, such as length of hospital stay, length of mechanical ventilation, morbidity, and mortality rate.[12] They defined early tracheostomy as performed within 24 hours from time of admission while those performed beyond 24 hours were classified as late tracheostomy. Results of this study showed that early tracheostomy in moderate and severe stage tetanus led to shorter length of hospital stay and length of mechanical ventilation than late tracheostomy.[12] With that in mind, early tracheostomy becomes a justifiable step in patients with moderate to severe tetanus.[8] Once tracheostomy is immediately initiated and management is early administered especially in moderate to severe cases such as Stage II and III, good prognosis, which can be manifested by decannulation, becomes more likely.

In our study, the case fatality rate increased with age, consistent with findings of the Research Institute for Tropical Medicine (RITM) report.[4] Sixty two percent (62%) of our patients had incubation periods of less than 7 days, and 58% of those patients were already assessed as Stage III or severe disease. Moreover, 62% of those with periods of onset of less than 3 days already had Stage III disease. Fasunla identified a short incubation period as one of the factors associated with more severe disease.[8] Miranda-Filho *et al.* identified a cut-off incubation period of $\leq$10 days and period of onset of $\leq$48 hours that indicate worse prognosis; those with incubation period of >10 days and period of onset of >48 hours are associated with better prognosis.[13]

Sixty one percent (61%) of those who did not receive any vaccination for tetanus were staged III during admission. Although a complete dose has not been proven to give lifelong protection against tetanus, it is still recommended that a complete dose be accomplished before 6 years of age followed by booster shots between ages 11 and 18 years and every 10 years in adults.[8] According to the Centers for Disease Control and Prevention, the antitoxin levels of most persons approach the minimal protective level by 10 years after the last dose. Therefore, routine boosters are recommended every 10 years.[14] Unfortunately, there was no mention of booster shots in the chart entries of our patients.

Dyspnea can be considered a deadly predictor of negative outcome. Another important parameter derived from logistic regression analysis is the coefficient estimate. The sign of the coefficient estimate tells the direction of the relationship between the dependent variable and outcome. A positive coefficient indicates an increased likelihood of an outcome from happening, while a negative one decreases its likelihood. With a negative coefficient estimate for outcomes "discharge" and "decannulation," tetanus patients are less likely to be discharged and decannulated due to such possible reasons as: "need for/connected to a mechanical ventilator," "infection," "complications (ventilator-associated pneumonia, comorbidities)," or more severe disease since they "already progressed to spasms of muscles of respiration."[7]

"Dyspnea" and "neck pain rigidity" showed a positive coefficient estimate in mortality outcome. This is consistent with the literature.[4,14] Tetanus follows a descending pattern from trismus or lockjaw to neck stiffness, dysphagia, rigid abdomen, progressing to laryngospasm and spasm of muscle of respiration.[11,14] As the course of the disease progresses, mortality becomes more likely.[4]

One limitation of this study is our small sample size. A larger sample size may provide more data and possibly include more patients in Stage I that did not undergo tracheostomy. Tracheostomy as a surgical procedure comes with various complications that is why some authors only recommend tracheostomy for moderate to severe stages of tetanus.[2,8] Another limitation of our study is that we did not further investigate the cause of death of some patients, and whether there were complications from tracheostomy. We recommend further studies to evaluate the complications of the procedure and perform a cost-benefit analysis in tetanus patients. Future studies may employ a larger sample size to explore and describe not only trends, but significant results and associations. Moreover, the inclusion of all presenting (head and neck, and non-head and neck) symptoms in the comparison and analysis may provide a more holistic approach to tetanus.

In conclusion, trismus and neck pain/rigidity are the most common initial head and neck symptoms of tetanus, with a significant relationship to decannulation. A patient with such symptoms should raise a high index of suspicion for tetanus so that early diagnosis and expeditious intervention (including tracheostomy) can be initiated. To secure the airway via tracheostomy among tetanus patients manifesting with potential difficult airway access heralded by trismus and neck rigidity may allow decannulation but not necessarily favor discharge or decrease in mortality. Nevertheless, early tracheostomy should decrease morbidity attributed to frequent or recurrent intubation. Securing the airway and initiating medical management improves prognosis, making survival and decannulation more likely.

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