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Tetanus Immunoglobulin G Assessment in Adults Trauma Patients

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Abstract

Background: *Clostridium tetani* is an anaerobic, gram-positive bacillus that causes tetanus infection. It usually enters the body through injury with contaminated objects. Tetanus differs from other diseases that can be prevented by vaccination in that it is not contagious and does not spread from person to person. The aim of this study is to evaluate the levels of Tetanus IgG in trauma patients admitted to the emergency department (ED).

Methods: The study was planned as cross-sectional, prospective, and single-center. The study was conducted from January to July 2018 in the Kahramanmaraş Sütçü İmam University Hospital. Totally, 178 patients aged ≥18 years were included. For measurement of the level of Tetanus IgG, Clostridium tetani toxin 5S IgG kit (NovaLisa, NOVATEC) was used to quantitatively detect IgG type antibodies by micro-ELISA method in accordance with the manufacturer's recommendation.

Results: In total, 143 cases were male and 35 were female. The mean age of the cases was 40 ± 16 years. Tetanus IgG levels were found to be 0.29 ± 0.6 IU/mL in cases from rural areas and 2.14 ± 1.64 IU/mL in cases from urban areas ($P < 0.001$). There was a negative correlation between age and Tetanus IgG level (r: (-) 0.479; $P < 0.001$). The protective level of Tetanus IgG was observed to be even lower, especially in patients aged ≥40 years (n = 43, 78.9%).

Conclusion: Measurements of Tetanus IgG levels should be performed as far as possible in the ED. In this way, unnecessary vaccination can be avoided.

Keywords: Emergency department, Tetanus Ig G, Trauma, Vaccination

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Introduction

Clostridium tetani is an obligate anaerobe and gram-positive bacillus that causes tetanus infection. Bacterial spores are most abundantly present in dust, soil, animal gut and fertilizer. The disease is transmitted into the human body as a result of the entry of bacteria through injured skin or after trauma. Once the body is infected, two important neurotoxins, tetanospasmin and tetanolysin, are released. Tetanospasmin is antigenic and the main toxin responsible in the pathogenesis. This toxin inhibits the release of gamma aminobutyric acid (GABA) and glycine that are inhibitory neurotransmitters in the neuromuscular region. Inhibition of neurotransmitters that inhibit muscle contraction increases muscle tone and the muscles enter a state of constant contraction. It causes the whole body to contract, especially in the jaw and facial muscles. When the muscles are locked due to masseter muscle spasm, it is called "trismus". Locking the facial muscles causes a fixed sarcastic grimace, called "*risus sardonicus*". If the muscles of the whole body are affected, it leads to the state called opistotonus.[1,2]

There are four different forms of clinical findings in tetanus, namely generalized, local, cephalic and neonatal. The most common type is the generalized type (80%).[3]

The World Health Organization (WHO) recommends a total of six doses of vaccine for tetanus; these include three doses of primary vaccine and three doses of booster. The WHO recommends three booster doses following a primary vaccination series of three doses of vaccine containing tetanus and diphtheria. Three doses of primer should be given starting from the age of six weeks and doses should be given with a minimum of 4 weeks between doses. Three booster doses should preferably be given in the second year of life (12–23 months), 4–7 years, and 9–15 years. Ideally, there should be at least 4 years between booster doses.[4] In our country, three doses of tetanus vaccine are given in 2–4–6 months after birth. The first booster dose is given at 18–24 months. In the childhood vaccination program, re-vaccination with adult type diphtheria-tetanus vaccine (Td) in primary schools is done in Grade 1 (7 years) and Grade 8 (14 years). Pregnant women as well as men going to the military are also vaccinated. Over time, however, the level of tetanus immunoglobulin G (IgG) falls below the protective level.[5] The aim of this study is to evaluate the levels of Tetanus IgG in trauma patients admitted to the emergency department.

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Patients and Methods

The study was planned as cross-sectional, prospective, and single-center. The study was conducted from January to June 2018 in the Kahramanmaraş Sütçü İmam University Hospital. A total of 178 patients aged ≥18 years who were admitted to the emergency department because of trauma were included in this study. Permission was obtained from cases and/or their relatives with an informed consent form. The age, gender, vaccination status, occupation (worker, housewife, student, farmer, civil servant, unemployed), type of injury (sharp objects, industrial accident, crush injury, traffic accident, trauma, firearm injury, fracture), place of injury (upper extremity, head and neck, lower extremity, trunk, multiple injuries) and place of residence (rural/urban) of the cases were recorded by questioning. Pregnant women, patients aged <18 years and those who were vaccinated with the tetanus vaccine in the last 5 years were not included in the study.

At the time of admission, blood was collected from the cases in 5 cc citrate tubes. The serum obtained from these blood samples was stored at -20°C until the day of the study. For measurement of the level of tetanus IgG, *Clostridium tetani* toxin 5S IgG kit (NovaLisa, NOVATEC) was used to quantitatively detect IgG type antibodies by micro ELISA method in accordance with the manufacturer's recommendation (Figure 1). According to the manufacturer's recommendation, the results were evaluated as follows; <0.1 IU/mL: no protective antibody response, do primer immunization or booster injection, look at antibody level after 4–6 weeks; 0.10–0.5 IU/mL: safe protection! Do booster injections and look at the antibody level after 4–6 weeks; 0.51–1.0 IU/mL: safe protection! There is no need for a booster injection. Look at the antibody level two years later; 1.1–5.0 IU/mL: long-term protection, look at the antibody level after 5–10 years; >5.0 IU/mL: long-term protection, look at the antibody level after 10 years.

Statistical evaluation of the data obtained in the study was performed using the SPSS 22.0 package program (IBM SPSS Statistics for Windows, Version 22.0. IBM Corp., Armonk, NY). Continuous data were summarized with means and standard deviations while categorical data were summarized with numbers and percentages. Continuous data in independent groups were compared using student *t* test. Chi-square test was used for comparisons of categorical data from two independent groups. The mean values were compared between groups using the analysis of variance (ANOVA) test. Tukey was used as post hoc test. Pearson correlation test was used in order to determine the relation between two continuous variables. Statistical significance level was accepted at $P < 0.05$.

Results

A total of 186 patients were included in the study and 8 patients were excluded due to serum loss. Of these, 177 cases (99.4%) were citizens of Turkey while only 1 case (0.6%) was a Syrian immigrant.

Considering the educational level of cases, 5.6% (n = 10) were illiterate, 48.4% (n = 86) had primary education, 32% (n = 57) had high school education and 14% (n = 25) graduated from university. The data showed that the Tetanus IgG level increased with increasing educational level (r: 0.634; $P < 0.001$). The demographic information of the patients is presented in Table 1.

With regard to the patients' occupation, more than half of the cases represented workers (61.8%). When the mean Tetanus IgG of the occupational groups was examined, it was observed to be the highest in civil servants, followed by students and worker groups. On the other hand, Tetanus IgG values of farmers, housewives and unemployed groups were found to be quite low. The data of the occupational groups compared based on tetanus IgG averages are presented in Table 2.

The characteristics of injury in the cases are presented in Table 3.

When the place of residence (rural/urban) of the cases were analyzed, 49 (27.5%) were living in rural and 139 (72.5%) were living in urban areas. Tetanus IgG levels were found to be 0.29 ± 0.6 IU/mL in cases from rural areas and 2.14 ± 1.64 IU/mL in cases from urban areas ($P < 0.001$).

A statistically significant correlation in the negative direction was observed between age and Tetanus IgG level (r: (-) 0.479; $P < 0.001$). The protective level of Tetanus IgG was observed to be even lower, especially in patients aged ≥40 years (n = 43, 78.9%).

Tetanus IgG levels and distribution according to age

Table 1. Demographic Information

	Male	Female	Total
Sex, No. (%)	143 (80.3)	35 (19.7)	178 (100)
Age (y), mean ± SD	39 ± 15	43.8 ± 19.6	40 ± 16
Educational level, No. (%)			
Illiterate	6 (60)	4 (40)	10 (100)
Primary education	67 (77.9)	19 (22.1)	86 (100)
High school	51 (89.5)	6 (10.5)	57 (100)
University	19 (76)	6 (24)	25 (100)
Occupational groups, No. (%)			
Worker	104 (94.5)	6 (5.5)	110 (100)
Housewife	0 (0)	22 (100)	22 (100)
Student	15 (83.3)	3 (16.7)	18 (100)
Farmer	15 (83.3)	3 (16.7)	18 (100)
Civil Servant	5 (71.4)	2 (28.6)	7 (100)
Unemployed	3 (100)	0 (0)	3 (100)

SD, Standard deviation.
* Chi-square (χ^2) test was used for comparisons of categorical data from two independent groups.

Table 2. Evaluation of Mean Tetanus IgG in Occupational Groups

	No. (%)	Tetanus IgG (IU/mL) Mean ± SD	Worker	Housewife	Student	Farmer	Civil Servant	Unemployed
						P*		
Worker	110 (61.8)	1.9 ± 1.6		<0.001	0.773	<0.001	0.164	0.520
Housewife	22 (12.4)	0.4 ± 0.8	<0.001		<0.001	0.998	<0.001	1.000
Student	18 (10.1)	2.4 ± 1.7	0.773	<0.001		<0.001	0.761	0.265
Farmer	18 (10.1)	0.2 ± 0.3	<0.001	0.998	<0.001		<0.001	1.000
Civil servant	7 (3.9)	3.3 ± 1.6	0.164	<0.001	0.761	<0.001		0.060
Unemployed	3 (1.7)	0.5 ± 0.4	0.520	1.000		1.000	0.060	

SD, standard deviation.
* One-way ANOVA test was used to compare the groups. Tukey was used for post hoc test.
P values < 0.05 were considered statistically significant.

groups are presented in Table 4.

Discussion

The incubation period of the anaerobic bacterial disease tetanus is 3–21 days whereas most cases occur within 14 days. The time elapsed between the first symptoms and the first reflex spasm is considered to be the onset time and this time is considered to be 1–4 days.[2,6]

Tetanus differs from other diseases that can be prevented by vaccination in that it is not contagious and does not spread from person to person. *C. tetani* is usually found in soil, dust and fertilizer. It usually enters the body through injury with contaminated objects. Almost all cases of tetanus consist of adults who have not received the tetanus vaccine or booster vaccination in the past 10 years.[7]

Maternal and neonatal tetanus cases are closely monitored by the WHO. Since 1989, the World Health Assembly has targeted global neonatal elimination. In 1999, the

Table 3. Characteristics of Injury in the Cases

	Number	Percent
Type of injury		
Sharp objects	92	51.6
Industrial accident	32	18.0
Crush injury	25	14.0
Traffic accident	17	9.6
Trauma	9	5.1
Firearm injury	2	1.1
Fracture	1	0.6
Place of injury		
Upper extremity	110	61.8
Head and neck	33	18.5
Lower extremity	30	16.9
Trunk	3	1.7
Multiple injuries	2	1.1
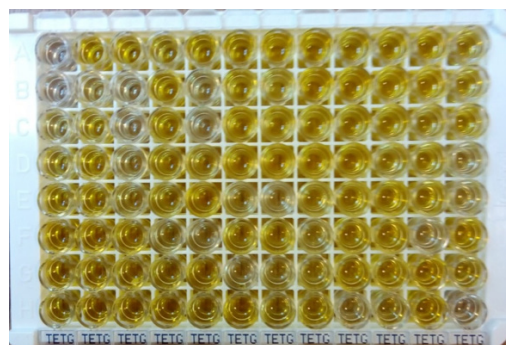
Figure 1. Tetanus IgG Study of Serum Samples by Micro ELISA Method.

Table 4. Tetanus IgG Levels and Distribution According to Age Groups

Age Groups (y)	Sex	Tetanus IgG Levels (IU/mL)					Total
		<0.1 No. (%)	0.10–0.5 No. (%)	0.51–1.0 No. (%)	1.1–5.0 No. (%)	>5.0 No. (%)	n
18–29	Female	3 (23.1)	1 (7.7)	2 (15.4)	7 (53.8)	0 (0)	13
	Male	2 (4.7)	3 (7.0)	8 (18.6)	27 (62.8)	3 (7.0)	43
30–39	Female	0 (0)	0 (0)	2 (66.7)	1 (33.3)	0 (0)	3
	Male	7 (18.4)	3 (7.9)	1 (2.6)	25 (65.8)	2 (5.3)	38
40–49	Female	1 (25.0)	2 (50.0)	1 (25.0)	0 (0)	0 (0)	4
	Male	10 (46.7)	3 (9.7)	6 (19.4)	12 (38.7)	0 (0)	31
50–59	Female	5 (83.3)	1 (16.7)	0 (0)	0 (0)	0 (0)	6
	Male	7 (46.7)	1 (6.7)	2 (13.3)	5 (33.3)	0 (0)	15
>60	Female	9 (100)	0 (0)	0 (0)	0 (0)	0 (0)	9
	Male	11 (68.8)	2 (12.5)	1 (6.3)	2 (12.5)	0 (0)	16
Total		55 (30.9)	16 (9.0)	23 (12.9)	79 (44.4)	5 (2.8)	178

initiative Maternal and Neonatal Tetanus Elimination (MNTE) was re-launched by the UNICEF, WHO and the United Nations Population Fund (UNFPA) to achieve its target as a public health problem. As of April 2018, only 14 countries have not accomplished the MNTE status. Six doses of vaccine are recommended in order to maintain this state safely in adulthood.[6]

In a study conducted by Şimşek et al, tetanus IgG levels were evaluated in patients admitted to the emergency department. The mean age of the cases included in the study was 40.9 ± 15.8 years and it was determined that 73.1% of the cases were male.[8] Another study conducted by Aydın et al showed that the mean age of the cases was 55 years and 86% of the cases were over 45 years of age. The female/male ratio of the cases was 1.3.[9]

In a study conducted by Cılız et al on health care staff, the seropositivity of tetanus was examined according to age groups. Tetanus seropositivity was found to be 100% at 15–24 years, 98.9% at 25–34 years, 85.7% at 35–44 years and 80% at ≥45 years. In terms of educational status, tetanus protection was determined at 80% in those with primary education, 100% in high school level , 92.7% in undergraduate level and 96.9% in post graduate level.[10] In a study conducted by Esteve et al in Brazil, the seropositivity rate of tetanus was found to be 84.7% in 215 participants and it was found that the protective effect of tetanus decreased with age.[11] Dos Santos et al investigated the protection of tetanus in healthcare workers in the newborn unit. When age groups were examined, it was found that the level of tetanus IgG level at the age of 50 years was at a low level of 0.53 IU / mL.[12] Another study by Mizuno et al reported that the mean value of tetanus IgG was 0.63 IU / mL at > 50 years of age.[13]

Jablonka et al assessed the levels of tetanus IgG in six refugee camps in Germany. Their results showed that age-related protection decreased and that vaccination programs for refugees should be done within strict guidelines.[14] In a study of 594 patients diagnosed with tetanus in Italy between 2001 and 2010, 80.2% of the cases were found to be > 64 years old.[15]

One study questioned the patients if they were vaccinated and afterwards, the level of tetanus IgG was determined. It was found that 23.9% of the cases had tetanus protection, 19% had no protection against tetanus, and 57.1% did not know about tetanus protection.[16] In the same group, 16% of the cases were not protective against tetanus according to the tetanus IgG levels observed after questioning. In a study on tetanus protection, it was reported that there was discordance between tetanus IgG level and knowledge of vaccination status.[8] Although all cases in our study reported that they were not protected against tetanus, only 30.9% of cases were found not to have protective levels.

Valuable results were obtained from this study. In this sense, we believe that this study will contribute to health workers in developing countries.

In conclusion, it is clear that tetanus protectiveness has decreased in later ages. For this reason, measurements of tetanus IgG levels should be performed. In this way, unnecessary vaccination can be avoided. If this is not possible, we believe it would be useful to vaccinate older adults.

Authors' Contribution
Idea/Concept: SN, HH, ARŞ; Design: SN, HH, ARŞ, FO; Control/supervision: SN, FO; Data collection and/or processing: HH, FO; Analysis and/or interpretation: SN, FO; Literature review: SN, FO; Writing the article: SN; Critical review: SN, HH, ARŞ, FO.

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