

Investigation of Tetanus Antitoxin Titer Levels in People Over Forty Years of Age

Kırk Yaşın Üzerindeki İnsanlarda Tetanoz Antitoksin Titre Düzeylerinin Araştırılması

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ABSTRACT Objective: Tetanus is a disease that can be prevented with vaccination, but protective antitoxin titers decrease to undetectable levels with old age. The aim of this study is to evaluate tetanus antitoxin levels in individuals over 40 years of age and to investigate the vaccination and physical injury status via survey. **Material and Methods:** A total of 361 participants, 178 men and 183 women, were enrolled in the study and blood was drawn from each participant to measure tetanus antibody level by enzyme immunoassay (EIA) method. **Results:** Tetanus antibodies were undetectable in 55 male (30.9%) and 71 female patients (38.8%) at the end of the study. It was determined that tetanus antitoxin levels significantly decrease with age in both women and men especially after 50 years of age which is accepted as the limit age in which antibody is likely to be negative. **Conclusion:** In adult age group, booster vaccination for tetanus is recommended every 10 years in developing and developed countries, but this recommendation can not be put into practice as anticipated. Similarly in our country, vaccination of adult age group is not common and tetanus vaccine is not generally administered at every ten years. The results of this study show that one dose of tetanus vaccine should be administered at least to individuals over 50 years of age, and individuals who do not recall their vaccination history should be taken into a three-dose vaccination program.

Key Words: Diphtheria-tetanus vaccine; tetanus antitoxin; tetanus toxoid

ÖZET Amaç: Tetanoz aşısı ile önlenilebilir bir hastalıktır fakat yaşla beraber koruyucu antitoksin titreleri saptanamayacak düzeylere düşer. Bu çalışmanın amacı 40 yaşın üzerindeki bireylerde tetanoz antitoksin düzeylerini değerlendirmektir. **Gereç ve Yöntemler:** Bu çalışmada 178 erkek ve 183 kadından oluşan toplam 361 katılımcıdan alınan kan örneklerinde enzim immunoassay (EIA) yöntemiyle tetanoz antitoksin düzeyleri çalışılmıştır. **Bulgular:** Tetanoz antikorunun erkeklerin 55 (%30,9)'inde ve kadınların 71 (%38,8)'inde ölçülemeyecek düzeyde olduğu, tetanoz antitoksin düzeylerinin kadınlar ve erkeklerde yaşla beraber azaldığı ve özellikle sınır yaş olarak kabul edilen 50 yaş ile beraber negatif olduğu saptanmıştır. **Sonuç:** Erişkin yaş grubunda gelişmiş ve gelişmemiş ülkelerde tetanoz için her 10 yılda bir rapel aşılması önerilmesine karşın bu öneri yeterince uygulanamamaktadır. Ülkemizde de erişkinlerin aşılması yaygın olmayıp 10 yılda bir tetanoz rapeli yeterince yapılamamaktadır. Çalışmamızın sonuçları 50 yaş üzerindeki bireylere en az bir doz tetanoz aşısı uygulanması gerekliliğini ve aşılama geçmişini hatırlamayan bireyler için üç doz aşılama programı uygulanmasının faydalı olacağını düşündürmektedir.

Anahtar Kelimeler: Difteri-tetanoz aşısı; tetanoz antitoksini; tetanoz toksoidi

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Tetanus is a disease that can be prevented with vaccination, but adult tetanus is still an important health issue, especially in the developing countries. With increasing age, serum antitoxin titers decrease to zero. Tetanus frequency increases with age in the adult age group and most

of tetanus cases are seen above 60 years of age in developed countries.¹⁻⁴ Puncture wounds of nail, thorn or splints, injury with various tools contaminated with soil as well as traffic accidents enclose risks for tetanus. Tetanus is seen more frequently in adults, elders with motor dysfunction and workers who work in the soil and dirty areas. Therefore, tetanus is seen frequently in male patients. Tetanus can never be eradicated since *Clostridium tetani* subsists in soil. Mortality rate of tetanus was cited between 10-90%, and most of the cases were unvaccinated patients.³⁻⁵

In this study, it was aimed to serologically determine tetanus antitoxin levels in serum samples of individuals over 40 years of age. In addition, a questionnaire was used to collect data about socio-demographic characteristics and risk factors (vaccination history, physical injury status etc.) of participants enrolled in this study.

MATERIAL AND METHODS

This is a cross sectional study which was planned to be conducted in Turgutlu District Center and its villages affiliated to Central Primary Health Care Units. Study population was consisted of the residents of Turgutlu, who were over 40 years of age. Subsequent to ethical committee approval, a questionnaire was filled by the population based on mid-year population introduced by City Health Directorate with face-to-face interview method; the "Informed Written Consent Form" was signed by all enrolled individuals, and then 10 cc blood was drawn from each participant to measure the tetanus antibody level. Dependent variable of the trial was tetanus antitoxin levels. Independent variables; age, gender, health insurance, education level, marital status, characteristics of living environment/house, history of physical injuries, history of tetanus vaccination (completed or not) and information of the timing of last vaccination were evaluated by survey forms. Study data were collected by nurses, midwives and health staff working in Primary Health Care Centers. Before the study, one-day training was conducted for these individuals on the scope of the study and data collection.

According to Manisa City Health Directorate data, a total of 36208 people over 40 years of age reside in villages affiliated to Turgutlu District Center and Central Primary Health Care Units.

The study sample was selected adjusting to 30%±5 (95% Confidence Interval). Based on this, the sample group needed to include at least 320 individuals consisting of 162 women and 158 men; due to rounding-off to whole numbers and the need to reach at least one individual from every age and gender group in each area, It was predicted that this figure could be increased and the study was carried out with 361 participants. Samples were selected randomly; it was weighted according to age groups and gender in seven different Primary Health Care Areas. For evaluation of the data, Epi-Info program was used. Analyses were performed with descriptive statistics and Chi square tests.

Tetanus antitoxin levels were determined by enzyme immunoassay (EIA) method (NovaLisa-Germany). Based on recommendations of the manufacturer company, serum samples were diluted by a ratio of 1/100 and tests were conducted by micro EIA method. Similarly, during the evaluation of results, based on test kit user manual, values under 0.10 IU/mL were regarded as absolute negative, values between 0.11-1.0 IU/mL as low-positive and values ≥1.10 IU/mL as strong positive. In this method, values under 0.01 IU/mL are regarded as absolute negative and due to nil levels of protective antibodies, full dose vaccination is recommended. Levels between 0.01-0.10 IU/mL are low-positive and not considered reliable in terms of protection; for these individuals, one booster dose and titer control after 4-6 weeks is recommended. Likewise, levels between 0.11-0.50 IU/mL are regarded as reliable protective levels, but for these individuals, one booster dose followed by antibody titer control after 4-6 weeks is recommended. Antibody titers between 0.51-1.0 IU/mL are reliable levels and no booster dose is needed, but in these individuals, titer control is recommended after 2-3 years. If the antibody titer is above 1.10 IU/mL, it is indicated that long term protection is present, and no booster dose is recommended; it is recommended to conduct titer controls after 5-10 years in these people.⁶⁻⁸

RESULTS

A total of 361 individuals residing in Turgutlu district center or villages were enrolled in the study; Of these participants, 178 were men with mean age of 57.62 ± 12.58 years (range 41-87) and 183 were women with mean age of 55.85 ± 12.19 years (range 40-98).

Immunity for tetanus in relation to various characteristics was summarized in Table 1 and distribution of immunity for tetanus according to age groups and gender were presented in Table 2.

Absolute negative status of tetanus antibody was determined in 30.9% of men and 38.8% of

women (Table 1). No statistically significant difference was detected between two genders regarding the determined tetanus antitoxin levels.

It is observed that absolute negativity ratio of tetanus antitoxin levels in women decreases with age. Although negativity levels were higher in the older men versus men at 40-49 years of age, it was found as 12 (19.4%) while the highest negativity ratio in 50-59 age group was 21 (42.9%) (Table 1).

The percentages of seronegativity according to age-groups in men was found as 19.4%, 42.9%, 37%, 32.1% and 25% in 40-49, 50-59, 60-69, 70-79, and over 80 years of age, respectively. On the other hand, in women at the same age-groups, these val-

TABLE 1: Characteristics of the participants with regard to their tetanus antibody statuses.

Characteristic	Immunity status			
	Absolute negative		Positive and strong positive	
	n	%	n	%
Gender				
Male	55	30.9	123	69.1
Female	71	38.8	112	52.5
Educational status				
Illiterate	26	38.2	42	61.8
Literate	24	50.0	24	50.0
Primary school (5 th grade)	60	31.6	130	68.4
Primary school (8 th grade)	7	38.9	11	61.1
High school	6	35.3	15	64.7
College-University	3	15.0	20	85.0
Age (years)				
40-49	37	27.4	98	72.6
50-59	38	39.2	59	60.8
60-69	26	42.6	35	57.3
70-79	19	39.6	29	60.4
≥ 80	6	30.0	14	70.0
Marital status				
Married	102	35.1	189	64.9
Bachelor	2	25.0	6	75.0
Divorced	2	28.6	5	71.4
Widow	20	37.7	33	62.3
Social insurance				
Social Security Organization for employees of private companies	74	37.2	125	62.8
Pension Fund for civil servants	8	20.5	31	79.5
Social security organization for artisans and the self-employed	26	41.3	37	58.7
Social security for people who earn less than the minimum wage	6	31.6	13	68.4
No insurance and others	12	30.0	28	70.0
Total	126	34.9	235	65.1

ues were found as 34.2%, 35.4%, 47.1%, 50%, and 37.5%, respectively (Table 2). It was determined that this decrease emerging in women with increasing age was not statistically significant ($p>0.05$). However, when 50 years was taken as cut off point, it was significant in men (Pearson Chi-square= 0.015) (OR= 2.45 %95 GA 1.17-5.11) (Table 2). The number of elderly participants over 70 years of age, especially over 80 years was smaller than the number of participants at other age-groups in both sexes. Nevertheless, the data show that decreased antibody titer can also be clearly observed in this age group.

When the number of pregnancies and tetanus vaccination during pregnancy were investigated, it was observed that 38 women (20.7%) had a pregnancy in the previous ten years. On the other hand, 31 of 167 (18.5%) women who had a history of pregnancy had a tetanus vaccination during pregnancy. Although tetanus prophylaxis during pregnancy is programmed routinely in our country, the vaccination ratio during pregnancy was low in this study since the number of women with a history of pregnancy in last ten years was only 38 (20.7%).

There was no relation between immunity levels and administration of tetanus vaccine during pregnancy in women under 50 years of age ($p>0.05$).

On the other hand, it was found that 61 of 178 men in this study had a tetanus vaccination history during their military service. No relation was found between administration of tetanus vaccine during military service and the immunity levels ($p>0.05$).

In this study, there were 159 (44%) participants that were working in risky jobs with regard to exposure to tetanus toxin such as gardening, farming and building construction. However, there were only 42 (11.6%) participants with a vaccination history in last ten years among all participants. Remaining 319 participants did not have a vaccination history.

When history of injury was taken into consideration, 89 (24.7%) of the participants had admitted to a hospital for treatment of an injury before, and 31 of them (8.6%) were vaccinated. No relation was observed between referring to a health care center due to a physical injury in the previous five years, social insurance, marital status and immunity levels of individuals for tetanus ($p>0.05$).

Regarding relationship between tetanus protective antibody levels and education; it was found that the ratio of protective antibody levels were 64.1% in illiterate participants and elementary school graduates and 70.9% in secondary school graduates and the ones with higher education levels, however the difference was not statistically significant ($p>0.05$). At the same time, regarding relationship between tetanus protective antibody levels and socioeconomic status, it was found that the ratio of protective antibody levels was 63.5% in participants with middle or lower socioeconomic status and 76.1% in participants with higher socioeconomic status; and similarly the difference was not statistically significant ($p>0.05$).

DISCUSSION

Although tetanus is a disease that can be prevented with vaccination, it is an infectious disease with incidence of about one million cases worldwide, the

TABLE 2: Age and gender distributions according to tetanus antibody status.

Gender and age	Immunity status*			
	Absolute negative		Positive and strong positive	
	n	%	n	%
Men				
40-49	12	19.4	50	80.6
50-59	21	42.9	28	57.1
60-69	10	37.0	17	63.0
70-79	9	32.1	19	67.9
≥ 80	3	25.0	9	75.0
Total	55	30.9	123	69.1
Women				
40-49	25	34.2	48	65.8
50-59	17	35.4	31	64.6
60-69	16	47.1	18	52.9
70-79	10	50.0	10	50.0
≥ 80	3	37.5	5	62.5
Total	71	38.8	112	61.2
General Total	126	34.9	235	65.1

* Row percentages were used.

majority occurring in developing countries with a high mortality rate.¹⁻⁴ In close correlation with vaccination procedures of countries, cases present as newborn tetanus and elderly adult cases. Similarly, in our country, even though the number of cases have decreased considerably, adult tetanus (especially elderly) is still observed and the majority of the cases have the disease due to insufficient vaccination in the adult age group.

Studies conducted in our country and other countries reported that tetanus antitoxin levels decrease with age and the levels are especially low in cases above 50-60 years of age.^{9,10}

One study conducted in Turkey reported that proportion of individuals with protective antibody for tetanus was 23.7% between 40-60 years of age and 34.5% over 60 years of age among 595 individuals over 20 years of age in Kocaeli province.¹¹ In Kayseri province, protective tetanus antitoxin levels were determined in only 63 (25.3%) individuals out of 249 individuals over 40 years of age.¹²

Another study conducted by Atabey et al. reported that antitoxin values decreased below protective levels in 86.7% of individuals in whom the last vaccine was administered more than 10 years ago.¹³ Similarly in Malatya province, insufficient tetanus antitoxin levels were found as 74.3% in 31-50 age group and as 85.7% in ≥ 51 age group among 175 individuals with ages ranging between 1-79 years.¹⁴ Saltoğlu et al. followed-up 53 tetanus cases between 1994-2000 in Çukurova University Hospital, Turkey and the mean age was 46.6 years and mortality rate was 52.8% in these cases.¹⁵ There was a history of incomplete primary immunization schedule in 38 of these cases (71.7%).

In another study conducted in three cities of Turkey between 2000-2001 covering 26 centers and 2465 individuals; insufficient tetanus antitoxin level rates were 40.6%, 51.4% and 67.4%, respectively.¹⁶ In a study conducted between 2000 and 2001 in Manisa province, tetanus antitoxin levels were investigated in a study group of 143 individuals between 17-72 years of age and in a control group of 50 individuals consisting of 25 high school

students and 25 pregnant women. In the study group, sufficient protective antitoxin levels were found in 74.8%, low-positive in 8.4% and negative in 16.8%. Protective antitoxin levels were observed to decrease with age; while insufficient antitoxin determination rates were found as 11% in 17-35 years age group, 14% between 36-49 and 29% in 50-70 years age group.¹⁷

In our study, insufficient antibody levels were found in 55 men (30.9%) and in 71 women (38.8%). It was also determined that tetanus antitoxin levels decreased with age in women, however the levels decreased significantly after 50 years of age in men which is considered as the age limit for the ones who were unprotected for tetanus. In addition, we found a progressive decline in protection with increasing age, and people older than 40 years of age should be vaccinated to provide a protective antibody level.

No relation was observed between administration of tetanus vaccine during pregnancy and antibody levels in women under 50 years of age and this result was associated with the fact that majority of the women had their last pregnancy more than 10 years ago. Of 178 men, 61 were vaccinated during their admission to their military service. No association was determined between administration of tetanus vaccine during military service and the antibody levels. Even though high immunity levels were expected in men who were vaccinated during their military service; immunization history was not evaluated completely due to the fact that they could not remember whether they had tetanus vaccine or not. The percentages of seronegativity according to age groups in men were found as 19.4%, 42.9%, 37%, 32.1% and 25% in 40-49, 50-59, 60-69, 70-79, and over 80 age groups, respectively. On the other hand, these values were found as 34.2%, 35.4%, 47.1%, 50%, and 37.5% in women in aforementioned age groups, respectively. The number of elderly participants, especially the ones over 80 years of age was smaller than the number of the participants in other age groups in both genders. Nevertheless, the data revealed that decreased of antibody titer can also be observed clearly in this age-group.

When the number of pregnancies and tetanus vaccination during pregnancy were investigated, it was observed that 38 women (20.7%) had a pregnancy history in the previous ten years. On the other hand, 31 women (18.5%) were vaccinated during their pregnancy among 167 women with a pregnancy history. Although tetanus prophylaxis during pregnancy is programmed routinely in our country, the low ratio of vaccinated women during pregnancy was an expected result since the number of women with a pregnancy history in the previous ten years in this study was only 38 (20.7%).

In this study, 159 (44%) participants had risky jobs such as gardening, farming and building construction, which could cause exposure to tetanus bacteria. However, there were only 42 (11.6%) participants that had a vaccination history in the previous ten years. Remaining 319 participants did not have a vaccination history.

Eighty nine participants (24.7%) had ever admitted to hospital for treatment of an injury and 31 of them (8.6%) were vaccinated.

For primary immunization for tetanus, three doses of vaccination is needed; the first and second doses are given 4-6 weeks apart and third dose is administered 6-12 months later after the second dose. Following primary immunization, every individual tetanus booster dose (recall dose) should be administered every 10 years. A three-dose vaccination schedule is recommended to people whose immunization history is unclear. Immunization can be administered with tetanus vaccine alone or

adult type diphtheria tetanus (Td) can be administered. ACIP (Advisory Committee on Immunization Practices) recommends inquiring of tetanus immunization history and a booster dose should be administered between 11-12 and over 50 years of age.^{2,3,7}

In our country, tetanus vaccination is administered in infancy and is followed by booster doses in primary school and high school. Furthermore, tetanus vaccination is administered free of charge to pregnant women, to men during their military service and women between 15-49 years of age. Although a booster dose is recommended every 10 years, vaccines are usually administered following a physical injury. Therefore, older people are expected to have a lower tetanus antitoxin level. Absolute negativity status of mean tetanus antitoxin level at or over 50 years of age has been determined as approximately 40% in our study. Although a random sampling method is used in the study, the number of people over 80 years of age who accepted to enroll in the study is small. This is the limitation of our study and therefore the number of people at or over 80 years of age may not fully represent this age group.

Eventually, it is concluded that, considering that adult vaccination is not a very common practice in our country, it would be a suitable strategy for protection against tetanus to raise awareness of public on the tetanus vaccination and booster doses every 10 years through mass communication tools and to immunize particularly people over 50 years of age who have not been previously vaccinated.

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