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Türk Hijyen ve Deneysel Biyoloji Dergisi

Tetanus immunisation status in the adult population: Investigation of IgG levels

Erişkin popülasyonda tetanoz bağışıklık durumu: IgG düzeylerinin incelenmesi

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ABSTRACT

Objective: Tetanus is a vaccine-preventable disease; however, approximately one million new cases of tetanus are reported worldwide each year. As a result of successful vaccination policies in developed countries, tetanus cases are observed in individuals who are not vaccinated or who have not completed the vaccination schedule. The aim of this study is to determine the quantitative tetanus antibody levels in patients admitted to our hospital and to analyse the correlation between age, sex and antibody levels.

Methods: The study included the serum of 408 adult patients over 18 years of age who were admitted to the outpatient clinics and services of our hospital between 01/01/2022 and 06/08/2024. Tetanus IgG antibody levels were quantitatively determined using the VIRCLIA ELISA device (Vircell, Spain) using the Tetanus VIRCLIA® IgG ELISA kit (Vircell, Spain) in the serum of patients arriving at our medical microbiology laboratory. The data analyzed with the SPSS (Statistical Package for Social Sciences) 20.0 package program. The conformity of the numerical data to the normal distribution was

ÖZET

Amaç: Tetanoz aşı ile önlenebilir bir hastalık olmasına rağmen dünya genelinde her sene yaklaşık bir milyon yeni tetanoz vakası olduğu bildirilmektedir. Gelişmiş ülkelerde uygulanan başarılı aşılama politikaları neticesinde tetanoz vakaları sadece aşılanmamış veya yetersiz aşılanmış bireylerde gözlenirken; gelişmemiş ülkelerdeki tetanoz vakaları yenidoğan mortalitelerine oldukça sık neden olmaktadır. Bu çalışmanın amacı; hastanemize başvuran hastalardaki tetanoz antikor düzeylerini kantitatif olarak saptayarak, yaş ve cinsiyete göre antikor düzeylerinin ilişkisini incelemektir.

Yöntem: Çalışmaya 01.01.2022-06.08.2024 tarihleri arasında hastanemizde çeşitli poliklinik ve servislere başvuran 18 yaş üstü 408 yetişkin hastanın serumları dahil edildi. Tıbbi Mikrobiyoloji laboratuvarımıza ulaşan hasta serumlarında Tetanus VIRCLIA IgG ELISA kiti (Vircell, İspanya) kullanılarak, VIRCLIA® ELISA cihazı (Vircell, İspanya) aracılığıyla kantitatif olarak tetanoz IgG antikor düzeyleri ölçüldü. Veriler SPSS (Statistical Package for Social Sciences) 20.0 paket programı ile analiz edildi. Sayısal verilerin normal dağılıma uygunluğu

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examined by visual (histogram) and analytical methods (Kolmogorov-Smirnov test). Mann Whitney U test was performed for pairwise comparisons in groups with significant differences between them. The statistical significance level for all tests was accepted as p<0,05.

Results: The mean ± standard deviation values of the ages of the adults included in the study were determined as 40.07±15.10. 233 (57.1%) of patients were female. In our study, non-protective tetanus antibody levels of <0.1 IU/mL were detected in 25 adults (6.1%) and protective tetanus antibody levels of ≥0.1 IU/mL were detected in 383 adults (93.9%). The median tetanus antibody level was 1.12 IU/mL in men and 0.99 IU/mL in women. However, there was no statistically significant difference between the sexes (p>0,447). A negative correlation was found between age and antibody level above 40 years of age (r=-0,334; p=0,001).

Conclusion: In our study, lower tetanus antibody levels were found in older ages, and antibody monitoring should be performed at older ages and a tetanus booster dose should be administered if necessary.

Key words: Tetanus, IgG, vaccine, antibody level, immunisation

görsel (histogram) ve analitik yöntemlerle (Kolmogorov-Smirnov testi) incelendi. Aralarında anlamlı fark bulunan gruplarda ikili karşılaştırmalar için Mann Whitney U testi uygulandı. Tüm testler için istatistiksel anlamlılık düzeyi p<0,05 olarak kabul edildi.

Bulgular: Çalışmaya dahil edilen yetişkinlerin yaşlarının ortalama ± standart sapma değerleri 40,07±15,10 olarak tespit edildi. Hastaların 233 (%57,1)'ünü kadın hasta oluşturmaktadır. Çalışmada 25 (%6,1) kişide <0.1 IU/ml düzeyinde korumasız tetanoz antikoru, 383 (%93,9) kişide ise ≥0.1 IU/ml seviyesinde koruyucu tetanoz antikoru tespit edildi. Erkeklerde ortanca antikor düzeyi 1.12 IU/ml, kadınlarda ise 0.99 IU/ml olarak saptandı. Cinsiyetler arası istatistiksel olarak fark saptanmadı (p=0,447). 40 yaş üstünde yaş ile antikor düzeyi arasında negatif korelasyon saptandı (r=-0,334; p=0,001).

Sonuç: Çalışmamızda ileri yaşlarda daha düşük tetanoz antikor düzeyi saptanmış olup, ilerleyen yaşlarda antikor takibi yapılarak gerekliyse tetanoz hatırlatma dozu uygulanmalıdır.

Anahtar Kelimeler: Tetanoz, IgG, aşı, antikor düzeyi, bağışıklama

INTRODUCTION

Tetanus is an acute disease caused by exotoxins produced by *Clostridium tetani*, an anaerobic bacillus, with a high mortality, usually involving the musculoskeletal system. There is a vaccine developed from the bacteria's toxin. Although it is a vaccine-preventable disease; it is an important public health problem that mostly affects newborns and young adults in developing and the elderly in developed countries (1). Tetanus is a notifiable disease and its incidence is estimated to be 18 per hundred thousand. Mortality rates due to tetanus vary between 30-50% worldwide. It is reported that at least half of the mortality cases belong to the neonatal period (2-4). Since 1948, diphtheria, tetanus and pertussis vaccines have been used as combined toxoid vaccines (5). Turkey's National Immunisation Program states that DaBT-IPA-Hib (Diphtheria, Acellular Pertussis, Tetanus, Inactivated Polio, *Haemophilus influenza* type B) is the first vaccination given in the second month of life.

The administration of three doses of vaccine continues at intervals of eight weeks. A booster dose is administered at 18 months. DaBT-IPA is administered as a single booster dose in the first grade of primary school and Td (Tetanus, Diphtheria) in the eighth year. Moreover, men receive a single dose of the

tetanus vaccine while serving in the military, while women receive two doses at least two weeks prior to delivery (3).The risk of developing the disease increases in older ages due to the decreasing tetanus antibodies with age. According to a study done in the US, the vaccination rate for individuals six years of age and older was 72.3%, while the rate for those over 70 was 31% (4).

In this study, tetanus immunoglobulin G (IgG) levels of patients over 18 years of age admitted to various outpatient clinics and wards in our hospital is aimed to be investigated quantitatively and the relationship of antibody titres with age and gender is analysed.

MATERIAL and METHOD

The tetanus antibody levels of the patients included in our study were obtained retrospectively from the hospital information system. All patients who were requested tetanus antibodies from various outpatient clinics and services between 01.01.2022 and 06.08.2024 were included in our study.

The serum of 408 adult patients over the age of 18 who applied to various outpatient clinics and services in Necmettin Erbakan University Medicine Faculty between 01.01.2022 and 06.08.2024 were included in the study. Tetanus IgG antibody levels were quantitatively detected by the VIRCLIA ELISA device (Vircell, Spain) using the Tetanus VIRCLIA® IgG ELISA kit (Vircell, Spain) in the serum of patients accepted in our Medical Microbiology laboratory.

Results were stated in International Units per mililiter (IU/mL). The detected antibody levels were grouped according to the investigations in the literature and kit recommendations. Antibody titers of <0.1 IU/mL were considered to be non-protective against tetanus, antibody levels between 0.1-1 IU/mL were considered protective, and antibody levels above 1 IU/mL were considered to be long-term protective against tetanus. Protection status and recommendations according to tetanus antibody levels are presented in Table-1 (6-8).

The data were analyzed with the SPSS (Statistical Package for Social Sciences) 20.0 package program. In the descriptive analysis, frequency data were shown as numbers (n) and percentages (%), while numerical data were given using minimum and maximum values. The conformity of the numerical data to the normal distribution was examined by visual (histogram) and analytical methods (Kolmogorov-Smirnov test). Mann Whitney U test was performed for pairwise comparisons in groups with significant differences. Chi-square test and Fisher's exact chi-square test were used to compare categorical data. The correlation of parameters that did not fit the normal distribution was analized by Spearman test. The statistical significance level for all tests was accepted as $p<0,05$.

Table 1. Protection, vaccination and antibody monitoring according to tetanus antibody levels

Tetanus IgG Levels	Protective Status	Vaccination and antibody monitoring
<0.1 IU/mL	No protection	A booster dose should be given, and the antibody level should be measured after 4-6 weeks.
0.1-0.5 IU/mL	There is protectiveness	A booster dose should be given, and the antibody level should be measured after 4-6 weeks.
0.5-1.1 IU/mL	There is protectiveness	Antibody level control is recommended after 2 years
1.1-5.0 IU/mL	There is protectiveness	Antibody level control is recommended after 5-10 years
>5.0 IU/mL	There is protectiveness	Antibody level control is recommended for 10 years

The study was approved by the Necmettin Erbakan University Non-Drug and Non-Medical Device Research Ethics Committee Ethics Committee (Date: 20.09.2024 and Number: 2024/5181).

RESULTS

The mean ± standard deviation values of the ages of the adults included in the study were determined as 40.07±15.10. Considering the average age of the patients in the study, two groups under the age of 40 and over the age of 40 were formed in terms of age. 233 (57.1%) of patients in the study were female.

In the study, the median tetanus IgG level of women was 0.99 (0.44-1.67) IU/mL and of men 1.12 (0.62-1.77) IU/mL (p=0,447). The median tetanus IgG level was found to be 1.28 (0.66-2.33) IU/mL in the group aged 40 and under, and 0.71 (0.23-1.36) IU/mL in those aged 40 and over.

The antibody level of 6.1% of the patients was below <0.1 IU/mL that is not protective against tetanus. The rate of having a protective antibody level against tetanus for 2-5 years was 25.2%. The rate of having a protective antibody level for 5-10 years was 42.4%. The rate of having a protective antibody level for more than 10 years was 7.1%. (Figure-1).

There was no statistically significant difference between the antibody levels in males and females (Figure-2).

Considering the relationship between antibody levels and patient ages, the high results obtained for tetanus IgG antibody levels in patients under 40 years of age was found to be statistically significant (Table-2).

There was moderate negative correlation between age and tetanus antibodies (r=-0,334; p=0,001).

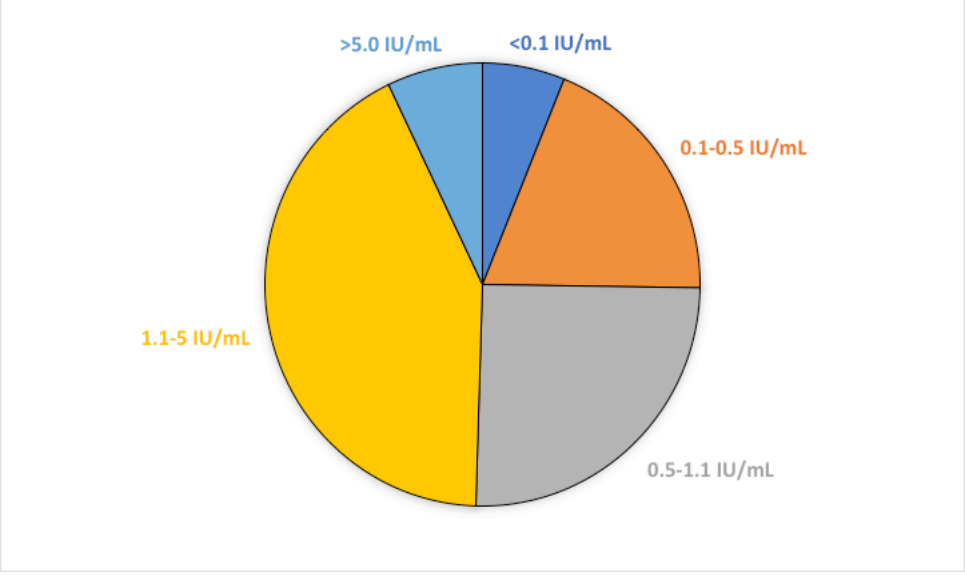

Figure 1. Antibody distribution of patients in the study.

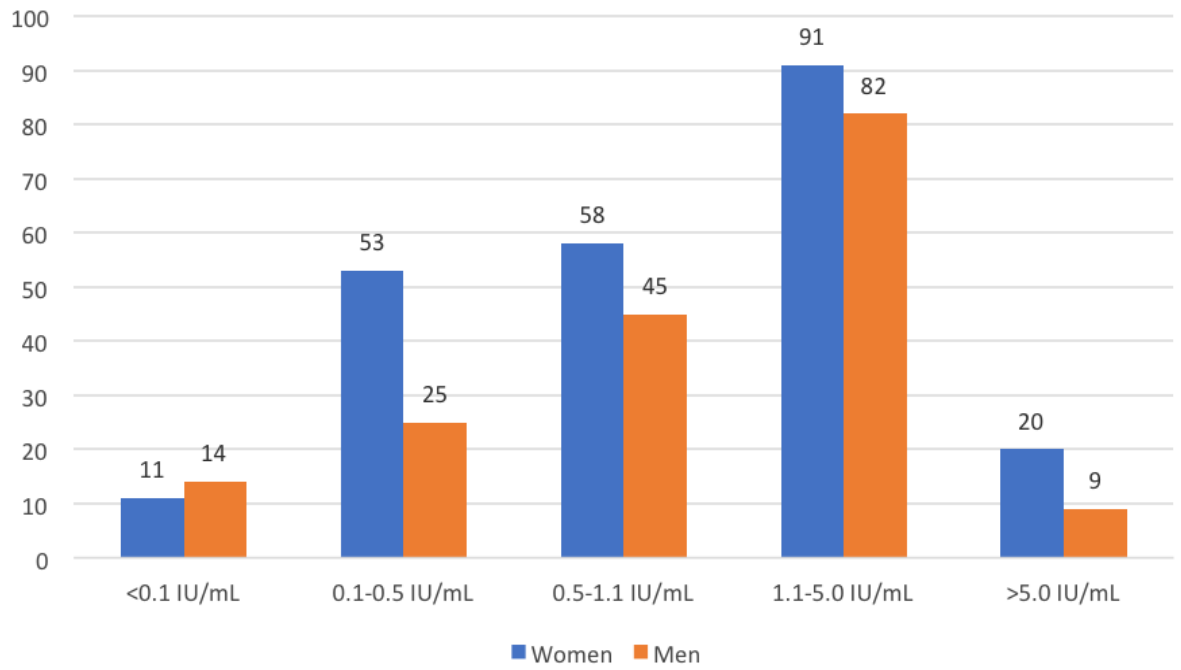

Figure 2. The relationship and distribution of antibody groups with gender

Table 2. The relationship and distribution of antibody groups with age

Tetanus IgG Level	Age group		p-value
	40 years and younger n (%)	Over 40 years old n (%)	
<0.1 IU/mL	2 (0.8)	23 (13.4)	0,001
0.1-0.5 IU/mL	32 (13.6)	46 (26.7)	
0.5-1.1 IU/mL	65 (27.5)	38 (22.1)	
1.1-5.0 IU/mL	117 (49.6)	56 (32.6)	
>5.0 IU/mL	20 (8.5)	9 (5.2)	

DISCUSSION

In our study, no statistically significant difference was found between genders in terms of tetanus antibodies, while a moderate negative correlation was found between age and antibody levels.

Tetanus is a vaccine-preventable disease with a high mortality and morbidity. For this reason, it is important to carry out vaccination programs in adulthood as well as childhood (9,10). Tetanus antibody levels vary depending on the development level and vaccination program of the country. A study

of 255 adults in India reported that 47% had antibody levels <0.1 IU/mL and were nonprotected against tetanus (11). In a study in Spain, tetanus antibodies were evaluated in 1296 people and 68.3% of people were found to have protective antibody levels (12). In a study conducted in healthcare workers in China, it was determined that 29.82% had an antibody level of <0.1 IU/ml (13). In a study conducted in 295 people in Edirne, protection against tetanus was found to be 98.6%, and in a study conducted in our hospital in 2021, protection against tetanus was found to be 82.5% (6,14). In our study, protection against tetanus was found to be 93.9% which is higher than the literature. We think that the reason for this may be due to the vaccination programs and the immune response of the patients included in the study.

In some studies in the literature, it is reported that higher tetanus antibody levels are seen in the male gender. It is reported that the reason for this situation may be the booster doses administered during military service and injury (12,15). In our study, although higher antibody titers were detected in the male gender, no statistically significant difference was found ($p>0.05$). The immune response to tetanus vaccination decreases over the years. Studies have shown that higher levels of antibodies are produced in young adults after vaccination than in the elderly. In the literature, it is reported that after 10 years or more, a booster dose should be given, especially in the elderly population (16). In many studies, antibody titers that are unprotected against tetanus (<0.1 IU/mL) have been detected, especially in the elderly population (17-19).

In our study, it was determined that 92% of the group with antibody titers lower than 0.1 IU/mL were adults over 40 years of age. In our study, similar to the literature, the decrease in tetanus antibodies as age increased was found to be statistically significant. ($r=-0.334$; $p<0.001$). The lower tetanus antibody levels in adults over 40 years of age were found to be statistically significant compared to adults aged 40 and under ($p<0.001$). Immigrants leaving countries where vaccination programs are not effectively implemented pose a significant risk of tetanus in the countries where they settle. In a multicenter study involving six European countries, it was found that 22.3% of migrants did not have a protective tetanus antibody titer (<0.1 IU/mL) (20).

Since our study is a retrospective study, the vaccination status of the individuals included in the study is unknown. We believe that more than 10 years have had passed since the vaccination of the adults included in our study whose tetanus antibody levels were not at a protective level.

Although tetanus is a vaccine-preventable disease with a high mortality and morbidity, it can still be seen worldwide. Preventive health services constitute the most important part of health policies in developed countries. After routine vaccination in our country since 1968, a single booster dose is recommended for men during military service and two doses during pregnancy for women.

It is essential to administer a booster dose to increase the levels of antibodies against tetanus that decrease in older ages. Especially for individuals over the age of 20, antibody levels should be followed every 10 years and a booster dose should be administered if necessary. The public should be informed about the risk factors, transmission routes, clinical findings and mortality of tetanus, and it should be ensured that the vaccinations of unvaccinated or of incompletely vaccinated people should be performed.

Since our study was planned retrospectively, we believe that the limitations of our study were the inability to obtain vaccination status, risk factors, and sociodemographic data of the individuals included in the study.

ETHICS COMMITTEE APPROVAL

* The study was approved by the Necmettin Erbakan University Non-Drug and Non-Medical Device Research Ethics Committee Ethics Committee (Date: 20.09.2024 and Number: 2024/5181).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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