Original Article

Epidemiological Study of Tetanus Seropositivity Levels in Different Age Groups in Ankara Province, Turkey, 2017

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SUMMARY: The aim of this study was to determine the seropositivity levels of tetanus vaccine by age group in Ankara province, identify possible factors that affect immune status, and develop public health recommendations, especially for those 50 years and older. This cross-sectional epidemiological study covered individuals aged 3 years and older who are registered in the Family Medicine Information System. We received blood samples from 992 individuals and included 968 surveys in the analysis. Protective tetanus antibody levels were 80.5% in the 3–5 years age group, 92.0% in the 6–12 years age group, 94.3% in the 13–20 years age group, 95.2% in the 21–39 years age group, 84.4% in the 40–49 years age group, and 57.3% in the 50 years and older age group. Tetanus seropositivity decreased with age. Awareness of the importance of tetanus vaccine boosters for adults should be increased by providing training, ensuring booster vaccination against tetanus at 10-year intervals, and if necessary, considering mandatory tetanus vaccination for those 50 years and older.

INTRODUCTION

Tetanus is a vaccine-preventable, global infectious disease caused by Clostridium tetani (C. tetani) (1). The U.S. Centers for Disease Control and Prevention receives between 35 and 70 reports of domestic cases each year. Most reported cases are patients older than 60 years, indicating that waning immunity is an important risk factor. Tetanus is always acute in onset and characterized by persistent tonic spasm, with brief, violent exacerbations (2).

In Turkey, nationwide vaccination of tetanus started in 1935 (3), and the vaccination schedule currently recommended by the Ministry of Health requires administering 4 doses of diphtheria-tetanus-acellular pertussis-inactive poliovirus-Haemophilus influenzae type b (DaBT-IPA-Hib) at ages 2, 4, 6, and 18 months, one dose of diphtheria-tetanus-acellular pertussis-inactive polio (DaBT-IPA) at 6 years, and one dose of tetanus adult diphtheria (Td) at 13 years (4). For adults, primary vaccination consists of 3 doses. The first 2 doses should be administered at 4-week intervals, and the third dose approximately 6–12 months following the second dose. It is recommended that adults who have completed primary vaccination receive Td boosters every 10 years and that one of these boosters be tetanus, adult diphtheria, acellular pertussis (Tdap) (5).

According to surveillance data collected by the Department of Vaccine Preventable Diseases in General Directorate of Public Health, while the number of cases of tetanus in Turkey has decreased over time between 1980–2016, cases do still occur (Fig. 1).

The purpose of this study is to determine the seropositivity levels of tetanus vaccine in different age groups in Ankara province, identify possible factors that could affect immune status, obtain information that can be used for additional tetanus vaccination studies, and develop public health recommendations, especially for those 50 years and older.

MATERIALS AND METHODS

Study group: This research was conducted in the province of Ankara and includes individuals 3 years and older registered in the Family Medicine Information System. This system covers 99.8% of Ankara residents. Since the tetanus vaccine is administered at 6 years, 13 years, and military age according to the Ministry of Health vaccination schedule, age groups were classified as follows: 3–5 years, 6–12 years, 13–20 years, 21–39 years, 40–49 years, and 50 years and older. To determine specific seroprevalence for each age group, sample sizes were calculated for each group using the OpenEpi statistical program. The expected level of immune response was 85% ± 5 for the population under 50 years of age and 50% ± 5 for the population 50 years and older. Sample size was separately calculated for every age group, and the total sample size was 1,957.

Data collection tools and methods: For this cross-sectional epidemiological study, we used a questionnaire...
The Tetanus Seropositivity in Ankara

15 form which included sociodemographic characteristics (age, sex, type of work, etc.), tetanus vaccination status, tetanus disease status, admission to healthcare facilities after injury, tetanus vaccination status after injury, access to vaccination services, and chronic diseases. The questionnaire form was completed during face-to-face interviews, and a venous blood sample was collected by healthcare personnel. Data collection started on June 5, 2017, and was completed on December 18, 2017. Blood samples were collected from 992 individuals. The nonresponse rate was 49%. We analyzed 992 blood samples in terms of age, sex, and tetanus antibody levels. Questionnaires that were accurately completed and included socio-demographic characteristics, such as educational level, economic status, and tetanus vaccination status, were included in the study. In total, 968 questionnaires were used in the analysis.

Definitions of seropositivity and seronegativity: We considered ≥ 0.1 IU/ml serum antibody levels as ‘Protective’, 0.01–0.099 IU/ml as ‘Partial Protective’, and < 0.01 IU/ml as ‘Negative’. For analysis, protective levels were defined as ‘Seropositive’ while partial protective and negative levels were defined as ‘Seronegative’.

Laboratory: Serological tests were carried out in the vaccine-preventable diseases laboratory of the Department of Microbiology Reference Laboratories and Biological Products. Tetanus IgG levels in serum samples were detected using a commercially available quantitative sandwich enzyme-linked immunosorbent assay test (IBL International, Frankfurt, Germany).

Ethical issues and permissions: Since the research was conducted by the General Directorate of Public Health to recommend effective interventions for public health purposes, this study did not receive ethics committee approval.

Data analysis: We used proportions, chi-square test for seropositive and seronegative intergroup comparisons, and odds ratio (OR) at 95% confidence interval (CI) for data analysis. Statistical significance level was accepted at 5%. For further analysis, logistic regression analyses were separately performed for all age groups using the IBM SPSS Statistical Program. Factors associated with seronegativity and factors with \( p < 0.20 \) were also included in the model when the logistic regression model was constructed, and a final model was constructed using the backward Wald method. The logistic model for the age group 50 years and older included sex, presence of chronic disease, education level, presence of tetanus vaccination in the past 10 years, and admission to healthcare facilities.

RESULTS

Of the participants, 48% were female and 52% were male. The mean age was 33 \( \pm \) 23, and the median age was 30 years with a range of 3–104 years. Among the 788 seropositive subjects, 45.2% were female and 54.8% were male. Tetanus-protective antibody levels were 80.5% in the 3–5 years age group, 92.0% in the 6–12 years age group, and 57.3% in those 50 years and older (Table 1).

As shown in Fig. 2, the levels of tetanus protection increased with age after tetanus vaccination and decreased after 50 years of age.

Variables that may affect tetanus immunity, including sex, educational status, family type, economic status, chronic illness, tetanus vaccination status, admission to healthcare facilities after injury, and tetanus vaccination after injury, were evaluated in 968 subjects. In the 6–12 years age group, 55% of the seropositives and 15% of the seronegatives were male. The odds of being male was 6.8 times higher (95% CI: 1.4–31.8) in seropositives \( (p = 0.005) \). In the 40–49 age group, odds of education level of primary school or lower was 3.8 times higher (95% CI: 1.1–14.0) in seropositives \( (p = 0.030) \) (data
In seropositive individuals 50 years and older, the odds of being male was 1.7 times higher, education level of secondary school or higher was 2.0 times higher, having at least one chronic disease was 1.9 times higher, tetanus vaccination in the past 10 years was 2.3 times higher, and admission to healthcare facilities after injury was 2.2 times higher than in other groups (Table 2).

Childhood vaccination status could not be determined for this age group as these records are not available in the electronic health record for patients of this age.

After controlling for external factors, adjusted odds ratio (OR_adj) was 2.5 in those with an education level of primary school or lower, 2.7 in those who had not received the tetanus vaccine within the past 10 years, and 2.6 in those who were not admitted to healthcare facilities after injury (Table 2). Childhood vaccination status could not be determined for this age group as these records are not available in the electronic health record for patients of this age.

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The primary reasons for non-vaccination in time were 'unawareness of the necessity of the next dose' and 'the gap of knowledge for timeliness of vaccination.' In addition, 50% of those indicating unawareness and two-thirds of those indicating gap of knowledge were 50 years and older.

**DISCUSSION**

Tetanus is a disease that can be prevented by vaccination. Although tetanus vaccination campaigns have been initiated in our country with extensive immunization programs, cases of tetanus still do occur. According to the Ministry of Health vaccination schedule, the tetanus vaccine is administered to school pupils younger than 13 years of age with no routine vaccination program after this period, except in pregnancy or those in the military. Adults are recommended to have a booster every 10 years, but since this is not mandatory, tetanus vaccination is administered to individuals electively in the hospital or after an injury. There is no surveillance for tetanus vaccination in adults in Turkey. If the tetanus vaccine booster is not administered, the level of tetanus-protective antibody decreases with age and the risk of illness increases. According to surveillance data collected by the Department of Communicable Diseases, 46 of 62 reported cases of tetanus (74.2%) diagnosed between 2012 and 2016 were 45 years and older. One of the objectives of our study was to determine the level of tetanus-protective antibodies in individuals aged 50 years and older and to develop recommendations that will ensure that necessary preventive measures can be taken.

Tetanus seropositivity decreased with age in our study, decreasing to 57.3% in those over 50 years. This result was expected for our country, and has been shown in other countries. Öncü et al. reported that tetanus seropositivity in a village of Aydin province in Turkey between March 2010 and June 2011 was 51.5% in those

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**Table 1. Tetanus antibody levels (%) by age groups**

| Age Group (yr) | Negative | Partial Protective | Protective | Total |
|----------------|----------|-------------------|------------|-------|
|                | n  | %    | n  | %    | n  | %    |
| 3–5            | 2  | 1.5  | 24 | 18.0 | 107 | 80.5 | 133 |
| 6–12           | —  | —    | 13 | 8.0  | 150 | 92.0 | 163 |
| 13–20          | —  | —    | 9  | 5.7  | 148 | 94.3 | 157 |
| 21–39          | 1  | 1    | 4  | 3.8  | 99  | 95.2 | 104 |
| 40–49          | —  | —    | 20 | 15.6 | 108 | 84.4 | 128 |
| 50 years and older | 1 | 0.3  | 130 | 42.4 | 176 | 57.3 | 307 |
| Total          | 4  | 0.4  | 200| 20.2 | 788 | 79.4 | 992 |

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**Fig. 2. Age-specific protective levels (%).**
The Tetanus Seropositivity in Ankara

17

50–59 years, 36.4% in those 60–69 years, and 9.5% in those 70 years (6). In a study conducted in Kocaeli province in Turkey, protective antibody level was found to be 65.5% in those over 60 years old (7). Similar results have been found in other countries. The prevalence of tetanus-protective antibodies in those 64 years and older in the Catalonia region of Spain was found to be 57.1% (8). In a study conducted in Korea in 2012, 6 groups above the age of 11 were formed. Seroprevalence of tetanus declined with increasing age; 92% in the 11–20 years age group, 33.3% in the 41–50 years age group, 17.3% in the 51–60 years age group, and 19.3% in the age group 61 years and older (9). Vaccination programs in these countries are similar to Turkey, with no mandatory vaccination for adults (8,9).

According to the Ministry of Health vaccination schedule, at least 4 doses of tetanus vaccine should be administered to children by the age of 3. It is expected that children of this age with all vaccinations will be protected by 99% (3). The reason that tetanus-protective antibody level was found to be 80.5% in the 3–5 years age group in our study could be that vaccination efforts did not reach all children in this population.

According to the literature, as the level of education decreases seropositivity level decreases and seronegativity increases (6,7,10,11). Evaluating the characteristics of the seronegative group separately, we found that 64% were 50 years and older (Table 1) and 59% of the seronegative group had an education level lower than secondary school (data not shown). Since tetanus seropositivity can be achieved with vaccination, vaccinated individuals are expected to be seropositive. The reason we observed this outcome in the lower educational levels could be that this group tends to have incomplete information regarding tetanus vaccination. For example, vaccinated individuals may not be aware that the vaccine should be re-administered every 10 years in adulthood. In our study, we found this reason to be particularly

| Characteristics | n (%) | Seropositivity n (%) | Seronegativity n (%) | OR (95%CI) | p |
|-----------------|-------|----------------------|----------------------|------------|---|
| Sex             |       |                      |                      |            |   |
| Male            | 135 (44) | 87 (49) | 48 (37) | 1.7 (1.1–2.6) | 0.025 |
| Female          | 172 (56) | 89 (51) | 83 (63) |            |     |
| Education status|       |                      |                      |            |   |
| Secondary school or higher | 121 (41) | 82 (48) | 39 (32) | 2.0 (1.2–3.2) | 0.006 |
| Primary school or lower | 172 (59) | 89 (52) | 83 (68) |            |     |
| Family structure|       |                      |                      |            |   |
| Nuclear         | 216 (78) | 127 (79) | 89 (77) | 1.1 (0.6–2.1) | 0.598 |
| Others          | 60 (22) | 33 (21) | 27 (23) |            |     |
| Perceived economic status|       |                      |                      |            |   |
| Poor            | 36 (12) | 23 (14) | 13 (10) |            |     |
| Fair            | 185 (63) | 104 (62) | 81 (65) |            |     |
| Well            | 72 (25) | 41 (24) | 31 (25) |            |     |
| Chronic disease |       |                      |                      |            |   |
| Yes             | 191 (64) | 99 (58) | 92 (72) | 1.9 (1.1–3.1) | 0.011 |
| No              | 106 (36) | 71 (42) | 35 (28) |            |     |
| Tetanus vaccination status |       |                      |                      |            |   |
| In the last 10 years | 63 (36) | 50 (42) | 13 (24) | 2.3 (1.1–4.9) | 0.017 |
| Later than 10 years | 110 (64) | 68 (58) | 42 (76) |            |     |
| Admission to health facilities after injury |       |                      |                      |            |   |
| Yes             | 103 (74) | 70 (80) | 33 (63) | 2.2 (1.04–4.8) | 0.037 |
| No              | 37 (26) | 18 (20) | 19 (37) | 2.0 (0.9–4.2) | 0.068 |
| Tetanus vaccination after injury |       |                      |                      |            |   |
| Yes             | 58 (46) | 42 (53) | 16 (36) |            |     |
| No              | 67 (54) | 38 (47) | 29 (64) | 2.0 (1.1–3.6) | 0.034 |
| Tetanus vaccination at pregnancy |       |                      |                      |            |   |
| Yes             | 32 (80) | 25 (83) | 7 (70) | 2.1 (0.4–11.2) | 0.387 |
| No              | 8 (20) | 5 (17) | 3 (30) |            |     |
| Tetanus vaccination at military |       |                      |                      |            |   |
| Yes             | 62 (70) | 37 (69) | 25 (74) | 0.8 (0.3–2) | 0.615 |
| No              | 26 (30) | 17 (31) | 9 (26) |            |     |

1): 148 people with unknown tetanus vaccination status were excluded from the study.
2): Fischer’s exact test.

Table 3. Possible risk factors for seronegativity in 50 years and older adults

| Risk factors | ORadj (95%CI) | Wald (p) |
|--------------|---------------|----------|
| Primary school or lower education | 2.5 (1.1–5.6) | 0.028 |
| Non-vaccinated by tetanus vaccine in the last 10 years | 2.7 (1.1–6.9) | 0.034 |
| People who didn’t admit to health facilities after injury | 2.6 (1.1–6.5) | 0.039 |
important in this age group.

Adults have the opportunity to receive vaccinations when they are seen in healthcare facilities after injuries. Among the elderly, accidents at home are more frequent due to decreased functional capacity and loss, muscle weakness, slowing of movements, and increased time spent at home (12,13). Chronic diseases and home injuries are expected to be more common in this age group, and injuries are also likely to occur. Vaccines are administered to patients electively when they visit a healthcare facility after injury. In our study, however, we observed that one out of 4 in this age group did not visit any healthcare facility after injury. In our study, however, we observed that one out of 4 in this age group did not visit any healthcare facility after injury (Table 2). Similarly, a study conducted in 2002 found that only 37.4% of the elderly who had an accident at home visited a healthcare facility (14).

As tetanus vaccination is not mandatory for adults, tetanus vaccination is not possible unless admitting to a medical center after injury, during pregnancy, or in the military. Increasing levels of tetanus antibodies following tetanus vaccine boosters indicate that the vaccine is effective and that booster doses are necessary. Our study shows that the level of tetanus-protective antibodies decreases with age, and many adults are not aware that a booster dose is necessary every 10 years.

It will be useful to increase awareness in adults of the importance of tetanus vaccine boosters through trainings, administer tetanus vaccine booster at 10-year intervals by monitoring, carry out studies to define protective tetanus antibody levels, and if necessary, consider mandatory tetanus vaccination for those 50 years and older. This can help to increase levels of tetanus-protective antibodies in older age groups.

Conflict of interest None to declare.

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