

Seroprevalence of Tetanus Antibody in the Thai Population: A National Survey

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SUMMARY Tetanus is a disease with high mortality and the most important measure for effective prevention is vaccination. Tetanus immunization has been introduced to Thailand's national immunization program for 30 years. Yet, the coverage and seroprevalence of tetanus antibody in vast parts of the population has not been assessed. This study has been performed on 1,277 subjects aged between 6 months and 60 years or above from four geographically distinct provinces of Thailand. Tetanus antibody levels were measured using a commercially available ELISA kit. Most of the Thai population had immunity against tetanus. The level of antibodies to tetanus, as demonstrated by the geometric mean titer of antibody (GMT) (and 95% confidence interval) was 2.62 (2.34-2.91) IU/ml. The highest and lowest GMT was found in subjects aged between 5 and 9 years, and above 60 years of age with GMT (and 95% confidence intervals) of 3.64 (3.34-3.96) and 1.24 (0.67-2.29) IU/ml respectively. The minimum protective level of antitoxin (>0.01 IU/ml) was detected in 99.7 % of subjects. More than 90% of subjects displayed durable antibody protection levels (DAPL) (≥ 1.0 IU/ml), except for subjects above the age of 60 years (82%). According to this study, the majority of the population expresses tetanus antibody levels that can confer long term protection. Yet, considering the lowest GMT and the highest incidence of tetanus cases found in subjects aged above 60 years, re-immunization should be targeted at this age group especially if they had sustained any tetanus-prone injury.

Tetanus, a disease caused by a toxin produced by *Clostridium tetani* in contaminated wounds, incurs a high mortality rate.¹ Obviously, vaccination represents the most important measure for effective and extensive protection against tetanus. Immunization against tetanus has been introduced to Thailand's national immunization program since 1977, and the coverage is targeted at 90%. Three doses of the vaccine are administered at two, four and six months of age, followed by the fourth dose at 18 months and the fifth dose at 4 to 6 years of age. The booster dose is given at the age of 12 to 16 years.

Since 1992, tetanus vaccine coverage in children below the age of one year has exceeded 90%. Yet, data on the coverage rate among older age groups has been limited. In 1977, tetanus immunization comprising two injections during the last trimester has been recommended to pregnant women to prevent

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neonatal tetanus. In 1993, the number of injections has been increased to three in order to ensure long term protection. Tetanus immunization coverage in pregnant women has been increased from 55% in 1986 to 85% in 1992 and 90% in 1999.² Tetanus toxoid is also given routinely to individuals with tetanus-prone wounds. Yet, the coverage has not been assessed. According to the records of the Ministry of Public Health of Thailand, in the year 2005 there have been 166 cases of tetanus (0.27/100,000) with 5 deaths, and 6 cases of neonatal tetanus with one death. In 2006, there have been 143 cases of tetanus (0.23/100,000) with 11 deaths, and 3 cases of neonatal tetanus (0.37/100,000 live births) with 2 deaths.² Tetanus cases in Thailand tend to occur among older age groups especially in the over 60-year old with the rate of 24%, 21% and 19% in population age > 65 years, 55-64 years and 45-54 years, respectively. The case rate and death rate has been declined since 1997.²

The minimum protective level along with seropositivity is considered to be 0.01 IU/ml and durable antibody protection levels (DAPL) are ≥ 1.0 IU/ml³. An antibody level below 0.01 IU/ml is a strong evidence that an individual either has never received the primary tetanus vaccine or has not received a booster injection during the preceding decade. In order to evaluate the impact of the national immunization program and arrive at an appropriate recommendation for tetanus immunization among the Thai population, it is necessary to determine tetanus antibody and the protective status among individuals of various age groups and within a larger population group.

MATERIALS AND METHODS

The ethics of this study were approved by the Ministry of Public Health and the Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.

Study population

In 2004, the populations studied were part of a separate research project investigating the seroprevalence of hepatitis A antibody in Thailand and the impact of universal mass vaccination against hepatitis B virus infection 12 years after hepatitis B

vaccine had been integrated into the national expanded program on immunization.^{4,5} The study was a hospital-based cross-sectional study. We selected Chiangrai, Udonrthani, Chonburi and Nakhon Si Thammarat as the geographical representations of people in the North, Northeast, Center and South of the country, respectively. In each province, the provincial hospital and two to three additional district hospitals were chosen provided that they had good medical service facilities and were situated at different geographical locations within the provinces. The details of the study have been reported elsewhere.^{4,5}

The participants were healthy children attending the well baby clinic or patients with acute illness, who attended either the out-patient clinic or the in-patient ward at those four provincial hospitals or the participating district hospitals. The sample size was calculated based on the pilot study on the prevalence of tetanus antibody by the Bureau of General Communicable Diseases, Department of Disease Control, Ministry of Public Health, Thailand. The subjects had to fulfill the following criteria: no chronic illness, not subjected to immunosuppressive therapy, no clinical signs or symptoms associated with either HIV infection or any immunodeficiency related diseases.

Either the participants themselves or their guardians answered questionnaires on education, occupation, annual income, medical history, vaccination, and gave their informed consent.

Laboratory tests

Blood samples were collected and stored at -70°C . Concentrations of tetanus antibody were measured in IU/ml, and the control standards were calibrated against the World Health Organization international reference 76/589. The minimum protective level of antitoxin was considered to be 0.01 IU/ml and durable antibody protection levels (DAPL) were ≥ 1.0 IU/ml. Tetanus antibodies were measured using commercially available solid phase enzyme-linked immunosorbent assay (ELISA) kits (IBL ImmunoBiological Laboratories, Hamburg, Germany) based on the sandwich principle. The specific antibodies of the sample binding to the antigen coated well were detected by the enzyme conjugated anti-human IgG antibody. Upon reaction completion,

the developed color is measured and compared with the standard curve to detect the amount of IgG antibodies in the respective samples.

Data analysis

The geometric mean titers (GMTs) were compared using the unpaired t test. The seroresponse rates were shown in percentage and compared using the chi-square test.

RESULTS

Taken from the 6,213 subjects participated in the previous study,⁴ a total of 1,277 individuals were randomly evaluated in this study. The population distributions of Chiangrai, Udonrthani, Chonburi and Nakorn Si Thammaraj as the geographical representations of people in the North, Northeast, Center and South of the country amounted to 27.1%, 27.9%, 22.1% and 22.9%, respectively, with 540 (42.3%) males and 737 (57.7%) females. Three hundred and thirty-two (36%) were children below the age of 15 years. Protective antibody levels according to age groups are shown in Table 1. The level of antibodies to tetanus, as demonstrated by the geometric mean titer of antibody (GMT) (and 95% confidence interval) was 2.62 (2.34-2.91) IU/ml. The highest and lowest GMT was found in subjects aged between 5 and 9 years, and above 60 years of age with GMT (and 95% confidence intervals) of 3.64

(3.34-3.96) and 1.24 (0.67-2.29) IU/ml respectively. The GMT in each age group and the total population is shown in Fig. 1.

A minimum protective level of antitoxin (> 0.01 IU/ml) was detected in 99.7% of the subjects. The proportion of subjects expressing durable antibody protection levels (DAPL) (≥ 1.0 IU/ml) was 94.6%. The proportion of subjects with protective antibody levels exceeded 95% in each age group. More than 90% of subjects from every age group displayed durable antibody protection levels, except for the group comprising subjects above the age of 60 where only 82% expressed high levels of tetanus antibody. As to the rate of immunity (99.4% vs. 99.9% $p = 0.78$) and GMT (3.29 vs. 3.34 IU/ml, $p = 0.63$), there was no significant difference between male and female subjects.

DISCUSSION

In this study we demonstrated that the majority of the Thai population are immune to tetanus with 99.7% of all subjects expressing protective antibody levels and 94.6% displaying durable antibody protection levels (DAPL). The highest GMT was found in the group of subjects aged between 5 and 9 years. This may be due to the booster effect of the fifth dose of tetanus vaccine which is given at the age of 4 to 6 years. The lowest GMT was found in subjects aged above 60 years which may be ex-

Table 1 Protective antibody levels according to age groups

Age group	N (% within age group)		Tetanus antibody level (IU/ml)		
			< 0.01	0.01-0.9	>1
0-4	123	(9.6)	0	5 (4.1)	118 (95.9)
5-9	118	(9.2)	0	1 (0.8)	117 (99.2)
10-14	91	(7.1)	0	0	91 (100.0)
15-19	79	(6.2)	0	2 (2.5)	77 (97.5)
20-24	79	(6.2)	0	2 (2.5)	77 (97.5)
25-29	78	(6.1)	0	4 (5.1)	74 (94.9)
30-39	240	(18.8)	0	13 (5.4)	227 (94.6)
40-49	244	(19.1)	1 (0.4)	18 (7.4)	225 (92.2)
50-59	190	(14.9)	2 (1.1)	15 (7.9)	173 (91.1)
≥ 60	35	(2.7)	1 (2.9)	5 (14.3)	29 (82.9)
Total	1,277	(100.0)	4 (0.3)	65 (5.1)	1,208 (94.6)

plained by the waning of antibody, the impairment of antibody production along with decreased immunological memory in older subjects. This finding may also be due to lack of immunization in this group since they had been born before the introduction of tetanus immunization into Thailand's national immunization program. In our study, there was no difference in tetanus immunity between male and female subjects, similar to the survey from Turkey.⁶ This result was in contrast with studies from some other countries such as the United States, Australia, and Spain⁶⁻¹⁰ which showed that more men than women were immune. The majority of the Thai population (94%) in this study had tetanus antibody in DAPL which are considered to convey long term and effective protection. Yet in the older age group, the proportion of subjects with antibody in DAPL dropped to 82%. The incidence of tetanus and tetanus neonatorum in Thailand has been consistently decreasing from 891 (1.72/100,000 population) and 564 (57.93/100,000 live birth) in the year 1985 to 143 (0.23/100,000 population) and 3 (0.37/100,000 live birth) cases in the year 2006, respectively,² which can be explained by our study showing tetanus

immunity in the majority of the Thai population. Yet, since herd immunity does not occur in tetanus, tetanus immunization has to be continued aimed at covering the entire population especially high risk groups such as pregnant women and the elderly.

In conclusion, the national immunization program in Thailand has been effective in providing tetanus immunity to the general population of all age groups. More than 99% of the Thai population are immune against tetanus with 95% expressing antibody levels that can confer long term protection. Young children had the highest levels of tetanus antibody. According to this study, the population above 60 years of age should be targeted for re-immunization especially if they had sustained any tetanus-prone injury.

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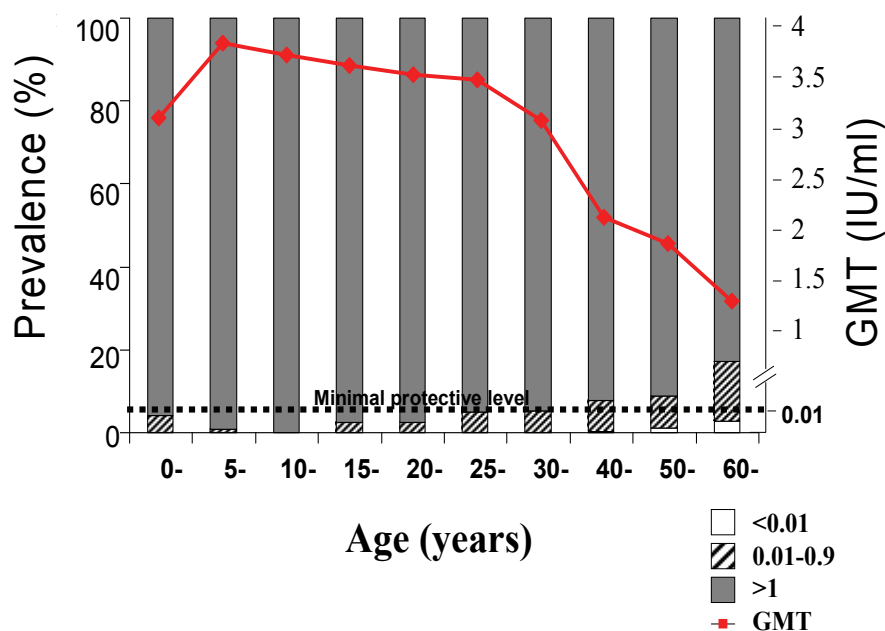


Fig. 1 Seroprevalence of tetanus antibody in the general population according to age groups. Bars indicate prevalence in percent. Line plot indicates GMT (IU/ml).

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