

A comparison of tetanus antibody levels between patients with high body mass indices and normal patients

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Abstract

Aim: It has recently been thought that obesity may cause metabolic diseases as well as being linked to immune system dysfunction. The purpose of this study was to compare tetanus antibody levels between patients with high body mass indices and healthy-weight individuals and to examine the effect of obesity on tetanus antibody levels in adults.

Materials and Methods: This cross-sectional research was performed at Duzce University, Faculty of Medicine from December 2018 to February 2019. The study group was composed of obese patients who had undergone tetanus immunization within the previous 10 years. The control group consisted of healthy-weight individuals who had also been immunized in the previous 10 years. An enzyme-linked immunosorbent assay kit (Euroimmun, Germany) was used to detect antibodies to tetanus toxoid.

Results: Sixty-seven individuals with obesity and 21 controls participated in this study. Anti-tetanus IgG antibodies were at protective levels in both groups, although the mean antibody level in the patients with obesity was significantly lower compared to the control group (0.788 ± 0.602 vs 1.112 ± 0.398 , $p=0.022$). Anti-tetanus IgG antibodies were significantly negatively correlated with BMI ($r=-0.269$, $p=0.016$).

Conclusion: The detection of low levels of tetanus antibody titers in patients with high BMI in this study compared to the control group suggests that greater attention is required in this population.

Keywords: Immunization; obesity; tetanus; tetanus antibody levels

INTRODUCTION

Obesity is the result of environmental and biological factors leading to excess adipose tissue deposition. This is also correlated to a greater prevalence of conditions linked to increased morbidity and mortality (1,2). Under the body mass index (BMI) classification recommended by the National Institutes of Health, individuals are regarded as underweight ($BMI \leq 18.5 \text{ kg/m}^2$), normal weight ($18.5-24.9 \text{ kg/m}^2$), overweight ($25.0-29.9 \text{ kg/m}^2$), obese ($30.0-34.9 \text{ kg/m}^2$), or severely obese ($\geq 35 \text{ kg/m}^2$) (3). BMI is also referred to as the Quetelet index, and is a valuable tool for identifying patients at risk of weight-associated complications, including a poor vaccine-associated immune response (4,5). Overweight and obesity have become significantly more prevalent worldwide over the last 30 years (40.3% and 42.2% in men and 39.7% and 43.3% in women, respectively), and are now severe threats to human health (6,7). Recent evidence seems to indicate that obesity may be linked to immune system dysfunction developing in parallel to increased weight (8).

Immunization is the most important and efficacious tool against several contagious diseases (9). However, despite this success, various sub-populations, such as individuals with obesity, exhibit a weak or poor response to immunization and are at risk of diseases that can be prevented through it (10). Studies have shown that leptin produced by adipocytes leads to an impairment in the immune response developing against vaccination and infection (11). Two studies observed significant decreases in the formation of antibodies against vaccines developed for tetanus and rabies, and reported that underlying factors associated with obesity limited the response to immunization and left many individuals vulnerable to disease-related complications (12,13). Tetanus, one of the diseases that can be prevented through immunization, is an infectious disease with high mortality affecting infants and young adults in developed countries and the elderly in developed countries (14,15). The Advisory Committee on Immunization Practices (ACIP) recommends that tetanus vaccinations be repeated once every 10 years in adults (16).

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However, there has been only limited research into the response to tetanus antibodies in overweight or obese adults.

The purpose of the present study was to evaluate tetanus antibodies in overweight and normal weight patients based on BMI values, and to investigate whether BMI is associated with levels of tetanus antibody titers.

MATERIALS and METHODS

Serum collection and study design

Sixty-seven obese individuals and 21 controls (≥ 18 years) participated in this cross-sectional study between December 2018 and February 2019. All patients were diagnosed at the Duzce University, Faculty of Medicine Patients with BMI values ≥ 30 constituted the obese group. The control group was selected from healthy volunteers with BMI values ≤ 24.9 . During our inquiry into histories of tetanus vaccination, individuals who had been vaccinated within the previous 10 years were enrolled from among the patients in both groups in order to ensure standardization. Individuals unable to remember their tetanus vaccination histories for the previous 10 years were excluded.

BMI measurement

Height was calculated using a standard calibrated stadiometer, and body mass using calibrated scales. These data were in turn employed to calculate body mass index (BMI) (weight / height²) values. BMI percentiles were also calculated for each adult based on the applicable standards published by the Centers for Disease Control, National Center for Health Statistics (3).

Overweight and control group demographic data (age, sex, weight, and education status), biochemical data (urea, creatinine, fasting blood sugar, cholesterol, triglyceride, and alanine aminotransferase) and Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) measurements (HOMA-IR= ((fasting insulin (mU/mL) x fasting glucose (mg/dL))/405)) were recorded.

Tetanus antitoxin measurement

Blood specimens collected from patients with BMI ≥ 30 and the control groups were centrifuged for 10 min at 3000 rpm. The resulting serum specimens were then placed into Eppendorf tubes and stored at -80°C until serological analysis. A commercially-available indirect enzyme-linked immunosorbent assay (ELISA) kit (Virotech, Germany) was employed to determine antibodies to tetanus toxoid. Anti-tetanus IgG antibody levels less than 0.1 IU/ml were regarded as indicating susceptibility, while levels between 0.1 and 1.0 IU/ml were regarded as protective, and levels exceeding 1.0 IU/ml were interpreted as being long-term protective (17).

Statistical Analysis

Statistical analysis was carried out on SPSS (Statistical Package for Social Sciences) for Windows 22 software. The Kolmogorov–Smirnov test was employed to assess the distribution of variables. Homogeneously distributed variables were expressed as mean \pm SD, and comparisons between these were performed using the independent

samples t-test. Student's t test was applied to compare mean Anti-tetanus IgG antibody levels in overweight and normal weight patients. Non-homogeneously distributed variables were expressed as median (minimum-maximum) values, and comparisons were performed by applying the Mann–Whitney U test. The χ^2 test was employed to compare categorical variables. Receiver operating characteristic (ROC) curve analysis was employed to calculate optimal cut-off values for identifying maximum sensitivity and specificity for determining antibody levels between the two study groups. Pearson's correlation analysis was applied to identify associations between age, weight, BMI and HOMA-IR parameters and Anti-tetanus IgG antibodies. p values < 0.05 were considered statistically significant.

RESULTS

Eighty-eight individuals were enrolled in the study, 67 patients with BMI ≥ 30 and a 21-member normal weight control group. The mean age of the high BMI patient group was 47 ± 14 years, and that of the control group was 39 ± 18 years ($p = 0.060$). Gender distributions between the two groups were similar, women constituting 86.5% of the obese group and 74.1% of the control group ($p = 0.179$). Significant differences were determined between the groups in terms of weight, BMI, glucose, HOMA-IR, triglyceride, high density lipoprotein (HDL) and ALT values ($p < 0.05$). Anti-tetanus IgG antibodies were found to be at protective levels (> 0.1 IU/ml) in both groups, although the mean antibody level in the obese patients was significantly lower than that of the control group (0.788 ± 0.602 vs 1.112 ± 0.398 , respectively, $p = 0.022$) (Table 1).

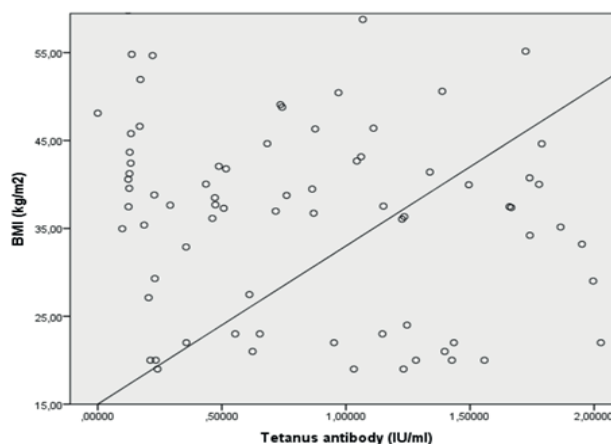


Figure 1. Correlation chart for BMI and tetanus antibody levels

Anti-tetanus IgG antibody levels were negatively moderately correlated with age ($r = -0.605$, $p = 0.000$), and negatively weakly correlated with BMI ($r = -0.269$, $p = 0.016$) and glucose ($r = -0.278$, $p = 0.010$). The negative correlations between the parameters investigated are presented in Table 2, and a correlation chart for BMI tetanus antibody levels is shown in Figure 1. An ROC curve for the Anti-tetanus IgG antibody levels between the patient and control groups is shown in Figure 2 and Table 3 (cut-off, 1.22 IU/ml, AUC = 0.666, $p = 0.022$; sensitivity 71% and specificity 58%).

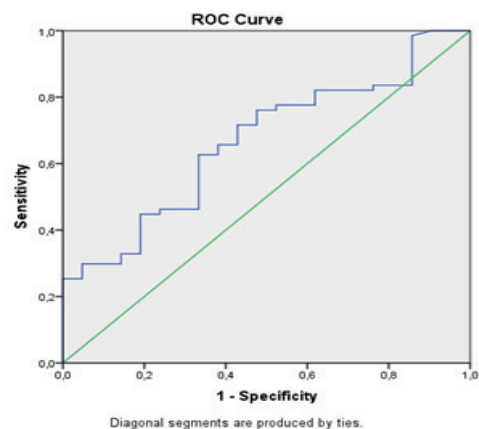
Table 1. Characteristics of the obese and control groups

Parameters	Obesity group (n=67)	Control group (n=21)	p value
Age(years), mean±SD	47±14	39±18	0.060
Sex (Female,%)	86.5	71.4	0.179
Education (n)			
Uneducated	5	2	
Primary school	38	10	0.056
High School	9	3	
University	15	6	
Weight (kg)	102.76±19.7	55.15±4.69	<0.001
BMI kg/m ²	44.59±15.73	21.19±1.63	<0.001
Glucose, mg/dl median (min-max)	123.71(73-561)	85(78-96)	<0.001
HOMA-IR	1.60(1.20-2.10)	5.14(3.20-14.2)	<0.001
Urea mg/dl	28.03±10.06	26.12±8.16	0.174
Creatinine mg/dl	0.78±0.04	0.64±0.02	0.143
Total cholesterol (mg/dl)	204.34±54.36	198.24±44.29	0.342
Triglyceride (mg/dl)	157.23±91.48	128±36.24	0.033
LDL (mg/dl)	125.05±41.79	104±21.24	0.080
HDL (mg/dl)	48.50±11.42	54.50±14.8	0.042
ALT (U/L)	24.67±11.87	18.74±7.84	0.037
Tetanus antibody (IU/ml)	0.78816±0.60271	1.11295±0.39870	0.022

HOMA-IR: Homeostatic Model Assessment of Insulin Resistance; ALT: Alanine aminotransferase; BMI: Body Mass Index; HDL: High-density lipoprotein; LDL: Low-density lipoprotein

Table 2. Correlations between antibody levels and other parameters

Parameters	r	p value
Age	-0.605	<0.001
Weight	-0.11	0.038
BMI	-0.269	0.016
Glucose	-0.278	0.010
HOMA-IR	-0.192	0.111



AUC	CUT-OFF	Sensitivity	Specificity	P
0.666	1.229	71%	58%	0.022*

p* < 0.05 p** < 0.01, AUC: Area under the curve

Figure 2 . Figure 2 and Table 3 ROC curve of tetanus antibody levels in the patient and control groups

DISCUSSION

Anti-tetanus IgG antibodies titers were significantly lower among obese adults with histories of standard immunization compared to normal weight individuals with such immunization. Recently emerging data appear to indicate that obesity may be linked to immune system impairment emerging in parallel with weight gain. An association has been reported between body fats mass and leptin, a pro-inflammatory cytokine involved in several immunological functions, since this is manufactured and released by adipocytes (18). Increasing fatty tissue and leptin levels in obesity can adversely impact the fight against infection (19). Increased risks of infection and impaired immune response to vaccines have therefore been observed in obese patients (2,8). Obesity was identified as an independent risk factor for morbidity and mortality associated with the H1N1 influenza pandemic of 2009, and also the 2020 COVID-19 pandemic (20,21). During the 2009 H1N1 pandemic obesity was observed to result in severe influenza complications by altering the functions of T cell responses in overweight and obese patients. The purpose of the present study was to compare tetanus antibody levels between high BMI and healthy weight patients, and to examine the effects of obesity on Anti-tetanus IgG antibody levels in obese adults.

Obesity is known to reduce antibody responses to the hepatitis B vaccine in adults and to the tetanus vaccine in children (10,13). The correlation between obesity and poor vaccine-induced immune response was first observed when obese healthy workers received the hepatitis B vaccine (10). A study from Iran identified obesity as an independent risk factor in terms of anti-HBs levels (22). BMI levels ≥ 25 kg/m² together with factors such as age, sex, and smoking were shown to be associated with a decreased antibody response in a meta-analysis (23). Anti-tetanus IgG antibodies were negatively correlated with BMI in the present study ($r=-0.269$, $p=0.016$).

Tetanus-specific IgG antibodies are responsible for providing tetanus immune protection; similarly to the seroconversion mechanisms discussed in association with the hepatitis B and influenza A vaccines. Few studies have assessed the relationship between tetanus antibody protection levels and obesity (12,24). One previous study demonstrated that children with BMI values exceeding the 85th percentile exhibited significantly lower tetanus-specific antibody levels (2.6 ± 0.6 IU/ml) than healthy weight children (4.2 ± 0.5 IU/ml) (12). In contrast, Petras M et al. showed a four-fold increase in tetanus antibodies following vaccination in overweight or obese adults compared to normal weight individuals (24). Similarly, the response of obese patients to the influenza vaccine was initially high, but after 12 months, a higher BMI was found to be associated with a greater fall in influenza antibody titers (25). Similarly in the present study, protection associated with vaccination in the previous 10 years was weaker in the obese individuals than in the control group.

In addition to studies of tetanus, hepatitis B and influenza, investigation of other antibody responses following immunization in obese patients has revealed no consistent correlation between obesity and results published after vaccination against rabies, hepatitis A, or pertussis (13,26,27). In terms of the relationship between hepatitis A vaccine and obesity, despite an increase following the second dose, a more gradual antibody response was observed to hepatitis A vaccination in overweight individuals in one study. Both weight and BMI emerged as significant predictors of a non-protective (anti-HAV titers < 10 mIU / mL) seroresponse when anti-HAV titers were measured after four weeks. The authors also reported that response rates increased as BMI values decreased (28). However, another study observed no difference in anti-HAV titers between healthy and obese individuals, the authors concluding that obesity has no significant impact on seroconversion after hepatitis A vaccination in some populations (26).

LIMITATIONS

This study has a number of limitations. First, the research was limited to the Düzce area of Turkey and may not be representative of all regions. Other limitations include the low patient number and the fact that no full standardization was achieved in the timing of the groups' tetanus vaccinations.

CONCLUSION

In conclusion the detection of low levels of tetanus antibody titers in patients with high BMI compared to the control group in this study suggests that greater attention is required in this population.

Competing Interests: The authors declare that they have no competing interest.

Financial Disclosure: There are no financial supports.

Ethical Approval: The study was approved by the ethics committee of the Duzce University Medical Faculty, and written informed consent was obtained from the patients (2018/236).

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