



Evaluation of Hepatitis B, Hepatitis A, Measles, Rubella, Mumps and Varicella Antibody Seroprevalences in Vocational School of Health Students

Sağlık Meslek Lisesi Öğrencilerinin Hepatit B, Hepatit A, Kızamık, Kızamıkçık, Kabakulak ve Suçiçeği Antikor Seroprevalanslarının Değerlendirilmesi

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Abstract

Objective: In the present study, we investigated the seroprevalence of antibodies against hepatitis B, hepatitis A, measles, mumps, rubella and varicella viruses in adolescent students of a Vocational School of Health and aimed to contribute to the future studies intended to increase the vaccination rates of adolescent and health care workers in our country.

Material and Method: Ninety-five students of the Vocational School of Health screened for hepatitis B, hepatitis A, measles, mumps, rubella and varicella who were referred to the vaccination unit of our hospital were included in this study.

Results: The mean age of the students was 16.4±0.7 years (14-18 years), 63.2% are girls, 36.8% are boys. None of the students received hepatitis A vaccine and varicella vaccine before. Of all the students, 16.9% tested positive for hepatitis B surface antibody, 8.4% tested positive for hepatitis A IgG, 77.9% tested positive for measles IgG, 92.3% tested positive for mumps IgG, 93% tested positive for rubella IgG and 88.5% tested positive for varicella IgG.

Conclusion: In the present study, it was concluded that catch-up vaccination seems necessary for hepatitis A and varicella because contracting these two infections in this age group increases the complication risk caused by the high seronegativity of hepatitis A and the high incidence of natural varicella infection. Conducting similar studies for adolescents and healthcare providers in our country is important to determine pre-contact and post-contact strategies, assess cost-effectiveness of pre-vaccination serology and establish screening and immunization programs.

Keywords: Adolescent, health care workers, seroprevalence, vaccination

Öz

Amaç: Çalışmada; adolesan olan Sağlık Meslek Lisesi öğrencilerinin hepatit B, hepatit A, kızamık, kabakulak, kızamıkçık ve suçiçeği virüslerine karşı antikor seroprevalansları araştırılmış olup, ülkemizde adolesanlar ve sağlık çalışanlarında aşılama oranlarının artırılması ile ilgili yapılacak olan çalışmalara katkı sağlanması amaçlanmıştır.

Gereç ve Yöntem: Çalışmada; hastanemiz Aşı Ünitesi'ne yönlendirilen hepatit B, hepatit A, kızamık, kabakulak, kızamıkçık ve suçiçeğine karşı antikor düzeyleri bakılmış 95 Sağlık Meslek Lisesi öğrencisi yer almıştır.

Bulgular: Öğrencilerin yaş ortalaması 16,4±0,7 yıldır (14-18 yıl) ve %63,2'si kız, %36,8'i erkektir. Öğrencilerin hiçbirine hepatit A aşısı ve suçiçeği aşısı yapılmamıştır. Öğrencilerin %16,9'unda hepatit B yüzey antijenine karşı antikor pozitif, %8,4'ünde hepatit A IgG pozitif, %77,9'unda kızamık IgG pozitif, %92,3'ünde kabakulak IgG pozitif, %93'ünde kızamıkçık IgG pozitif, %88,5'inde suçiçeği IgG pozitif bulunmuştur.

Sonuç: Çalışmada; hepatit A seronegatifliğinin yüksek olması, suçiçeğinin ise doğal enfeksiyon şeklinde yüksek oranda geçirilmesi nedeniyle, her 2 enfeksiyonun bu yaş grubunda geçirilmesi komplikasyon riskini artıracığından, hepatit A ve suçiçeği için yakalama aşılması yapılması gerekli gözükmektedir. Ülkemizde adolesanlarda ve sağlık çalışanlarında benzer çalışmaların yapılması, temas öncesi ve temas sonrası stratejilerin belirlenmesi, aşılama öncesi seroloji bakılmasının maliyet-etkinliği, tarama ve bağışıklama programlarının oluşturulması için önemlidir.

Anahtar kelimeler: Adolesan, sağlık çalışanları, seroprevalans, aşılama



INTRODUCTION

Immunization is the process whereby a person is made immune or resistant to an infectious disease, typically by the administration of a vaccine. Vaccines stimulate the body's own immune system to protect the person against subsequent infection or disease. Immunization aims to prevent the emergence of diseases in the short term and eradicate infectious diseases globally in the long term. Childhood immunization in our country is well positioned in terms of implementation and delivering the goal. Over the years, vaccination rates have increased and reached 96%–98%.^[1] However, waning of the immunity acquired by vaccination in childhood over time results in increase in morbidity of vaccine-preventable diseases in adolescents. Also, adolescents with incomplete vaccination are a source of infection for high-risk children, adults and the elderly in the community. Maintaining the importance given to immunization in infancy and early childhood also in the adolescent period plays a critical role in controlling and eliminating vaccine-preventable diseases.^[1,2] In adolescents who seek to gain independence, disease mortality and morbidity are high due to risky behaviors; however, the fact that most adolescents do not accept the healthcare offered for them is a cause of the low rate of immunization in adolescents. In addition, healthcare professionals and families with insufficient knowledge about the recommended vaccines, suspicions about the efficacy and safety of vaccines, detailed and complicated vaccination recommendations, uncertainty about costs, vaccines not covered by insurance and expensive vaccines are challenging factors to set and maintain the vaccination goals in adolescents. In developed and developing countries, compared with the infancy, adolescents belong to an age group that is neglected in terms of health assessments. Lack of regulatory-legal obligations and a regular registration system are the reasons for insufficient data on adolescent vaccinations.^[3,4]

In Turkey, hepatitis B vaccine in 1998, the measles–mumps–rubella (MMR) vaccine and Haemophilus influenzae type b (Hib) vaccine in 2006, the diphtheria, tetanus and acellular pertussis-inactivated poliovirus-Hib (DTaP–IPV–Hib) vaccine in 2008, DTaP–IPV vaccine instead of tetanus, diphtheria (Td) vaccine and Oral Poliovirus vaccine in 2010 for the grade 1 students at primary schools, 13-valent pneumococcal vaccine in 2011, hepatitis A vaccine in 2012, and lastly, varicella vaccine in 2013 have been added to the National Immunization Schedule.^[5]

Adolescent vaccines recommended worldwide around the age of 11–12 include tetanus–adult type diphtheria–adult type acellular pertussis (Tdap) vaccine, human papillomavirus (HPV) vaccine, meningococcal vaccine and influenza vaccine. In Turkey, the National Immunization Schedule incorporates only Td for the grade 8 students at primary schools. Human papillomavirus and meningococcal vaccine are not included in our routine National Immunization Schedule.^[6,7]

Today, several programs have been established to improve

and increase the safety of employees and patients in health facilities. Vaccination of healthcare providers (HCPs) at risk is one of the most addressed infection control measures among these infection control programs. However, programs concerning the recommended and compulsory occupational vaccines differ from country to country and even from centre to centre.^[8]

The world's leading healthcare authorities such as Centers for Disease Control and Prevention (CDC), Advisory Committee on Immunization Practices and American Academy of Pediatrics recommend that health care providers should have complete immunity against measles, mumps, rubella, varicella and pertussis agents, must be administered seasonal influenza vaccines and one of the vaccines for immunity against diphtheria–pertussis–tetanus should be administered in the form of Tdap vaccine. It is recommended that all healthcare providers who may be exposed to blood or body fluids are immune to the hepatitis B virus. All new employees should receive a prompt review of their immunization status prior to starting to care for patients; in addition, all employees should have an annual review to ensure that immunizations remain up to date. Medical students should be screened and immunized before get in contact with patients. Immunization is recommended when prior vaccine administration cannot be documented, unless the HCP has a contraindication to vaccine administration.^[9,10]

In the present study, the antibody seroprevalences against hepatitis B, hepatitis A, measles, mumps, rubella and varicella viruses were evaluated in the students from Vocational School of Health who were admitted to the vaccination unit of our hospital between January 01, 2017 and December 31, 2018, before starting their internship in healthcare facilities. Students included in the study group were in the adolescent age group as well. The results of the present study are intended to contribute to the studies aimed at increasing vaccination rates in HCWs as well as to the regulations to be made concerning adolescent vaccination in our country.

MATERIAL AND METHOD

The present study was a retrospective study conducted at the University of Health Sciences, Ankara Child Health and Diseases Hematology Oncology Training and Research Hospital Vaccination Unit. The study included 95 students from Vocational School of Health who were referred to the vaccination unit in our hospital by their educational institution to have their antibody levels screened against hepatitis B, hepatitis A, measles, mumps, rubella and varicella viruses before starting their internship at the healthcare facilities, to have their immune status examined and to get a vaccination plan if needed.

Enzyme-linked immunosorbent assay (ELISA) method was used to detect hepatitis B surface antigen, antibody against hepatitis B surface antigen (anti-HBs) for hepatitis B virus

(Radim SpA, Italy). Microplate based ELISA was used for the determination of Hepatitis A virus-specific IgG type antibody (Etimax-3000, Diasorin, Italy). Measles, mumps, rubella and varicella virus-specific IgG type antibodies were also examined by ELISA method (Vircell Microbiologist, Spain) according to the manufacturer's instructions.

Information about the age, gender, presence of a chronic disease, the vaccination information, and history about infection in the students was retrieved from their files. Infection history of students is clinical diagnosis. None of the students had chronic diseases.

Childhood vaccines in the National Immunization Schedule compatible with the birth years of all students were complete. All the students received one dose of measles vaccine; 97.9% (93/95) of them received two doses of measles vaccine with the first dose at the age of 1 years and the second dose administration, given as MMR, in grade 1 of primary school. [5] None of the students had received hepatitis A vaccine and varicella vaccine before. Vaccines of students who had seronegativity were planned.

Statistical analyses

Data analysis was performed using IBM SPSS Statistics 23.0 package program. Descriptive statistics were performed. Mean and standard deviation, upper and lower values (minimum–maximum) were calculated for the quantitative data. Chi-squared test was used to assess categorical data. $P < 0.05$ value was considered the reliability coefficient.

Ethical approval was obtained for this study numbered 2019-003 from the University of Health Sciences, Ankara Child Health and Diseases, Hematology Oncology Training and Research Hospital.

RESULTS

The mean age of the students was 16.4 ± 0.7 years (14–18 years), 63.2% are girls (60/95), 36.8% are boys (35/95). Although the mean age of girls is higher than boys, the difference is not statistically significant. All students have social security. All students were born and live in Ankara. Serology of students against infection agents is shown in **Table 1**. It was noticed in **Table 1** that the serological examination was performed mostly for hepatitis B.

Table 1. IgG serology of students hepatitis B, hepatitis A, measles, mumps, rubella and varicella.

Microorganism	IgG positive n (%)	IgG negative n (%)	Total n (%)
Hepatitis B	16 (16.9)	79 (83.1)	95 (100.0)
Hepatitis A	7 (8.4)	76 (91.6)	83 (100.0)
Measles	60 (77.9)	17 (22.1)	77 (100.0)
Rubella	67 (93.0)	5 (7.0)	72 (100.0)
Mumps	72 (92.3)	6 (7.7)	78 (100.0)
Varicella	69 (88.5)	9 (11.5)	78 (100.0)

Table 2 shows the distribution of the serology of the students create against infection agents by gender, and the differences are not statistically significant ($p > 0.05$).

The relationship between students' infection histories and serologies is shown in **Table 3**. An infection history was found to be significant only for varicella.

Table 2. Distribution of students' hepatitis B, hepatitis A, measles, mumps, rubella and varicella IgG serology by gender.*

	Girls n (%)	Boys n (%)	Number of students undergoing serology
Hepatitis B			95
seropositive	11 (18.3)	5 (14.3)	
seronegative	49 (81.7)	30 (85.7)	
Hepatitis A			83
seropositive	4 (7.7)	3 (9.7)	
seronegative	48 (92.3)	28 (90.3)	
Measles			77
seropositive	39 (78.0)	21 (77.8)	
seronegative	11 (22.0)	6 (22.2)	
Rubella			72
seropositive	42 (93.3)	25 (92.6)	
Seronegative	3 (6.7)	2 (7.4)	
Mumps			78
Seropositive	48 (92.3)	24 (92.3)	
Seronegative	4 (7.7)	2 (7.7)	
Varicella			78
Seropositive	46 (88.5)	23 (88.5)	
Seronegative	6 (11.5)	3 (11.5)	

* $p > 0.05$

Table 3. The relationship between students' history of infection and hepatitis B, hepatitis A, measles, mumps, rubella and varicella IgG serology.

The infection history	IgG positive n (%)	IgG negative n (%)	P value
Hepatitis A			
yes	1 (14.3)	0 (0.0)	0.084
no	6 (85.7)	76 (100.0)	
Measles			
yes	2 (3.3)	0 (0.0)	1.000
no	58 (96.7)	17 (100.0)	
Rubella			
yes	8 (11.9)	1 (20.0)	0.498
no	59 (88.1)	4 (80.0)	
Mumps			
yes	5 (6.9)	0 (0.0)	1.000
no	67 (93.1)	6 (100.0)	
Varicella			
yes	46 (66.7)	0 (0.0)	*0.000
no	23 (33.3)	9 (100.0)	

* $p < 0.05$

DISCUSSION

In the current study, we searched the seroprevalence of antibodies against hepatitis B, hepatitis A, measles, mumps, rubella and varicella viruses in the adolescent students from Vocational School of Health who were admitted to the vaccination unit in our hospital.

Serologic screening for immunity is generally not considered cost-effective. Yet, study results on this topic differ. In a study conducted among 1255 health care workers (HCWs) in

Turkey, 94%, 90%, 97% and 98% were found to be immune to measles, mumps, rubella and varicella, respectively. The positive predictive value of histories of measles, mumps, rubella and varicella were found to be 96%, 93%, 100% and 98%, respectively. The negative predictive values of histories of measles, mumps, rubella and varicella were found to be 13%, 17%, 5% and 2%, respectively. It was reported that the cost of vaccination without screening was significantly more expensive for varicella, although vaccination without screening was inexpensive for MMR. However, it was also reported that some HCWs (2-7%) would be unprotected against these contagious illnesses because of the unreliability of their measles, mumps, rubella, and varicella history if pre-screening is not conducted, thereby concluding that the screening of HCWs before vaccination therefore continues to be advisable.^[9-11] In another study conducted with 320 nursing students in Turkey; seroprevalence of students in hepatitis A, hepatitis B, measles, mumps, rubella and varicella 17%, 93%, 82.2%, 93.7%, 98.6% and 93% were found respectively. While all of these students were vaccinated against hepatitis B, measles, rubella and mumps, only 4.4% had hepatitis A vaccine.^[12]

All students were tested serologically for hepatitis B virus, whereas rates of serology testing for other agents were lower. This shows the necessity of increasing the awareness of the units that provide healthcare service to these two vulnerable groups (Vocational School of Health Students and adolescents) about vaccination through periodic screening. In a French study, the vaccination coverage for obligatory vaccinations among HCPs was found to be 91.7% for hepatitis B, 95.5% for the booster dose of diphtheria-tetanus-polio (DTP) and 94.9% for BCG. For non-compulsory vaccinations, coverage was found to be 11.4% for the 10-year booster of the DTP containing vaccine, 49.7% for at least one dose of measles, 29.9% for varicella and 25.6% for influenza.^[13] Although there is no hesitancy about hepatitis B vaccine being the most efficient way to prevent HBV infection, there are a few questions as to the duration of protection, the necessity of a booster dose and timing, and whether protection will continue if the anti-HBs titer fall below <10 mIU/mL.^[14-16] In our study, all the students received the first three-dose series of hepatitis B vaccine. While more than 15 years have passed since vaccination in 98.9% of these students, this period was between 10 and 15 years in 1.1%, and 83.1% of the students had a negative hepatitis B serology. However, the high level of anti-HBs negativity can be related to the time passed over the vaccine. However, none of these students had positive serology for hepatitis B infection. It has been shown that vaccine induces active production of anti-HBs antibody accompanied by HBsAg specific immunological memory that provide continuous protection in the absence of antibody.^[15,16] Several factors have been associated with nonresponse to hepatitis B vaccine. These factors include vaccine factors (e.g., dose, schedule, injection site) and host factors. Male gender, obesity, smoking, and chronic illness have been independently

associated with unresponsiveness to hepatitis B vaccine.^[17] In a study of 159 HCWs who were vaccinated between the ages of 18 and 60 years, approximately 75 percent of them had protective anti-HBs levels 10 to 31 years after they received their initial vaccine series.^[18] Anti-HBs positivity at protective levels was 98% in a Poland-based study and 62.7% in a study conducted in Turkey.^[19,20]

The primary strategy for preventing hepatitis A infection in HCWs is strict infection control practices. Nosocomial outbreaks are rare when proper infection control practices are followed.^[21] Turkey has intermediate endemic for hepatitis A virus (HAV) virus infection. The seroprevalence of HAV infection in Turkey shows significant differences according to geographical regions, age and socioeconomic status. In a study including 10 centres from Turkey, hepatitis A antibody positivity was found to be 91.1% in 2107 individuals. In this study, it has been concluded that hepatitis A antibody seronegativity was high in individuals under the age of 20 years, which is followed by the group of individuals in the age group of 21-30 years, and that the contact with HAV is shifting to older ages in our country that has intermediate endemicity.^[22] In our study, none of the students were administered hepatitis A vaccine. Thus, the seronegativity of hepatitis A was quite high (91.6%). As contracting the disease at this age leads to an elevated risk for the course of disease, implementation of a catch-up vaccination program covering this vulnerable group in Turkey is required.^[23]

The risk of acquiring measles in hospital personnel is estimated to be thirteen times greater than for the general population.^[24] All health care providers (medical with and without patient care responsibilities, non-medical, paid, volunteer, full-time, part-time, student) should have a formal assessment of immunity to measles and mumps regardless of year of birth and those who are susceptible should be immunized. The same recommendation is made for all female health care providers with respect to rubella immunity and immunization.^[25] As recommended by the CDC, HCWs without evidence of immunity should be provided with 2 doses of MMR for measles and mumps protection, one dose of MMR for rubella protection.^[9] In the present study, although 98% of the students were given two doses of measles vaccine at 1 year of age and in grade 1 of primary school, it was observed that seropositivity decreased the fastest in measles (78%) among the three agents. However, studies have shown that the level of antibodies decreases slowly over the years following the administration of the measles vaccine, not leading to measles sensitivity.^[26] Various studies conducted in Turkey also revealed that the seroprevalences of these agents increased with aging—similar to other countries—during the time when MMR vaccines were not included in the vaccination program.^[27,29] We expect that the high rate of rubella and mumps seroprevalence (93%, 92.3%, respectively) is due to the MMR vaccination administration that was performed in 98% of the 1st graders in primary school. This clearly demonstrates the benefit of incorporating the MMR vaccine into the National

Immunization Schedule. However, the outcome may also be related to the fact that the students had the infection naturally and sub-clinically or did not remember that they contracted the disease.

Rubella is a mild virus infection that occurs with fever and exanthema. Congenital rubella infection usually develops in the first trimester of pregnancy arising from the infection of the mother who does not have enough immunity against this virus, and leads to malformations of the fetus. Therefore, women in childbearing age are asked to be seropositive against rubella. In a study involving 530 non-vaccinated individuals between the ages of 1 and 29 from Turkey, rubella IgG seronegativity was found to be 23.3%. The proportions of susceptible individuals were reported to be 61.7%, 29.5%, 12.4%, 10.3% and 8.4% in the age groups of 1–4, 5–9, 10–14, 15–19 and 20–29 years, respectively. It has been noted that the history is not sufficient in evaluating rubella infection and that the disease can be manifested with nonspecific findings. In our study, it was also observed that the history was not very distinctive in seropositive and seronegative cases for rubella.^[29,30]

Varicella infection is a highly contagious disease characterized by a common vesicular rash. The disease usually progresses mildly. However, serious complications such as secondary skin infection, otitis media, pneumonia and encephalitis can be seen. Complications were seen to have emerged in adults rather than in children.^[31] The CDC recommends the varicella vaccine for health care providers, because of the risk of serious complications of natural disease in adults, the risk of further transmission in health care facilities, and immunization is cost-effective. HCWs with a laboratory or health care provider confirmation of prior disease or written documentation of two varicella vaccine doses can be considered immune, but all others should have serologic testing. HCWs who are seronegative should be immunized with two doses of the varicella vaccine administered at least four weeks apart. Approximately 14%–40% of HCWs are estimated to be susceptible to varicella.^[32,33] Despite the fact that all the students included in the present study were unvaccinated, the high rate of seropositivity (88.5%) that was observed was associated with natural infection. In the current study, it was observed that negative and positive history related to varicella infection was significantly correlated with serology.^[11] In another study, seropositivity was found in 48% of the adolescents who did not have a history of varicella infection or were not known to have the infection.^[34] As varicella infection may result in more serious complications in older ages, we suggest that a catch-up vaccination program involving this vulnerable adolescent group, which had missed the varicella vaccine introduced in the National Immunization Schedule in 2013, is necessary.^[5]

In conclusion, it is evident that the introduction of the hepatitis A vaccine in 2012 and the varicella vaccine in 2013 into the our National Immunization Schedule will have significant benefits in time for the protection of both adolescents and

individuals who will take part in healthcare services. Until this period is completed and considering that there are vaccines not included in the National Immunization Schedule for this group, the institutions, organizations and HCPs providing services for both groups should be aware of the necessity of vaccination, and admit the presence of additional and new vaccines complementary to childhood vaccination and the need to be committed to implementation. As our results show, because the hepatitis A seronegativity is high and varicella is acquired at high rate as a natural infection, getting these infections in this age group increases the risk of complications. Although our study is not a cost-effectiveness study, we conclude that it is necessary to perform catch-up vaccination for this age group for both infection agents. We also recommend that before the vaccination, serology testing should be conducted for varicella and that serology testing is not required for hepatitis A. In addition, conducting similar studies in adolescents and HCPs in Turkey will help establish pre-contact and post-contact strategies, assess the cost-effectiveness of pre-vaccination serology and create screening and immunization programs.

ETHICAL DECLARATIONS

Ethics Committee Approval: Ethical approval was obtained for this study numbered 2019-003 from the University of Health Sciences, Ankara Child Health and Diseases, Hematology Oncology Training and Research Hospital.

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients. .

Status of Peer-review: Externally peer-reviewed.

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