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RESEARCH ARTICLE

MEASLES, MUMPS, RUBELLA, VARICELLA AND HEPATITIS B SEROPOSITIVITY OF MEDICAL AND DENTAL STUDENTS AT KING ABDULAZIZ UNIVERSITY

Rahila Iftikhar[1,*] and Razaz Tawfiq[2]

[1]Assistant Professor, Community and Family Medicine Department, King Abdulaziz University, Jeddah, Saudi Arabia
[2]Consultant Family Physician, General Practice Department, King Abdulaziz University Hospital, Jeddah, Saudi Arabia

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ABSTRACT

Background
Medical and dental interns are at risk of acquiring (or transmitting) vaccine-preventable diseases, such as measles, mumps, rubella, varicella and hepatitis B. We aimed to determine the seroprevalence of mumps, measles, rubella, varicella, and hepatitis B among medical and dental interns.

Methods
A cross-sectional survey was performed on medical and dental students who applied for internship at King Abdulaziz University in 2013. The 2010 medical records of the students were reviewed and blood samples were collected and analyzed to determine the students' immune status to measles, mumps, rubella, varicella, and hepatitis B. Students who did not have immunity were vaccinated and tested post-vaccination. Data were analyzed using the Statistical Package for the Social Sciences.

Results
We included 170 students (131 medical and 39 dental) aged 22-25 years (mean ± SD, 23.9 ± 0.7 years). Most medical and dental interns were measles, mumps, rubella, and varicella seropositive and only a few interns lacked immunity to these infections. A total of 108 students (63.5%) had received all three doses of hepatitis B vaccine when they presented for screening in 2013; thirty-five students (21.6%) had received two doses, while 19 (11.7%) had received only one dose. The hepatitis B vaccination history of eight students was undocumented. Overall, we documented 29 cases (17.1%) of non-response to HBV vaccine. Revaccination with hepatitis B vaccine elicited response in 18 (62.1%) of the non-responders.

Conclusions
A large proportion of students who are not immune to HBV are allowed to start clinical training. Thus, medical and dental students should be screened for vaccine-preventable diseases as early as in their preclinical years.

INTRODUCTION

Students in healthcare professions are considered to be at substantial risk for acquiring or transmitting measles, mumps, rubella, varicella, and hepatitis B owing to their frequent exposure to blood or body fluids (Wicker *et al.*, 2007). Employers and healthcare personnel, including students and trainees, should take reasonable precautions to prevent transmission of vaccine-preventable diseases in order to avert occupationally acquired infections and avoid causing harm to patients. It is therefore essential to vaccinate medical and dental students against vaccine-preventable diseases, such as measles, mumps, rubella, varicella, and hepatitis B (CDC, 2011), which are reported to be the most frequent amongst these diseases (Wicker *et al.*, 2007; Sheek-Hussein *et al.*, 2012).

***Corresponding author: Rahila Iftikhar**. Assisstant Professor, Community and Family Medicine Department, King Abdulaziz University, Jeddah, Saudi Arabia*

Immunization is a cost-effective measure that protects students in healthcare professions. In addition, immunization may prevent outbreaks of infectious diseases within the healthcare vicinity (Arunkumar *et al.*, 2013), where inpatients, particularly immunocompromised patients, are already challenged by nosocomial infection. Several authors have reported cases of healthcare students who were exposed to infectious body fluids and cases of needle stick injury (Norsayani and Noor Hassim, 2003; Joob *et al.*, 2013). In one study, the authors found that all final year medical students were exposed to infectious body fluids and 14.1% reported that they sustained a needle stick injury during training (Varsou *et al.*, 2009). Findings from a recent report from Australia (Torda, 2008) also show that the self-reported history of previous vaccination by medical students is inaccurate. Hence, vaccination surveillance is necessary to know the protection levels of individuals that are at higher risk of exposure. Surveillance studies can help to identify immunization gaps

and susceptibility to infectious diseases to ensure the immunization status of healthcare personnel (Torda , 2008). This will consequently result in fewer lost work days and hospitalizations as well as fewer follow-up surveys after exposure (Shamsizadeh *et al.*, 2012). According to the Centers for Disease control and Prevention (CDC) guidelines, trainees must be vaccinated before they have contact with blood because the risk to acquire vaccine-preventable infections is higher during the professional training period; vaccination should be offered in schools of medicine, dentistry, nursing, laboratory technology, and other allied health professions (CDC, 2012). Although these guidelines are recommended at most health colleges and universities in Saudi Arabia, they are not strictly enforced (Al-Ajlan *et al.*, 2011; Darwish *et al.*, 2013). This study aimed to assess serological immunity against measles, mumps, rubella, varicella, and HBV amongst medical and dental students at King Abdulaziz University, Saudi Arabia. We also aimed to evaluate the seroconversion rate to hepatitis B vaccine in non-responders after hepatitis B revaccination.

MATERIALS AND METHODS

Participants and procedure

The medical and electronic databases of King Abdulaziz University Hospital were searched for the 2010 medical records of medical and dental students who applied for internship at King Abdulaziz University in 2013. According to the policy of our institution, medical interns should be screened for vaccine-preventable diseases during their preclinical year. All students who are found to lack immunity to a particular disease are accordingly vaccinated and followed up for seroconversion. Appropriate interventions are undertaken for non-responders, as recommended by the CDC (2011). The students are screened again, after three years, when they apply for internship at the university. We included students provided they met the following inclusion criteria: (1) they were graduates applying for internship during the 2013-2014 academic year and (2) they were seronegative for anti-hepatitis B surface antigen (anti-HBs) in 2010. Students who had achieved immunity against HBV (anti-HBs titers ≥ 10 mIU/mL) in 2010 and all cases of missing laboratory data were excluded from the analysis. Of the 439 graduates (323 medical and 116 dental students) who presented to the Staff Health Clinic in 2013, we excluded 225 students because they had achieved immunity against HBV. A further 44 students were excluded for missing laboratory data. Of these, the results of anti-HBs assays were unavailable for ten students. For all students included in the study, we collected blood samples and performed antibody titers to assess response to measles, mumps, rubella, varicella, and HBV vaccine. All students who had not achieved immunity to any of these infections were vaccinated accordingly. The records of non-responders who had received three doses of hepatitis B vaccine were reviewed after one to four months to determine their seroconversion status.

Laboratory testing

An enzyme-linked immunoassay was used to measure serum antibody titers against measles (Bioactiva Diagnostica® Measles Virus IgG-ELISA; Bad Homburg, Germany), mumps (Bioactiva Diagnostica® Mumps Virus IgG-ELISA; Bad Homburg, Germany), rubella (Cobas® Rubella IgG; Roche Diagnostics, Burgess Hill, West Sussex, UK), varicella (Bioactiva Diagnostica® Varicella-Zoster Virus IgG-ELISA; Bad Homburg, Germany), and HBV (Cobas® HBsA II; Roche Diagnostics, Burgess Hill, West Sussex, UK). All tests were conducted according to the manufacturers' instructions; all results were also interpreted as per the manufacturers' instructions.

Ethical considerations

Permission to conduct the study was granted by the Biomedical Ethics Committee of King Abdulaziz University. Medical files are created at King Abdulaziz University Hospital in accordance with the hospital policy that stipulates that patients' results are confidential but may be used for the purpose of research. Thus, for all electronic medical records created at King Abdulaziz University Hospital, patients consented to have their results used for research purposes.

Working definitions

1. **Responders:** Persons determined to have anti-HBs titers≥10 mIU/mL.
2. **Non-responders:** Persons determined to have anti-HBs titres <10 mIU/mL [14].

Statistical analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, US), version 20. Descriptive statistics was computed for all variables. Results are expressed as frequency (percent), mean ± standard deviation (SD) and range.

RESULTS

We included 170 students (131 medical and 39 dental) of both genders (74 men and 96 women) aged 22-25 years (mean ± SD, 23.9 ± 0.7 years).

Measles, mumps, rubella, and varicella immune status in medical and dental interns

Most medical and dental interns were measles, mumps, rubella, and varicella seropositive and only a few interns lacked immunity to these infections (Table 1).

Hepatitis B seroprevalence in medical and dental interns

A total of 108 students (63.5%) had received all three doses of HBV vaccine when they presented for HBV screening in 2013. Fifty-four students (33.3%) had not completed the HBV vaccine schedule. Of these, 35 (21.6%) had received two doses, while 19 (11.7%) had received only one dose. The HBV vaccination history of eight students was undocumented. Thirty-five of the 39 dental students (89.7%) achieved immunity to HBV as against 106 (80.9%) in the medical student group. Overall, we documented 29 cases (17.1%) of non-response to HBV vaccine (Table 1). Revaccination with hepatitis B vaccine elicited response in 18 of the non-responders (62.1%).

Table 1. Measles, mumps, rubella, and hepatitis B seroprevalence in medical and dental interns[a]

Status	Medical Interns (n = 131)	Dental Interns (n = 39)	Total
Measles[b]			
Seropositive	120 (91.6)	37 (94.9)	157 (92.4)
Seronegative	11 (8.4)	2 (5.1)	13 (7.6)
Mumps[c]			
Seropositive	118 (90.1)	33 (84.6)	151 (88.8)
Seronegative	13 (9.9)	6 (15.4)	19 (11.2)
Rubella[d]			
Seropositive	127 (96.9)	38 (97.4)	165 (97.1)
Seronegative	4 (3.1)	1 (2.6)	5 (2.9)
Varicella[e]			
Seropositive	122 (93.1)	35 (89.7)	157 (92.4)
Seronegative	9 (6.9)	4 (10.3)	13 (7.6)
Hepatitis B[f]			
Seropositive	106 (80.9)	35 (89.7)	141 (82.9)
Seronegative	25 (19.1)	4 (10.3)	29 (17.1)

[a]Data are presented as frequency (percent).
[b]A positive result is > 1.30 absorbance value and negative < 0.200.
[c]A positive result is > 1.30 absorbance value and negative < 0.200.
[d]A positive result is > 10 IU/mL and negative 0.0 to 4.9 IU/mL.
[e]A positive result is > 1.30 absorbance value and negative < 0.200.
[f]A positive result is a cutoff index ≥ 1.0 and negative a cutoff index < 0.90

DISCUSSION

We found that most medical and dental interns were seropositive for measles, mumps, rubella, and varicella IgG antibodies. Although Saudi Arabia implements the World Health Organization Expanded Program on Immunization and a royal decree in 1982 made vaccination compulsory for issuing the birth certificate of a Saudi child, a few students demonstrated immunity gaps to measles, mumps, rubella, and varicella. This might be because immunity against some of these vaccine-preventable infections weans off in time and results in unsustainable protection in adults (Baer *et al.*, 2005). The seronegativity rate to mumps (9.9%) in our medical interns is higher than that reported from another study conducted in Turkey (Kutlu *et al.*, 2011), where it was reported that 2.8% of the medical students were seronegative for mumps antibodies. On the other hand, the rate of seronegativity to mealses in our medical interns (8.4%) is lower than that reported in a study conducted in the United Arab Emirates. In their study, Sheek-Hussein *et al*. (2012) found that up to 46% of Emirati medical students were susceptible to measles although they all reported having received childhood immunization. In Saudi Arabia, the hepatitis B vaccine was included in the *Expanded Program on Immunization* (EPI) in 1990, and between 1990 and 1996, a "catch up" vaccination campaign that targeted school children was launched (Al-Faleh *et al.*, 1992). Therefore, it is expected that all of our students did not receive HBV vaccine at birth, but some may have received the "catch up" vaccine at school. All the students who lacked immunity against any of the vaccine-preventable diseases were offered vaccination when they presented to our clinics in 2010; however, the hospital records showed that 33.3% of the students (medical and dental) did not receive all three doses of HBV vaccine, which may explain why up to 17.1% of our students did not achieve anti-HBs titers ≥ 10 mIU/mL when they presented to the clinic three years later. In general, approximately 5-10% of immunized individuals fail to develop antibody titers ≥ 10 mIU/mL [18]. Other research demonstrated that 15–50% immunocompetent children who responded to the complete primary three-dose vaccination series with anti-HBsAg concentrations ≥ 10 mIU/mL had low or undetectable concentrations of anti-HBsAg at 5–15 years after vaccination (Plotkin *et al.*, 2008).. Furthermore, the authors observed that adults had rapidly decreasing anti-HBsAg titers within the first year after primary vaccination; 30–60% of the subjects had anti-HBs titers of <10 mIU/mL within 9–11 years after vaccination. Because some students who did not receive all three doses of HBV vaccine may have taken the vaccine at another health institution, this shows that the vaccination records of our students do not accurately reflect their immunity status for indicated vaccine-preventable diseases. In addition, some students who lack antibodies against HBV actually begin clinical training, which places them at increased risk for acquiring these diseases. Although healthcare workers and students recognize the importance of effective immunization (Oates *et al.*, 1993). We believe that the gaps in immunization among our students might be due to lack of compliance on the part of the students, coupled to the fact that our institution fails to enforce or formulate a comprehensive vaccination policy for all healthcare personnel. Furthermore, it is possible that many of our students who failed to receive three doses of HBV vaccine were unaware of the risks of vaccine failure and the consequent lack of protection in believing that immunity is for life, which has been previously reported (Sivarajasingam *et al*., 1995).

The seroconversion rate to hepatitis B vaccine revaccination was 62.1%. In general, persons who do not respond to a primary three-dose vaccine series respond to an additional vaccine dose in 25%–50% of the cases, and 44%–100% respond to a three-dose revaccination series using standard or high dosage vaccine (Averhoff *et al*., 1998, Kim *et al.*, 2003), which was the case in our students. Better response to revaccination has been reported in persons who have measurable but low (1–9 mIU/mL) levels of anti-HBs after the initial series than in those who have no anti-HBs (Clemens *et al.*, 1997). Persons are either infected with HBV or can be considered primary non-responders when they do not have protective levels of anti-HBs one to two months after revaccination; however, the Advisory Committee on Immunization Practices does not recommend more than two vaccine series in non-responders (CDC, 2006). In accordance with this recommendation, we did not vaccinate students who did not achieve immunity after HBV revaccination. We believe that an awareness program should be implemented for interns who do not develop immunity even after revaccination, so that they can be cautious when dealing with exposure. The results of this study should be interpreted in light of its limitations. The cross-sectional design of the study precluded any inferences being drawn about the vaccination status of the interns prior to 2010. Therefore, it was impossible to accurately differentiate non-responders from those who had missed the child and adolescent, catch-up, and adult immunization schedules. A further limitation is that some students who received less than the recommended three doses of HBV were lost to follow up. Hence, we could not determine whether these students completed the three-dose hepatitis B vaccine series, as recommended by the CDC (CDC, 2011). Future studies should not only focus on the demographic and serologic status of students, but these should also take into account a history of previous infection and immunization schedules in childhood.

We also recommend that in order to ensure that the vaccination status of medical and dental students is up-to-date, reminders should be sent to students through the hospital call centers or through a short messaging system. Taken together, our findings demonstrate that most medical and dental interns at King Abdulaziz University are immune to measles, mumps, rubella, and varicella. Given that up to 17.1% of the interns were anti-HBs seronegative after vaccination, and those who had not yet achieved seroprotection were allowed to start clinical training, we suggest that medical and dental students should be screened for vaccine-preventable diseases as early as in their preclinical years.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

RI conceived and designed the study, supervised sample and data collection, wrote the manuscript, and analyzed and interpreted the data. RT participated in writing the first draft of the manuscript and supervised laboratory testing. Both authors reviewed and approved the final version of the manuscript.

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