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RESEARCH ARTICLE

Seroprevalence of Pertussis Antibodies and Infection Risk Among Female Medical Students

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Abstract:

Objectives:

Pertussis seroprotection among neonates depends on maternal antibodies before receiving their first childhood acellular pertussis (DTaP) vaccination. Therefore, childbearing women need to have adequate seroprotection, either before conception or during the antenatal period, to protect their neonates from contracting neonatal pertussis. Given the global rise in neonatal pertussis incidence, there is a need to address the importance of protection against this infection by promoting booster vaccinations among female medical students as a preventive measure for their future generation. This paper addresses a part of our study on the seroprevalence of anti-PT IgG antibodies in female medical students who are more prone to acquire infections from the patients during their clinical rotations.

Methods:

A cross-sectional study was conducted for three months by recruiting female medical students of RAK Medical and Health Sciences University, Ras Al Khaimah, UAE. The antibody levels (IgG) of pertussis (anti-PT) in blood sera of the study population were quantitated by enzyme-linked immunoassay. A 60 – 125 IU/mL titer was considered the positive titer level (p-value <0.05 being statistically significant).

Results:

Among 90 ethnically different student participants (mean age of 21 years), forty-four percent (n=40) showed detectable titers of anti-PT IgG antibodies. Whereas fourteen percent of participants (n=13) had high positive titers above 125U/mL, four percent (n=3) showed positive titers ranging from 60-125IU/mL. Two percent (n=2) were in borderline with 55 - <60IU/mL and twenty three percent (n=21) were < 55IU/mL titres. The mean ± SD of IgG titers was 42 ± 74.93 IU/mL with a range of 0-267 IU/mL

Conclusion:

Only forty-four percent had detectable titers of anti-PT IgG antibodies, among whom fourteen percent (n=13) had high positive titers indicating recent infection. The results signify a low level of seroprotection among female medical students that emphasizes the need to promote booster vaccination for the high-risk group who work in the health profession.

Keywords: Seroprevalence, Pertussis seroprotection, Neonate, DTP, Immunization.

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1. INTRODUCTION

Infections by several bacteria in neonates, especially in the respiratory tract, are easily preventable by current vaccines [1]. Despite the widespread availability of vaccinations, pertussis, caused by Bordetella pertussis, has re-emerged, causing significant complications in neonates [2]. Globally, a dramatic reduction (>90%) in the incidence and mortality due to pertussis following large-scale vaccination during the 1950s and 1960s [3]. However, the CDC reported that in 2018, there were 24.1 million pertussis cases and 160,700 deaths in children younger than five years worldwide [4]. Globally, pertussis re-emergence is a challenge in developed and developing countries, with high morbidity and mortality rates in young children [5]. Despite the high vaccination rate in the

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United Arab Emirates, there is a substantial increase in the incidence of pertussis, with 72% of the reported cases being neonatal pertussis from one emirate [6].

Pertussis is a gram-negative, pleomorphic coccobacillus that causes whooping cough in humans. It is most severe among infants with the highest risk of complications, including pneumonia, encephalopathy, and seizure leading to high morbidity and fatality [1]. Neonate has an immature immune system that cannot protect them from infectious diseases such as pertussis. To overcome this, antibodies from their mother passively protect them for the first few weeks of life. However, without pertussis vaccination during pregnancy, maternal pertussis antibodies in the infant decline substantially by six weeks of age and become undetectable by about 4months of age [6]. Age before the first vaccination is the crucial period when the infant is most susceptible to the life-threatening disease, with a high incidence of deaths in the first six months of life [7].

The antibody titers required for protection against pertussis are not well defined, but the higher levels of antibodies seem to correlate with protection [8]. A protective level of specific-IgG antibodies must be present in the mother's blood to ensure postnatal protection of the newborn [9, 10]. The higher the concentration of the antibodies in the mother's blood, the longer the fetus will be protected after birth [9 - 11].

The chances of contracting infectious illnesses among the medical students visiting patients during clinical rotations are comparably high than in the general population. Hence, the study aimed to test the antibody profile of the medical students to establish the potential risk of acquiring vaccine-preventable infectious diseases during their patient contact hours. Given the global rise in neonatal pertussis incidence, there is a need to address the importance of protection against this infection by promoting booster vaccinations among female medical students as a preventive measure for their future generation. This paper addresses a part of our study on the seroprevalence of anti-PT IgG antibodies in female medical students who are more prone to acquiring infections from the patients during their clinical rotations. This study intends to assess the seroprevalence of anti-PT IgG antibodies among female medical students.

2. MATERIALS AND METHODS

This exploratory cross-sectional study was conducted by convenient sampling among healthy medical female students between February 2019 and April 2019. The study occurred at the RAK Medical and Health Sciences University (RAKMHSU), Ras Al Khaimah, United Arab Emirates. The inclusion criteria included healthy female medical students between 18–25 years of age who received childhood vaccinations per their countries' vaccination schedule and were willing to participate by providing written signed informed consent. The exclusion criteria comprised individuals below 18 years of age and above 25 years of age, individuals with acute febrile illness or any other infections, and individuals with any genetic conditions or who were immune-compromised and were on any immunosuppressive agents.

RAK Research Ethics Committee, Ministry of Health and Prevention (United Arab Emirates) (No MOHAP/REC /2019/2-2019-UG-M) approved the study. Confidentiality was ensured by using identifiers for the questionnaire. Blood samples were coded using the same reference number used in the questionnaire.

The data, namely, demographic characteristics and participants' immunization status, as per their birth country's vaccination schedule, was collected at the time of enrolment. Approximately up to 5 mL of blood samples were collected from all participants. Serum was separated by centrifugation, and samples were stored at -20°C. The samples were analyzed at the Central Research Laboratory, Ras Al Khaimah Medical and Health Sciences University. The pertussis IgG levels in IU/mL were measured using the commercially available validated ELISA kit (Sero Pertussis Toxin IgG, Catalog No.1231-01D, Savyon Diagnostics Ltd, Ashdod, ISRAEL) for the quantitative determination of specific IgG antibodies to Pertussis toxin in serum specimens. The test was performed and interpreted as directed by the kit manufacturer. The assay was valid when the reagent blank, negative control, calibrator, and positive control were within their respective ranges. All invalid results were considered to be excluded from the analysis. The immune status ratio (ISR) value for each specimen was calculated by dividing the specimen's optical density (OD) value by the manufacturer's cut-off value. ISRs 1.1 were interpreted as seropositive. For data analysis, values below 1.1 were considered negative. The anti-PT antibody titers in IU/mL were categorized into groups according to the interpretive criteria provided by the manufacturer. They were <55 IU/mL–negative, 55–<60 IU/mL–borderline, 60–125 IU/mL–positive, and >125 IU/mL–strongly positive.

The age distribution of the participants was expressed as number and percentage. Other demographic and baseline characteristics were expressed as descriptive statistics. Statistical significance was tested using the appropriate chi-square test, and a $P \leq 0.05$ was classed as statistically significant.

3. RESULTS AND DISCUSSION

3.1. Result

During the period between February 2019 to April 2019, 117 female medical students were contacted for their participation in the study. Among them, 103 were eligible for the study; seven were below 18 years; five students were absent at the time of blood sampling, and two were suffering from acute febrile illness. A total of Ninety students participated in the study, and 13 participants were not willing to take part in the study. All the participants had previously received DTP vaccination during childhood, and none were married. However, no participant had a booster DTP vaccination in the past five years. None gave a history of symptoms suggestive of pertussis in the past six months. The participants were ethnically diverse, with 10 Emirati and 80 from the expatriate population, as shown in (Table **1**). Among 90 blood samples collected, 40 samples showed detectable titers of anti-PT IgG antibodies. Thirteen blood samples showed high positive titers above 125U/mL, four of which showed positive titers ranging from 60–125 IU/mL. Two samples were in borderline 55–<60 IU/mL, and twenty-one

samples tested had values less than 55 IU/mL. Undetected titres were found in fifty samples that is equal to 74.4% of samples were seronegative with values less than 55 IU/mL. The mean ± SD of IgG titers was 42 ± 74.93 IU/mL with a range of 0-267 IU/mL. All blood samples were tested for PT IgG antibodies, and no missing sample had an error. The sample was then stratified based on antibody titers into high positive, positive, borderline, and negative groups, as shown in (Table **2**)

Table 1. Baseline sociodemographic data of all the participants.

Variable characteristics	Total participants (n=90)
Age (years) Mean± SD	21.12 ± 1.74
Education levels	Frequencies (%)
I year (n=5)	5.6
II year (n=12)	13.3
III year (n=20)	22
IV year (n=31)	34.4
V year (n=18)	20
Interns (n=4)	0.4
Nationality	
Emirati (n=10)	11.1
Expatriates (n=80)	88.9

Table 2. Comparison of determinant characteristics among high positive, positive/ borderline, and negative groups.

	High positive PT IgG n = 13	Positive /Borderline PT IgG n=6	Negative PT IgG n=71
Mean of the titres (SD)	208.38 (49.92)	80.66 (23.37)	8.32 (15.94)
Mean age (SD)	21.30 (1.23)	19.80 (1.06)	21.05 (1.93)
Education levels	Frequencies% (n)	Frequencies % (n)	Frequencies% (n)
I year (n=1) II year III year (n=1) IV year V year Interns (n=1)	1.11(n=1) 3.33(n=3) 1.11(n=1) 4.44(n=4) 3.33(n=3) 1.11(n=1)	Nil 1.11(n=1) 3.33(n=3) 1.11(n=1) 1.11(n=1) Nil	4.44(n=4) 8.89(n=8) 16.78(n=16) 28.89(n=26) 15.56(n=14) 3.33(n=3)
Total	14.4(n=13)	6.67(n=6)	78.89 (n=71)
Nationalities	Frequencies%(n)	Frequencies %(n)	Frequencies %(n)
Emirati	3.33(n=3)	Nil	7.78(n=7)
Expatriates	11.11(n=10)	6.67(n=6)	71.1(n=64)

PT IgG= Pertusis toxin immunoglobulin G, High positive are >125 IU/mL; positive titres are 60–125 IU/mL; borderline are 55 – <60 IU/mL; negative titres are <55 IU/mL

A chi-square test of independence was analyzed to explore the relationship between education level (II to V year) and the groups based on titers. The relationship between these was insignificant, X^2 (N =81), p >0.05. Exploring any relation between ethnic groups and whether titers are high positive or negative also revealed no statistical significance by chi-square statistic, (N=84) p >0.05.

4. DISCUSSION

Our study results show low seroprotection among female medical students. As medical students are involved in various health care programs as part of their curriculum, they are exposed to the risk of infection during their patient contact hours during clinical rotations. The female gender is more prone to infection and goes unrecognized during adolescence [12]. Further, the low seroprevalence of pertussis infection among females of childbearing age is a potential risk of increased neonatal pertussis. The reason is a lack of protective antibodies to pass on the protection against the pertussis infection transplacentally.

Several earlier studies have done a seroprevalence of pertussis protection in females of reproductive age. The study on asymptomatic first-year medical students found that 42% of females and 54% of males were seropositive [13]. Seropositivity was found in 70.2% of adolescent females in Israel due to a better immune response or a recent infection [14]. At the same time, the study among university students with persistent cough found 26% of recent pertussis infections [15].

Narchi *et al*. reported high seronegativity, with 72.4% of pregnant women of the mean gestational age of 25.5 weeks showing anti-PT IgG < 10IU/mL, indicating the need for pertussis vaccination during pregnancy. The remaining 24% of women were in the 10-100 IU/mL range, and 3.6% were in the high positive titers range [16]. In our study, seventy-one students (n=71; 74.4%) had negative titers of less than 55 IU/mL. However, only six students (n=6; 6.7%) showed protective/borderline titers and 14.44% (n=13) had high positive titers. 88.88% (n=80 out of 90) of our population were mostly expatriates, whereas Narchi *et al*. included 63.3% of Emirati participants. In another cross-sectional study by Hashemi *et al*., among 288 pregnant women, 35% had antibodies against pertussis. However, antibody titer higher than 24 U/ml was considered seropositive [17]. The cut-off antibody titer for seroprotection depends on various factors, such as the laboratory kits used. In another study, only 6% of pregnant women had anti-pertussis IgG antibodies [7].

It is well regarded that infection-acquired immunity lasts longer and starts waning after 4-20 years, whereas vaccination-acquired immunity wanes after 4-12 years [18]. Thus vaccination during childhood may not provide adequate seroprotection throughout childbearing age. The growing evidence suggests the role of pertussis vaccination in pregnancy to prevent neonatal pertussis [19].

Further, in many cases, seropositivity does not differentiate the recent infection from vaccine-acquired immunity [20]. 14.44% of our study group had high positive titers that could be due to recent infection or exposure to contacts, though none of them gave a history of symptoms suggestive of pertussis in the past six months. This is alarming since chances of unrecognized or asymptomatic pertussis are common among adolescents [12] and health professionals, as in our study.

Unrecognized pertussis infection incidence was high when the serologically positive infections were compared with clinically reported [21]. Another seroepidemiology study

demonstrated that estimated peaks of recent infections were maximum during 15-19 years and subjects above 60 years [22]. Similarly, in a seroepidemiology study involving 1313 healthy subjects aged 0-95, only 8.9% of individuals had pertussis IgG levels above 30 IU/mL [23]. In a more extensive seroepidemiological study conducted in Thailand, protective antibodies against pertussis infection were consistently low after 11 years [24]. This finding implicates the need for a booster dose in adolescence for sustained protection.

According to the Advisory Committee on Immunization Practices (ACIP) practice guidelines, all adolescents should receive a booster dose of Tdap consisting of tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine, followed by booster tetanus and diphtheria toxoids (Td) every ten years [25]. Though minimal adverse reactions have been reported with multicomponent acellular vaccines (aP vaccines), they have low efficacy compared to the whole-cell vaccine (wP vaccines). However, they are more effective than low-efficacy wP vaccines [26]. Pregnant women should receive Tdap in the third trimester irrespective of a previous booster dose. Infants and children should receive a 5-dose series of diphtheria, tetanus toxoids, and acellular pertussis (DTaP) vaccines [25]. However, some evidence suggests vaccination during the second trimester has better antibody titers in the newborn as compared to third-trimester vaccination [27]. There is also evidence for the Cocoon strategy, which involves vaccinating postpartum mothers and all people in close contact with the newborn [10]. However, it has the demerits of being difficult in the implementation and susceptibility of infection during the first two weeks of the newborn. Hence, prenatal vaccination during pregnancy is recommended [25, 28].

Addressing the need for health care professionals, especially young medical students, with robust evidence is the strength of this study; however, smaller sample size and single-center study are the study's limitations.

CONCLUSION

Our results show low seroprotection for *B pertussis* infection among female medical students, considered a high-risk group in the health profession. Though the sample size is small to generalize the results, the present study provides supportive evidence to the existing studies emphasizing the need for booster immunization, especially for health care professionals.

LIST OF ABBREVIATIONS

ACIP	=	Advisory Committee on Immunization Practices
aP vaccines	=	Multicomponent acellular pertussis vaccines
CDC	=	Centers for Disease Control and Prevention
DTaP	=	Diphtheria Tetanus, and acellular pertussis vaccination
ISR	=	Immune status ratio
IU	=	International Units
OD	=	Optical density
PT	=	Pertussis Toxin
SD	=	Standard Deviation
Td	=	Tetanus and diphtheria toxoids
wP	=	Whole cell pertussis vaccines
X^2	=	Chi-square test

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

RAK Research Ethics Committee, Ministry of Health and Prevention (United Arab Emirates) (No MOHAP/REC/2019/2-2019-UG-M) approved the study.

HUMAN AND ANIMAL RIGHTS

No animals were used in this research. All human research procedures followed were per the ethical standards of the committee responsible for human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2013.

CONSENT FOR PUBLICATION

Informed consent was obtained.

STANDARDS OF REPORTING

STROBE guideline was followed.

AVAILABILITY OF DATA AND MATERIALS

The data are available on request from the corresponding author. The data are not publicly shared due to the privacy of study participants.

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CONFLICT OF INTEREST

The author declares no conflict of interest, financial or otherwise.

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