Journal of Ideas in Health

e ISSN: 2645-9248 Journal homepage: www.jidhealth.com Open Access

Original Article

Medical students carry more virulent microorganisms at their throat than that of patients' accompaniers

Hanan Raheem Hassooni [1*], Abbas Aboud Farhan[1], Hameed M. Jasim[2], Adil Hassan Alhusseiny[3]

Abstract

Background: Transition of medical students from a non-clinical to a clinical situation carries a great risk that needs further investigation. This study aims to detect and compare the throat bacterial colonization between medical students and patients' accompaniers in a tertiary hospital.

Methods: Across-sectional descriptive study was conducted at the out-patient clinics of the Baquba Teaching Hospital at the Faculty of Medicine, Diyala University, Iraq. A total of 120 throat swabs collected from sample of 70 medical students (fifth stage) and 50 volunteers as a control group who were selected conveniently during their outpatient visits over the September 2018. Aerobic and anaerobic culture methods were recruited to investigate the samples following the standard microbiological procedures.

Results: Finding of this study indicate a high rate of bacterial throat colonization among medical students compared to control group. Male gender showed high susceptibility for infection than females. The most common bacteria isolated among medical students were Staphylococcus aureus and Escherichia coli 26 (37.1%), followed by Streptococcus pneumoniae appeared in 23 samples (32.8%), Viridians streptococci 19 (27.1%), Acinetobacter spp.14 (20%), Enterobacter spp. 4 (5.7%), Candida spp. 3 (4.2%), Pseudomonas aeruginosa 2 (2.8%) respectively.

Conclusion: Our findings suggest that medical students may contribute significantly for transmission and dissemination of nosocomial pathogens among patients and vice versa.

Keywords: Medical students, patients' accompaniers, throat, normal flora, Baquba, Diyala, Iraq

Background

Normal flora (resident normal flora) or sometimes called commensals are defined as a group of different microorganisms such as bacteria, fungi, protozoa, and viruses that continuously inhabited the human body. normal flora have been detected at six important human body openings-related sites that usually exposed to external environment including the skin, eyes and ears, respiratory tract, oral cavity (mouth), gastrointestinal tract, and urogenital tract. Bacteria are the most commonly seen normal flora, compared to fungi and other commensals [1,2] Normal flora play an active role in prevention of diseases and maintaining the health. It help in prevention of colonization by pathogens via bacterial intervention mechanism [2,3]. As usual, the fetus and the internal body organs such as the spleen, liver, pancreas, bladder, lymph, blood and cerebro spinal fluids (CSF) are free of normal flora, however the opportunistic microbes can easily attack the fetus or body organs and cause infection when the number of normal flora significantly reduced. The number and variety of normal flora depend on multiple factors which might be physiological (such as the change in body temperature), the geographical habitat (such as hospital attendance), diet (presence of certain nutrient in mouth), age (neglected kids and old age), gender, the immune system status (immune deficiency diseases) and chronic disease [3,4]. Frandah et al. (2013) found that "patients with diabetes and a history of recent proton pump inhibitors (PPIs) use are more likely to have abnormal oral flora on admission to the medical intensive care unit (MICU)" [5].

Unfortunately, visitors of hospital, whether had been admitted or in an outpatient clinics and even their accompaniers are most likely to have a risk of the transmission of pathogens from health workers and hospital instruments. Microorganisms have been isolated from the white coat of medical doctors and students [6,7], medical uniforms [8], nasal cavity of medical students [9-11] and other health workers [11], hands of medical

*Correspondence: hanan6319@gmail.com
[1]Department of Biology, Faculty of Education for Pure Science, Diyala University, Iraq.
Full list of author information is available at the end of the article

doctors and students [12-15], stethoscopes, medical students' cell phone [16], medical charts [17], ward fomites [18,19], and the frequently touched objects in hospital [20]. The objectives of this study were (1) to determine the normal flora or the bacterial growth in the throat of medical students who are undergoing training education in the hospital and being in direct contact with patients, (2) to determine the bacterial growth or the normal flora in the throat of control group of the patient's accompaniers, (3) to compare the results of isolated bacterial growth between medical students and the control group.

Methods

Study design and subjects

A cross-sectional descriptive analytical study was performed among medical students, faculty of medicine, Diyala University, Iraq. Data were collected from September 1st to 30th, 2018. To investigate the normal flora in the throat, all the fifth stage medical students (academic year of 2018-2019) who were undergoing clinical training and being in direct contact with patients at the Baquba Teaching Hospital of Diyala University were included. Because of inclusion and exclusion criteria (Table 1), swabs were collected from the throat of 70 medical students compare to 50 volunteers in control group, who were accompanying patients during their outpatient visits. At the time of study, both of the sample and control groups were clinically examined. Table 1 presents the main inclusion and exclusion criteria.

Table 1 Inclusion and exclusion criteria.

Inclusion and exclusion criteria	Medical Student	Control Group
Fifth stage medical students.	+	-
Patient's accompaniers who visited the hospital.	-	+
Willing to participate.	+	+
Acute or chronic rhinitis.	-	-
Pharyngitis, cryptic tonsillitis, sinusitis, otitis media.	-	-
Sino bronchial syndrome.	-	-
Disorders related to airways or nasopharyngeal way.	-	-
Smoking and alcohol drinking. Diabetes or hypertensive.	-	-
Current antibiotic therapy (oral or systemic) use or used in the preceding 2 weeks.	-	-
Recent tonsil or throat surgeries.	-	-
Dental surgery in the preceding 2 weeks.	-	-

+: referred to inclusion criteria; -: referred to exclusion criteria

Collection of the sample

Researchers followed the standard clinical methods to collect throat swab samples. All samples were extracted in a well-lit room, considering the comfortable sitting of participants and facing a light source. Precautions were taken to avoid swab contamination before and after swab collecting procedure. A sterile tongue blade or spoon was used to depress the tongue. Attention was given not to touch all sides or top of the mouth including the tongue while moving the swab. A firm and quick rubbing of the swab on the back of the throat, and on the tonsils has performed. Swabs were soon placed in the provided culture medium.

Transport of sample

In order to ensure the viability of pathogens, samples were sent directly to the microbiology department of Baquba teaching hospital in a sterile transport medium. Moreover, each sample was provided with an individual participant data such as name, date, age, and gender to facilitate data collection for analysis.

Stain and culture process

Blood, Chocolate and MacConkey agars were separately used to culture the organisms. According to the standard microbiological methods, "Five percent sheep blood agar and MacConkey agar plates were incubated aerobically, while chocolate agar was incubated under 5% CO2 atmosphere at 37°C for 24–48 h". The isolates then stained with Gram stain to identify the shape and color of the colonies under the microscope. The isolates were cultured on the differential and diagnostic medium and were then diagnosed with VITEK-2 compact system.

Statistical analysis

Data was collected and analyzed using Microsoft Excel Spreadsheet. Descriptive analysis was performed concerning the most common pathogen isolate in both of medical student and control groups and the gender differences.

Results

Descriptive analyses

More than half (55.7%, 39) of the 70 throat swab samples collected from fifth class medical school students were females compared to 44.3%, 31 males. In the control group, the 50 throat swab samples were equally distributed between the male and female participants (Figure 1). Each participant of medical students and control group was in average age of 22 years old.

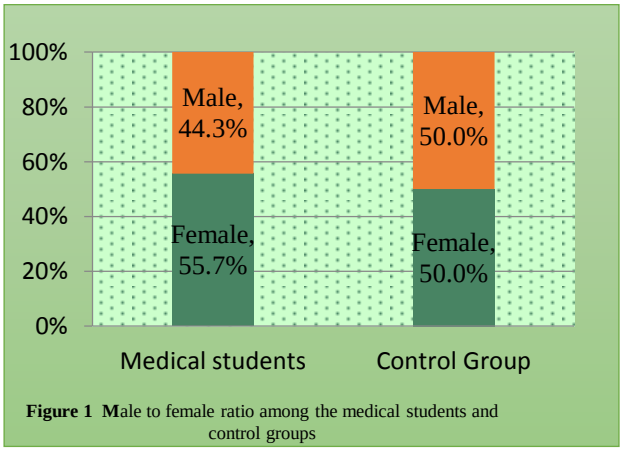

Figure 1 Male to female ratio among the medical students and control groups

Table 2 presents the bacterial growth in the medical students and control groups. The most common bacterial growth in the samples of medical students were Staphylococcus aureus, Escherichia coli, Streptococcus pneumoniae, Viridians streptococci, Acinetobacter spp.

The highest percent 26 (37.1%) was reported at an equal rate among Staphylococcus aureus and Escherichia coli. While Streptococcus pneumoniae appeared in 23 samples (32.8%), Viridians streptococci 19 (27.1%), Acinetobacter spp. 14 (20%), Enterobacter spp. 4(5.7%), Candida spp. 3(4.2%), Pseudomonas aeruginosa 2(2.8%). However, the lowest percent was at equal percentage of 1.4% (1 sample) for each of Proteus spp., Streptococcus pyogenes, Staphylococcus albicans. Regarding the control group, the bacterial growth was limited to five spp.; Haemophilius spp., Viridians streptococci, Streptococcus pneumoniae, Staphylococcus aureus and Streptococcus pyogenes at a percent of 21(42%), 18(36%), 9(18%), 4(8%) and 1(2%) respectively.

Table 3 presents the bacterial growth according to gender. There is a difference between males and females within the students and control groups in this study. In the student samples, almost all isolated bacterial spp. (Staphylococcus aureus, Escherichia coli, Streptococcus pneumoniae, Viridians streptococci, Acinetobacter spp.) recorded high bacterial growth among the male gender compared to female gender. However, the opposite was reported in control group, where the isolated bacterial growth such as Haemophilius spp. appeared more among female gender than the male gender.

Table 2 Bacterial growth in the healthy students and Control group

Medical students			**Control group**		
Bacteria	**N**	**%**	**Bacteria**	**N**	**%**
Staphylococcus aureus	26	37.1	Haemophilius spp.	21	42
Escherichia coli	26	37.1	Viridians streptococci	18	36
Streptococcus pneumoniae	23	32.8	Streptococcus pneumoniae	9	18
Viridians streptococci	19	27.1	Staphylococcus aureus	4	8
Acinetobacter spp.	14	20	Streptococcus pyogenes	1	2
Enterobacter spp.	4	5.7			
Candida spp.	3	4.2			
Pseudomonas aeruginosa	2	2.8			
Proteus spp.	1	1.4			
Streptococcus pyogenes	1	1.4			
Staphylococcus albicans	1	1.4			

Table 3 Bacterial growth in the healthy students and Control group according to sex

Medical students			**Control group**		
Bacteria	**Male**	**Female**	**Bacteria**	**Male**	**Female**
Staphylococcus aureus	15	11	Haemophilius spp.	9	12
Escherichia coli	17	9	Viridians streptococci	9	9
Streptococcus pneumoniae	15	8	Streptococcus pneumoniae	4	5
Viridians streptococci	10	9	Staphylococcus aureus	2	2
Acinetobacter spp.	8	6	Streptococcus pyogenes	0	1
Enterobacter spp.	3	1			
Candida spp.	2	1			
Pseudomonas aeruginosa	2	0			
Proteus spp	0	1			
Streptococcus pyogenes	0	1			
Staphylococcus albicans	1	0			

Discussion

In this study, different numbers and different types of bacterial growths have been detected in the throats of both of medical students and control groups. Twelve different bacterial spp. (Table 2) have been isolated from throats of medical student group compare to five bacterial spp. (Table 3) from the control group. Results of the study confirmed the existence of two different environments [11] with a marked changes happened in the nature of the resident normal flora in the throats of students. Most of normal flora components are harmless in healthy individuals, however normal flora could be changed to an inflammatory agent when have being stimulated by other organisms [1, 4]. Upper respiratory tract (URT) is often the main colonization place by pathogens compare to the lower respiratory tract (LRT) which is usually stay sterile, due to the difficulty of bacteria to reach it [1,21,22]. Collins (2008) identified three essential elements for the transmission of disease within health institutions: “a source of infecting microorganisms, a susceptible host, and a means of transmission for the microorganism to the host” [23]. Health care personnel including medical students are vulnerable to bacterial infection when they have direct contact with the

patient or any of his or her contaminated discharges [23]. This can explain partly the possibility of medical students in our study might have been exposed to microorganisms from patients during their training education in the hospital. Furthermore, despite the fact that the undergraduate medical students are out of the normal medical staff in health institutions, however they contribute seriously to being a source and mean of transmitting nosocomial infections because health training requires frequent and direct contact with patients. [10,24-27]. Findings of this study showed that the prevalence rate of S. aureus and Escherichia coli throat colonization was 37.1% among the sample of medical students compared to 8.0% among the sample of control group.

Although it is a normal inhabitant of the oral cavity, throat and nose [28], however S. aureus is considered among the most common pathogens responsible for a number of infectious diseases in both of community and health institutions [29]. Bhatta et al. (2018) in his study among Nepalese medical students, found that "the prevalence of s. aureus was significantly higher among clinical sciences students compared to preclinical sciences students" [30]. Al-Tamimi et al. (2018) reported that the prevalence rate of S. aureus nasal colonization among medical students as international trend was in range of 14 to 45%, which is close to our findings of 37.1% throat colonization among medical students [10]. In fact, results showed that medical students throat colonization with another group of infectious pathogens (Escherichia coli, Streptococcus pneumoniae, Viridians streptococci, Acinetobacter spp.) which were no less dangerous than S. aureus. International research indicated that most of these organisms act as resistant bacteria in oral cavities [31-34]. The results of the research may explain on the basis of either the medical students were exposed to direct nosocomial infections from the hospital because of direct contact with patients and this is what was discussed in this research or the behavior of the medical students agreed with the nature of the community of excessive and unjustified use of antibiotics, which results in bacterial resistance and this is beyond the current research.

Although "females were generally more interested in training improvement and higher education than males" [35], which normally required them to attend more training and clinical sessions in hospital, however finding of this study showed that most of bacterial growing were among the males group compared to females (Table 3). In fact, two main factors (genetic differences and endocrine immune reactions) were reported to determine the immunological differences between the sexes [36]. Differences in gene expression and sex steroid hormones help to obtain a difference in immune responses between males and females [37,38]. Females showed a strong immune response to antigenic challenges such as infection and vaccination and subsequently more resistant to infection thane males [36,39]. Females give more frequent and severe reactions to viral and bacterial vaccines than men [36,40] however they are more susceptible to the autoimmune disorders and diseases than their counterparts [41]. Prediction of transmission of serious pathogens from patients to medical students or the reverse can be reached by doing a regular screening of clinical medical students.

The clinical medical students are more likely responsible to transmit and disseminate the pathogens within the health care institution than other health care providers, because the medical students are undergoing to rotational training program in different wards/units of hospital, while doctors and nurses are usually working in predetermined wards/units depending on their specialty.

In the light of our results and other similar studies, the availability of data will greatly help to reduce the transmission of diseases among hospital departments, especially among the high-risk patients such as ICU, burn, postoperative and neonates patients. Policy about the standard medical practice including awareness/orientation program should be strictly implemented in the level of health care personnel and medical students to avoid the transmission of nosocomial pathogens.

The strength of this study lies in comparing medical students with patient's accompaniers belonging to two different environments. However, this study had complaint from some limitations. First: we collected our data during the autumn/summer season (September), however the seasonal variation in the colonization rate was ignored in this study. Second: antibiotic sensitivity of the isolated pathogens was not done. Third, the transmission of isolated pathogens from the sample of medical students to control group, patients or the other healthcare personnel, and the vice versa was not included in the current study. Fourth: results of this study cannot be generalized to other medical students, because the sample was from one medical college of Diyala University, Iraq.

Conclusion

This study compared sample of undergraduate medical students (fifth class) with patients' accompaniers attending outpatient clinics. Student are usually visiting different departments within the hospital following their clinical teaching curriculum. Results of this study found that the medical students complaint from high rate of bacterial throat colonization compared to control group. Such evidence may increase the possibility that medical students play role in transmission and dissemination the infection among patients and health care personnel. Efforts should be adequate to rise the knowledge and awareness among medical students, in addition to strong adherence to infection control protocols to minimize the transmission of nosocomial diseases in healthcare institutions.

Declarations

Abbreviations

CSF: Cerebro Spinal Fluids PPIs: Proton Pump Inhibitors MICU: Medical Intensive Care Unit URT: Upper Respiratory Tract URTI: Upper Respiratory Tract Infection LRT: Lower Respiratory Tract

Acknowledgement

We render our special thanks to all directors in Diyala university and Baquba Teaching Hospital. We are also grateful to all the medical students for their help, time and openness during the data collection

Funding

The author (s) received no financial support for the research, authorship, and/or publication of this article.

Availability of data and materials

Data will be available by emailing hanan6319@gmail.com

Authors' contributions

HRH is the principal investigator of the study who designed the study and coordinated all aspects of the research including all steps of the manuscript preparation. She is responsible for the study concept, design, writing, reviewing, editing and approving the manuscript in its final form. AAF, HMJ and AHA contributed in the study design, analysis and reviewed and approved the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

We conducted the research following the Declaration of Helsinki, and the protocol was approved by the Center of Training and Human Resource Development, Diyala Province Health Directorate, Ministry of Health, Iraq (Ref: official letter No. 303 issued in 21st January 2018). Confidentiality was assured with signed informed consent.

Consent for publication

Not applicable

Competing interest

The authors declare that they have no competing interests.

Author details

[1]Department of Biology, Faculty of Education for Pure Science, Diyala University.[2]College of Biotechnology, Al-Nahrain University, Baghdad, Iraq. [3]Department of Internal Medicine, Faculty of Medicine, Diyala University, Iraq.

Article Info

Received: 11 November 2018
Accepted: 21 December 2018
Published: 23 December 2018

References

1. Abhilash A, Zainab A, GangadharaS, Annet O, Sunil P. A clinical study of oropharyngeal microbial flora in laryngopharyngeal reflux disease. Journal of microbiology and biotechnology 2014; 3(2):14-18.

2. Cui L, Morris A, Ghedin E.The human mycobiome in health and disease. Genome Med 2013; 5(7): 63.

3. Lynne VM. Normal flora: diversity and functions, Microbial Ecology in Health and Disease 2000; 12(4):193-207.

4. Jayashree K, Sanjeev D, Inam D. An Initial Study on Normal Commensel Flora of Throat, Journal of Dental and Medical Sciences 2016; 15(7): 132-134.

5. Frandah W, Colmer-Hamood J, Mojazi Amiri H, Raj R, Nugent K. Oropharyngeal flora in patients admitted to the medical intensive care unit: clinical factors and acid suppressive therapy. J Med Microbiol. 2013;62(Pt 5):778–84.

6. Noor F, Jayanthi RS. The study of microbial flora on doctors white coats in tertiary care hospital in outskirts of Hyderabad, Telangana, India. Int J Res Med Sci. 2016; 4(7): 2705-2712.

7. Qaday J, Sariko M, Mwakyoma A, Kifaro E, Mosha D, Tarimo R, et al. Bacterial Contamination of Medical Doctors and Students White Coats at Kilimanjaro Christian Medical Centre, Moshi, Tanzania. Int J Bacteriol. 2015; 2015: 507890.

8. Du ZY, Zhang MX, Shi MH, Zhou HQ, Yu Y. Bacterial contamination of medical uniforms: a cross-sectional study from Suzhou city, China. J Pak Med Assoc. 2017; 67(11): 1740-1742.

9. Susethira AR, Vigneshwari RS, Krishnaveni M, Uma A, Thirumalaikolundusubbramaniam S, Jeyaseelan Senthinath T, et al. Nasal floral changes among medical students on exposure to formaldehyde. Int J Curr Microbiol App Sci. 2013; 2(6): 246-253.

10. Al-Tamimi M, Himsawi N, Abu-Raideh J, Abu jazar D, Al-jawaldeh H, Sameer Mahmoud A, et al. Nasal colonization by methicillin-sensitive and methicillin-resistant Staphylococcus aureus among medical students. J Infect Dev Ctries. 2018; 12(5): 326-335.

11. Muhammed SA, Mohammed AW, Wadi AS, Mohammed DL. A comparative study on detecting bacterial flora of the nasal cavity in normal healthy workers that work in cement factory and the healthy Students in Koya University. IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS) 2014; 9(4): 07-15.

12. Monistrol O, López ML, Riera M, Font R, Nicolás C, Escobar MA, et al. Hand contamination during routine care in medical wards: the role of hand hygiene compliance. J Med Microbiol. 2013; 62: 623–629.

13. Amin TT, Al Noaim KI, Bu Saad MA, Al Malhm TA, Al Mulhim AA, Al Awas MA. Standard precautions and infection control, medical students' knowledge and behavior at a Saudi university: the need for change. Glob J Health Sci. 2013; 5(4): 114–25.

14. Chauhan K, Mullan S. Evaluation of contamination of hands of the medical students in a medical teaching tertiary care hospital. Advances in Microbiology 2017; 7: 666-671.

15. Longtin Y, Schneider A, Tschopp C, Renzi G, Gayet-Ageron A, Schrenzel J, et al. Contamination of stethoscopes and physicians' hands after a physical examination. Mayo Clin Proc 2014; 89(3): 291–299.

16. Jalalmanesh S, Darvishi M, Rahimi M, Akhlaghdoust M. Contamination of senior medical students' cell phones by nosocomial ınfections: a survey in a university-affiliated hospital in Tehran. Shiraz E-Med J 2017; 18(4): e43920.

17. Chen K-H, Chen L-R, Wang Y-K. Contamination of Medical Charts: An Important Source of Potential Infection in Hospitals. PLoS ONE 2014; 9(2): e78512.

18. Xiao S, Tang JW, Li Y. Airborne or Fomite Transmission for Norovirus? A Case Study Revisited. Int. J. Environ. Res. Public Health 2017; 14: 1571.

19. Nwankwo E. Isolation of pathogenic bacteria from fomites in the operating rooms of a specialist hospital in Kano, North-western Nigeria. Pan Afr Med J 2012; 12: 90.

20. Bhatta DR, Hamal D, Shrestha R, Hosuru Subramanya S, Baral N, Singh RK, et al. Bacterial contamination of frequently touched objects in a tertiary care hospital of Pokhara, Nepal: how safe are our hands?. Antimicrob Resist Infect Control 2018; 7: 97.

21. Bista M, Amatya M, Basnet P. Tonsillar microbial flora: A comparison of infected and noninfected tonsils. Kathmandu University Medical Journal 2006; 4 (1): 18-23.

22. Hassooni H, Fadhil S, Hameed R, Alhusseiny A, Ali Jadoo SA. Upper respiratory tract infection and otitis media are clinically and microbiologically associated. Journal of Ideas in Health 2018; 1(1): 29-33.

23. Collins AS: Preventing health care-associated infections. Patient Safety and Quality: an Evidence-Based Handbook for Nurses. Edited

by: Hughes RG. 2008, Rockville (MD): Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services.
24. Zakai SA. Prevalence of methicillin-resistant Staphylococcus aureus nasal colonization among medical students in Jeddah, Saudi Arabia. Saudi Med J 2015; 36: 807-812.
25. Okamo B, Moremi N, Seni J, Mirambo MM, Kidenya BR, Mshana SE. Prevalence and antimicrobial susceptibility profiles of Staphylococcus aureus nasal carriage among pre-clinical and clinical medical students in a Tanzanian University. BMC Res Notes 2016; 9: 47.
26. John A, Tomas ME, Hari A, Wilson BM, Donskey CJ. Do medical students receive training in correct use of personal protective equipment? Med Educ Online 2017; 22: 1264125.
27. Orlin I, Rokney A, Onn A, Glikman D, Peretz A. Hospital clones of methicillin-resistant Staphylococcus aureus are carried by medical students even before healthcare exposure. Antimicrob Resist Infect Control 2017; 6: 15.
28. McCormack MG, Smith AJ, Akram AN, Jackson M, Robertson D, Edwards G, et al. Staphylococcus aureus and the oral cavity: An overlooked source of carriage and infection? Am J Infect Control 2015; 43: 35–37.
29. Rodriguez M, Hogan PG, Burnham CA, Fritz SA, et al. Molecular epidemiology of Staphylococcus aureus in households of children with community-associated S. aureus skin and soft tissue infections. J Pediatr 2014; 164: 105–111.
30. Bhatta DR, Hamal D, Shrestha R, Parajuli R, Baral N, Subramanya SH. Nasal and pharyngeal colonization by bacterial pathogens: a comparative study between preclinical and clinical sciences medical students. Can J Infect Dis Med Microbiol 2018; 2018: 7258672.
31. Bryskier A. Viridans group streptococci: a reservoir of resistant bacteria in oral cavities. Clin Microbiol Infect 2002; 8(2): 65-69.
32. de LV, Malosh RE, Aiello AE, Foxman B. Prevalence of Escherichia coli carriage in the oropharynx of ambulatory children and adults with and without upper respiratory symptoms. Ann Am Thorac Soc. 2015; 12: 461–463.
33. Wang L, Qiao X, Ai L, Zhai J, Wang X. Isolation of antimicrobial resistant bacteria in upper respiratory tract infections of patients. Biotech 2016; 6(2): 166.
34. Deepthi M, Narsimloo K. Role of usage of antibiotics in pharyngitis: a prospective study. Int J Otorhinolaryngol Head Neck Surg 2017; 3(2): 303-307.
35. Al-Samarrai MA, Ali Jadoo SA. Iraqi medical students, are still planning to leave after graduation. Journal of Ideas in Health 2018; 1(1): 23-28.
36. Anna R, Simona A, Antonell D, Luciana G, Marina V. The influence of sex and gender on immunity, infection and vaccination, Ann Ist Super Sanità 2016; 52(2): 198-204.
37. Pinheiro I, Dejager L, Libert C. X-chromosome-located microRNAs in immunity: might they explain male/female differences? The X chromosome-genomic context may affect X-located miRNAs and downstream signaling, thereby contributing to the enhanced immune response of females, Bioessays 2011; 33(11): 791-802.
38. Ying SY, Lin SL. Current perspectives in intronic micro RNAs (miRNAs). J Biomed Sci 2006; 13: 5–15 .
39. Klein SL, Jedlicka A, Pekosz A. The Xs and Y of immune responses to viral vaccines, Lancet Infect Dis 2010; 10(5):338- 49.
40. Cook IF. Sexual dimorphism of humoral immunity with human vaccines. Vaccine 2008; 4; 26(29-30): 3551-5.
41. Voskuhl R. Sex differences in autoimmune diseases. Biol Sex Differ 2011; 2(1):1-21.