

Original Article

Nasopharyngeal Colonization and levofloxacin Susceptibility of *Streptococcus pneumoniae* among Healthcare Workers in a Teaching Hospital in Tehran, Iran

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Abstract

Background: *Streptococcus pneumoniae* commonly asymptotically colonizes the human upper respiratory tract and the carriage rate varies between geographical regions. The colonized individuals are not only at risk of infections but also can be a source of transmission of the pathogen. The risk of the droplet or airborne transmission of pneumococcal strains healthcare workers is considerable. The current study aimed to determine the extent of nasopharyngeal colonization with *S. pneumoniae* and their levofloxacin susceptibility at a tertiary hospital in Tehran, Iran.

Materials and Methods: During a six-month period, the nasopharyngeal swab samples collected from 300 volunteer healthcare workers of Imam Hossein Hospital. Samples screened for *S. pneumoniae* using standard conventional biochemical methods. The minimum inhibitory concentration (MIC) of levofloxacin was determined using a commercially available strip antibiotic test according to the clinical laboratory standards institute (CLSI) guidelines.

Results: A total of 19 (6.3%) enrolled healthcare workers were colonized with *S. pneumoniae*. Amongst the enrolled volunteers, nurses had a higher rate of pneumococcal colonization (47.3%) followed by interns (21%) and laboratory workers (15.8%). Our analysis revealed that there was a significant correlation between smoking and pneumococcal colonization. The antimicrobial susceptibility testing showed that all of the isolates were susceptible to levofloxacin (MIC \leq 2 μ g/ml).

Conclusion: This low rate of pneumococcal colonization amongst healthcare professionals may be attributed to the low risk of horizontal transmission of severe pneumococcal infections in the hospital. Additionally, our findings indicated that levofloxacin was an effective antimicrobial agent for the treatment of pneumococcal infections.

Keywords: *S. pneumoniae*, Health care workers, Nasopharyngeal carriage, Colonization, Levofloxacin

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Introduction

Streptococcus pneumoniae (also called

pneumococcus) commonly asymptotically colonize the human upper respiratory tract, but occasionally can cause a wide range of infections ranging from non-

invasive infections, such as sinusitis and acute otitis media, to serious lethal invasive diseases such as pneumonia, septicemia or meningitis¹⁻³. Despite the availability of effective antimicrobial agents and the application of pneumococcal vaccines, the world health organization (WHO) reported that pneumococcal diseases were responsible for about 1.6 million deaths around in 2008 worldwide⁴. Young children and the elderly are particularly vulnerable to pneumococcal disease due to the lack of an adequate immune system and recurrent contacts to pneumococcal strains⁵.

The nasopharyngeal carriage rate of pneumococcus varies between geographical regions⁶. As a matter of fact, the clinical outcome of pneumococcal infections are preceded by asymptomatic colonization of the human nasopharynx by pneumococcal strains and the colonized strains are prerequisite of invasive diseases⁷. Moreover, nasopharyngeal carriage of pneumococcal strains is an important risk factor as it is the major source of horizontal spread of this pathogen in both healthcare and community settings⁸. Therefore, understanding the carriage rate among carriers is important for the understanding of pneumococcal burden particularly in health-care settings⁹. Monitoring and surveillance of pneumococcal carriers in health-care settings seems to be essential for several reasons. First, carriers can serve as reservoirs for *S. pneumoniae* transmission to others in the hospital. Second, pneumococcal colonization in healthy persons is a risk factor to develop invasive and non-invasive pneumococcal diseases¹. Horizontal transmission of pneumococcal strains to non-carriers occurs through direct contact with respiratory droplets from an asymptomatic carrier or a patient. Increased risk for developing the pneumococcal disease is documented in close contact between healthcare workers and unimmunized patients, including children younger than 2 years of age and patients with AIDS, sickle cell disease, certain immunodeficiency syndromes, asplenia and malignant neoplasms¹⁰.

Management of severe *S. pneumoniae* infections is currently being compromised by increasing resistance of the pathogen to several antibiotics, which are commonly used for the treatment of pneumococcal diseases^{11,12}. Several investigations of penicillin-

resistant pneumococci in the last years indicate that the emerging and spread of penicillin resistance is principally associated to spread of a few successful clones¹³. On the contrary, there is a lack of surveillance studies investigating fluoroquinolone resistance in several countries such as Iran. Although the incidence of levofloxacin-resistant pneumococci is reported to have increased throughout many parts of the world, the rate of such levofloxacin-resistance is unclear among pneumococcal strains in Iran.

Therefore, the current study aimed to investigate the colonization rate of *S. pneumoniae* in healthcare workers who have constant contact with wide varieties of patients and to determine levofloxacin susceptibility for the pneumococcal isolates in Imam Hossein Hospital in Tehran.

Methods

Study population: This study was carried out from April to October 2018. A total of 300 healthcare workers from various hospital wards and departments of Imam Hossein Hospital, Tehran, Iran, who had direct contact with patients or handling clinical samples enrolled in our study. All grades of healthcare workers including nurses, cleaners, contract staff, graduates medical students, and interns were included in this study. The Ethics Committee of School of Medicine, Shahid Beheshti University of Medical Sciences approved this study (IR.SBMU.MSP.REC.1397.401). A written informed consent was obtained from all subjects before enrolling in this study.

Sample collection and bacterial identification: The nasopharyngeal swab specimens were collected from volunteer healthcare workers of Imam Hossein Hospital who did not have any clinical evidence of infection and screened for *S. pneumoniae* by standard techniques. The collected swabs cultured for bacterial growth on tryptic soy agar plates (Merck Co., Germany) supplemented with 5% sheep blood followed by incubation for 24 hours at 37°C, 5% CO₂. Phenotypic and conventional biochemical tests performed on suspected alpha-hemolytic colonies from blood agar. Gram stain, catalase and optochin (ethylhydrocupreine hydrochloride) susceptibility tests were carried out to identify *S. pneumoniae* isolates; when necessary, a bile (sodium deoxycholate) solubility test was also performed according to the standard procedure¹⁴.

Levofloxacin susceptibility testing: Susceptibility to levofloxacin evaluated in all pneumococcal isolates. The minimum inhibitory concentration (MIC) of levofloxacin was determined using a commercially available strip antibiotic test (Liofilchem Co., Roseto, Italy) according to the clinical laboratory standards institute (CLSI) guidelines 2018. The antibiotic susceptibility pattern of each pneumococcal isolates was analyzed based on the CLSI breakpoint for levofloxacin (MIC of ≤ 2 $\mu\text{g/ml}$, susceptible, MIC = 4 $\mu\text{g/ml}$, intermediate resistance, and MIC of ≥ 4 $\mu\text{g/ml}$, resistant).

Results

Among the 300 healthcare workers enrolled during the study period, 19 (6.3%) had been colonized with *S. pneumoniae*. Amongst the enrolled volunteers, nurses had a higher rate of pneumococcal colonization (47.3%) followed by interns (21%) and laboratory workers (15.8%), while the lowest rate of colonization was found amongst the residents (5.2%).

In this study, various potential risk factors for colonization also were analyzed. There was no significant association between gender/marital status/duration of employment in hospital/ previous history of upper respiratory tract infection/ previous history of pneumococcal diseases/ history of antibiotic intake in preceding 15 days or throat examination findings and pneumococcal colonization. Our analysis revealed that there was a significant correlation between smoking and pneumococcal colonization ($p=0.001$). Demographic characteristics and personal details of the healthcare worker volunteers, as well as the risk factors for pneumococcal colonization, summarized in Table 1.

The antimicrobial susceptibility testing showed that all of the isolates were susceptible to levofloxacin (MIC ≤ 2 $\mu\text{g/ml}$). The range of MIC against levofloxacin in pneumococcal isolates was between 0.25 to 2 $\mu\text{g/ml}$, in which MIC50 and MIC90 values of levofloxacin were 1 $\mu\text{g/ml}$ and 2 $\mu\text{g/ml}$, respectively.

Discussion

Asymptomatic nasopharyngeal colonization by encapsulated *S. pneumoniae* is very frequent,

especially in children and healthcare workers, and the prevalence of carriers varies globally. It should be pointed out that nasopharyngeal colonization by pneumococcal strains is a prerequisite for pneumococcal infections^{15,16}. The risk of nasopharyngeal colonization and pneumococcal infections increases with overcrowding, and hospitalization is an important risk factor for developing pneumococcal diseases¹⁷. *Pneumococcus* was previously reported to cause epidemics within closed populations and settings, including military bases, hospitals, daycare centers, shelters, jails, and nursing homes¹⁸. Moreover, *S. pneumoniae* is recognized as one of the causes of nosocomial infections, which is responsible for 5% of nosocomial bacterial meningitis, 4% of nosocomial acute sinusitis, and 2% of bacteremia and about 1% of nosocomial pneumonia¹⁹. As a matter of fact, cases of cross-infection with *S. pneumoniae* in the hospital have been described in some specific age groups and debilitated individuals, such as the elderly, hospitalized neonates and infants, asplenic patients, and other immunocompromised patients and with ultimately fatal diseases²⁰. The burden of nosocomial pneumococcal infections is reported to be significantly higher in developing countries²¹. Healthcare workers are considered as potential carriers for the transmission of pneumococcal strains. Moreover, medical students particularly could be potential source of pneumococcal infections in the community²². Therefore, comprehensive surveillance is essential to screen healthcare professionals and medical students for colonization by pneumococcal strains.

Accurate data on the rate of carriage of pneumococci in healthy healthcare professionals in Iran are lacking. In this investigation, the rate of pneumococcal colonization in healthy healthcare workers in a teaching hospital in Tehran who do not suffer from pneumococcal infection was 6.3%. This colonization rate was less than those reported by Subramanya et al. in Nepal (30%)²². Mackenzie and colleagues reported that pneumococcal carriage prevalence was 26% among adults and 67% among children in Australia²³. The differences in prevalence mentioned above can be explained by geographic variance, public immunization, and other risk factors. In Iran, there are a few data indicating pneumococcal carriage rate in

Table 1: Demographic characteristics of the enrolled healthcare worker volunteers and also various risk factors for colonization with *S. pneumoniae*.

Characteristics	No. (%), N = 300	Colonized, n = 19 (%)	Not colonized, n = 281 (%)
<i>Gender</i>			
Male	178 (59.3%)	14 (63.1%)	164 (58.4 %)
Female	122 (41.7%)	5 (36.9%)	115 (41.6%)
<i>Smoking</i>			
Yes	77 (25.6%)	14 (63.1%)	63 (22.4%)
No	223 (74.3%)	5 (36.9%)	218 (77.6%)
<i>Designation</i>			
Nursing staffs	89 (29.6%)	9 (47.3%)	78 (28.5%)
Interns	73 (24.3%)	4 (21%)	69 (24.5%)
Laboratory staffs	19 (6.3%)	3 (15.8%)	16 (5.7%)
Other staffs	61 (20.4%)	2 (10.7%)	59 (21%)
Residents	58 (19.4%)	1(5.2%)	57 (20.3%)
<i>Marital status</i>			
Single	136 (42%)	8 (42.1%)	128 (45.5%)
Married	174 (58%)	11 (57.9%)	163 (54.5%)
<i>Duration of employment in hospital</i>			
>5 years	174 (58%)	7 (63.3%)	167 (59.4%)
5-10 years	93 (31%)	9 (23.3%)	84 (29.9%)
>10 years	33 (11%)	3 (13.3%)	30 (10.7%)
<i>History of RTI</i>			
Yes	29 (9.7%)	5 (6.7%)	24 (8.5%)
No	271 (90.3%)	14 (93.3%)	257 (91.4%)
<i>History of pneumococcal diseases</i>			
Yes	0 (0%)	0 (0%)	0 (0%)
No	300 (100%)	19 (100%)	281 (100%)
<i>History of antibiotic use in preceding 15 days</i>			
Yes			
No	24 (8%)	2 (10.5%)	22 (7.8%)
	276 (92%)	17 (89.5%)	259 (92.2%)
<i>Throat examination</i>			
Normal	287 (95.6%)	18 (94.7%)	269 (95.7%)
Inflamed tonsils	13 (4.4%)	1 (5.3%)	12 (4.6%)

healthy children. Accordingly, Mousavi et al., reported that 26.7% of healthy in Tehran were colonized by *S. pneumoniae*²⁴. In another

investigation, 1300 healthy children less than 10 years old of age in Tehran were shown pneumococcal nasopharyngeal carriage rate of 44.1%²⁵.

Numerous studies have indicated that pneumococcal conjugate vaccines (PCVs) can prevent severe pneumococcal infections and induce herd immunity against the pathogen through colonization reduction in vaccinated individuals, and unvaccinated persons indirectly²⁶. Accordingly, the pneumococcal colonization rate in the conjugate vaccine era has reported significantly lesser than the regions that do not have the pneumococcal immunization program²⁷. To the extent of our knowledge, currently, there is no public immunization schedule against *S. pneumoniae* in Iran. Hence, pneumococcal vaccines are of particular importance in the reduction of pneumococcal colonization rates and pneumococcal diseases. Vaccination by PCVs appears to be the most effective approach in order to prevent occupational pneumococcal colonization and infections in healthcare workers.

Smoking is established as an important independent risk factor for pneumococcal colonization and infection among adults. The high rate of pneumococcal colonization among smoker volunteers in our investigation was found. These findings are consistent with those reported by previous studies^{28,29}. These data emphasize that exposure to smoke markedly increases the pneumococcal colonization rates and thus reducing smoking, tobacco consumption, and smoke exposure could reduce pneumococcal carriage.

Antibiotic resistance among colonized pneumococci has can be used to predict response to antibiotic therapy of invasive pneumococcal disease³⁰. Peterson et al., in 2009 described that 96–99% of multidrug-resistant *S. pneumoniae* (MDRSP) strains were susceptible to levofloxacin; thus, levofloxacin was introduced as an effective antimicrobial against these isolates³¹. However, in recent years, a trend towards the increasing emergence and spread of levofloxacin non-susceptibility has been reported in Asian countries^{32,33}. In contrast with these data, our finding indicated that the levofloxacin non-susceptibility rate was 0% among *S. pneumoniae* isolates. Therefore, *in vitro* levofloxacin susceptibility assay showed that levofloxacin has remained effective for the treatment of pneumococcal infections. In light of these results, previously, a study conducted by Houry *et al.* showed no levofloxacin-resistant *S. pneumoniae* isolate in

pediatric patients¹².

Conclusion

This low rate of pneumococcal colonization amongst healthcare professionals may be attributed to a low risk of horizontal transmission of severe pneumococcal infections in the hospital. A strategy of continuous surveillance of pneumococcal colonization among healthcare workers and medical students could help to predict the transmission of pneumococcal infections in healthcare settings. Therefore, regular screening programs and restriction of colonized healthcare professionals should be implemented particularly in high-risk units in order to minimize the transmission of severe pneumococcal infections. In addition, an appropriate immunization of healthcare workers using PCVs is recommended to reduce pneumococcal carriage and therefore pneumococcal diseases. Finally, according to our findings levofloxacin has remained an effective antimicrobial agent for the treatment of pneumococcal infections.

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