ORIGINAL ARTICLE

Staphylococcus aureus nasal carriage rates among children between one-to-five years in Barangay Pio Del Pilar, Makati City

AUTHORS: Ceres Paulino, MD, Robert Dennis Garcia, MD, Shirley Ong, MD *
*Makati Medical Center

KEYWORDS:
Staphylococcus aureus; MRSA; nasal colonization

CORRESPONDENCE:
Dr. Ceres Paulino
Email: cerespaulino@gmail.com

ABSTRACT

Objective: This study aims to determine the staphylococcal nasal carriage rates of children who are between one-to-five years old and residing in Botanical Gardens, Barangay Pio Del Pilar, Makati City. The following shall also be investigated: antibiotic resistance patterns of isolates, factors associated with *S. aureus* nasal carriage, and other pathologic organisms colonizing the anterior nares in this population.

Methods: Nasal swabs were taken from each subject and cultured after informed consent was obtained. Statistical analysis was performed to determine factors with significant association with nasal colonization.

Results: Ten (12.9%) out of 77 subjects were positive for *S. aureus* nasal colonization, one of which was oxacillin-resistant. Only the gross monthly income showed significant association with nasal carriage (p=0.03, OR = 0.59, 95% CI). Four subjects (5.1%) were carriers of *S. pneumoniae.*

Conclusions: The study shows a relatively low rate of Methicillin Sensitive *S. aureus* (MSSA) and Methicillin Resistant *S. aureus* (MRSA) nasal carriage. The MRSA isolate was sensitive to all other anti-staphylococcal drugs tested, similar to other studies on Community Acquired-MRSA (CA-MRSA). Local surveillance studies are essential in the control of CA-MRSA and in guiding local antibiotic policies for staphylococcal infections. Further studies on a bigger population are needed to determine rates, resistance patterns and risk factors associated with nasal colonization.

INTRODUCTION

Methicillin resistance among *S. aureus* isolates has steadily increased worldwide. In the late 1990s, studies conducted in the United States, as well as in other countries have revealed a significant prevalence of community-acquired methicillin-resistant *S. aureus* (CA-MRSA) colonization or infection in both children and adults.[1] There is increasing evidence that CA-MRSA is spreading among healthy individuals, especially children.[2]

In local studies, prevalence of nosocomial oxacillin-resistant *S. aureus* at the Philippine General Hospital is 53%.[3] In antimicrobial resistance surveillance data conducted in 2012 by Carlos, 54.9% of *S. aureus* from different sentinel hospitals were oxacillin-resistant.[4] A study conducted in 2000 at the St. Luke's Hospital showed a methicillin resistance rate of 13.6%.[5] At the Makati Medical Center, methicillin resistance was observed in 46.9% of *S. aureus* isolates in 2010, which has increased to 49.1% in the first five months of 2011.[6]

Staphylococcus aureus nasal carriage plays a major role in the epidemiology and pathogenesis of infection. Approximately 20% of individuals are persistently nasal carriers of *S. aureus*, and 30% are intermittently colonized.[7] According to previous studies, the carriage rates in the general population are comparable to those found in health care workers and in admitted or hospitalized patients.[8] Self-inoculation causes recurrent skin infections in carriers, and individuals with chronic furunculosis were found to have higher nasal carriage rates.[9] In a study on patients with staphylococcal skin lesions, 80% were *S. aureus* nasal carriers and 65% had the same phage type in the nose and lesion.[10] Three sets of observations show that nasal carriage is an important risk factor for staphylococcal septicemia: carriers develop infection more frequently compared to non-carriers; infected individuals harbor the same strain in the nose as the infecting strain; and treatment of nasal carriage significantly reduces infection.[11] According to a systematic review done in the United States in 2008, nasal colonization increases the risk of staphylococcal infection four-fold.[11,12] Colonization also increases the risk of transmission among individuals in both health care and community settings.[7]

In our country, however, there is no data on nasal carriage rates among children in the community. This study aims to determine the rate of nasal carriage in children in a densely populated urban community in Makati City and to determine the antibiotic resistance patterns of the isolates.

MATERIALS AND METHODS

This is a prospective, cross-sectional study conducted between August 27 and September 3, 2011.

Study Participants and Data Collection

The study included children who are between 12-to-59 months old and residing in Botanical Gardens, Barangay Pio del Pilar, Makati City. This is a 2.4 km^2 area with an estimated population density of 1,041/km^2 and an average gross monthly income of seven thousand pesos (Php7, 000) per household. The population for this specified age group is 113. For a level of confidence of 95%, the calculated sample size is 77. Subjects were chosen by simple random sampling.

In addition to the demographic data (date of birth and gender), the following data were collected prior to the procedure: past medical history (previous hospitalizations, history of skin infections and treatment given, history of antibiotic use, diagnosis of asthma, atopic dermatitis, eczema or allergic rhinitis, immunization status), personal and social history (family members working in health care institutions, number and ages of siblings, household size, educational attainment and employment of parents, gross monthly income, school attendance, habits such as nose picking, nail biting or thumbsucking, bathing frequency, exposure to smoke or pets) and breastfeeding status. These variables were hypothesized to be potential factors associated with *S. aureus* nasal colonization.

The subjects were checked for the presence of illness during the time of study, including fever or upper respiratory tract infections. A physical examination was done to check for height, weight and presence of skin lesions.

Exclusion criteria included chronic illnesses such as chronic renal failure, chronic cardiovascular diseases, liver cirrhosis, chronic lung disease, diabetes mellitus, congenital immunodeficiency or malignancy.

Collection of nasal samples and laboratory methods

After obtaining written, informed consent, a nasal swab was performed on the subjects. The tip of the collection swab moistened with sterile water was inserted into the anterior nares and rolled four times in each nostril. The swab was then placed in a properly labeled Amies transport media with charcoal and sent to the MMC bacteriology laboratory for culture and antimicrobial susceptibility testing within four hours of collection. Culture and sensitivity were performed by medical technicians blinded to the patient's clinical data; a clinical pathologist validated the reports before release of results.

The nasal samples were swabbed on a glass slide for Gram's staining, inoculated on BAP, CAP and MaC plates and thioglycolate broth, and incubated at 35°C. Identification and drug susceptibility testing were performed on all cultures with pathogenic organisms. For susceptibility testing of *S. aureus*, disk diffusion method and an automated test using microdilution on VITEK System were performed. The inoculum was adjusted to a McFarland 0.5 turbidity standard and swabbed onto an agar plate. Antibiotic disks were placed onto the agar surface and incubated for 16-to-18 hours at 34°C –to-35°C. The diameter of inhibition zone was read to the nearest whole millimeter.

Statistical Analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 17.0. Prevalence of *S.aureus* was estimated with 95% confidence intervals. The risk factors were analyzed using Chi square test, Fischer's exact test or Independent T test, whichever was appropriate. Factors with a p value <0.1 were included in the final multiple logistic regression model and odds ratio were adjusted for age and gender.

RESULTS

All 77 subjects were eligible for the study. The age and sex of the study population are found in Table 1. Ten (12.9%) were positive for *S. aureus* nasal carriage, one of which was oxacillin-resistant.

Of the nine methicillin-sensitive *S. aureus* (MSSA), six were sensitive to all antibiotics tested; two isolates were resistant to trimethoprim-sulfamethoxazole; and one was multi-drug resistant (resistant to clindamycin, erythromycin and tetracycline with intermediate resistance to ciprofloxacin) (Table 2).

Table 1. Age and gender of study population

Age (yrs)	Gender		Total
	Female	Male	
1 to <2	8	8	16
2 to <3	13	6	19
3 to <4	9	13	22
4 to <5	6	14	20
Total	36	41	77

The following risk factors had p values <0.1 on univariate analysis and were included in the multiple logistic regression model: gross monthly income (p=0.004), second-hand smoke exposure (p=0.005) and maternal (p=0.043) and paternal education (p=0.059). On multivariate analysis, only the gross monthly income remained statistically significant which showed that for every P10,000 increase in monthly income, the odds of having *S. aureus* nasal carriage decreases by 41% (p=0.03, OR = 0.59) (Table 3).

DISCUSSION

To our knowledge, this is the first local study on the rate of *S. aureus* nasal carriage among children in a community setting. The results showed that 12.9% of the study population, who were between one-to-five years old, were nasal carriers of *S. aureus*. Only one isolate was oxacillin-resistant, which was susceptible to other non-beta lactam antibiotics. A significant correlation was found between nasal colonization and a lower gross monthly income. There was no significant association with the other factors studied. Nasal carriage of *S. pneumoniae* was found in 5.1% of the study population.

Table 2. Antibiotic resistance patterns of *S. aureus* isolates.

Case	Oxacillin	Tetracycline	Levofloxacin	Ciprofloxacin	Linezolid	Erythromycin	Clindamycin	Vancomycin	TMP/SMX	Gentamicin	Moxifloxacin
1	S	S	S	S	S	S	S	S	S	S	S
2	S	S	S	S	S	S	S	S	S	S	S
3	S	S	S	S	S	S	S	S	R	S	S
4	R	S	S	S	S	S	S	S	S	S	S
5	S	R	S	I	S	R	R	S	S	S	S
6	S	S	S	S	S	S	S	S	S	S	S
7	S	S	S	S	S	S	S	S	S	S	S
8	S	S	S	S	S	S	S	S	S	S	S
9	S	S	S	S	S	S	S	S	S	S	S
10	S	S	S	S	S	S	S	S	R	S	S
Susc %	90	90	100	90	100	90	90	100	80	100	100

S: susceptible; I: intermediate resistance; R: resistant

Table 3. Multiple logistic regression analysis of factors associated with *S. aureus* nasal carriage.

	B	Sig	Adjusted OR	95% CI	
				Lower	Upper
Age	-0.096	0.878	0.909	0.267	3.098
Gender (M vs F)	2.102	0.182	8.182	0.374	178.775
Father's Education *					
Elementary	-21.683	1.01	0.000	0.000	.
High School	-20.572	1.00	0.000	0.000	.
College	-16.473	1.00	0.000	0.000	.
Mother's Education*					
Elementary	1.893	0.329	6.638	0.148	297.10
High School	-1.278	0.514	0.279	0.006	12.89
College	-2.188	0.356	0.112	0.001	11.713
Gross Monthly Income	-0.521	0.030	0.594	0.371	0.951
Second Hand Smoke Exposure	20.56	0.997	8.55	0.000	.

*Logistic regression was used with "no education" as reference variable

Based on the literature, the rate of *S. aureus* nasal colonization in children ranges between 6.3%[13] to 57.1%[14] (Table 4). Our study result showed a figure at the lower end of this range. There are several reports in literature which studied the same age group. In Taiwan, a study done in the community showed a nasal carriage rate of 15.4%,[15] which was close to our findings. This was a large-scale study which included two-

Table 4. Nasal carriage rates of Methicillin-Sensitive *S. aureus* (MSSA) and Methicillin-Resistant *S. aureus* (MRSA) in literature

Author	Year of Publication	Country	Age group	Setting	Sample size	MSSA (%)	MRSA (%)
Adler I[30]	2010	Israel	2 to 12 months	Community	555	48	5.7
Buck[37]	2008	USA (Minnesota)	Kinder to Grade 3	School	611	33	0.50
Chaterjee[29]	2009	India	5 to 15 years	Community	489	52.30	3.89
Chen[15]	2011	Taiwan	2 to 60 months	Community	6,057	15.40	7.80
Ciftci[39]	2007	Turkey	4 to 6 years	Community	1,134	28.40	0.30
Creech[27]	2005	USA (Nashville)	2 weeks to 21 years	Outpatient clinic	500	36.40	9.20
Datta[20]	2008	Switzerland	Not specified	Hospital	1350	41.20	1 child
Erdenizmenili[40]	2004	Turkey	1 to 16 years	Outpatient clinics	115	19.1	not specified
Faden[41]	2010	USA (New York)	Newborn to 18 yrs	Hospital	90(control group)	21	not specified
Fan[42]	2011	China	Kindergarten	School	801	18.4	1.1
Fritz[43]	2008	USA (Washington)	Birth to 18 years	Outpatient clinics	1,300	24.20	2.60
Gorwitz[25]	2008	USA (nationwide)	1-19 years	Community	4772 (2001-02); 4338 (2003-04)	36.9; 34.6	0.6; 1.3
Halabhab[14]	2010	Lebanon	6 to 10 years	Community	not specified	57.10	not specified
Hisata[44]	2005	Japan	Nursery and Kindergarten	School	818	28.20	4.30
Huang[45]	2007	Taiwan	2 months to 5 years	Outpatient Clinic	3,046	23	7.3
Hussain[46]	2001	USA (Chicago)	≤16 years	Outpatient clinic	500	24.4	2.5
Lamaro-Cardoso[17]	2009	Brazil	2 months to 5 years	Day care centers	1,192	31.10	1.20
Lear[47]	2011	USA (Ohio)	14-18 years	School (football players)	190	23.1	None
Lo[48]	2008	Taiwan	Birth to ≤14 years	Outpatient Clinic or School	3,200	25.80	11.60
Lu[49]	2005	Taiwan	2 to 18 years	Community	987	31.8	3.3
Miller[28]	2011	USA (Virginia and North Carolina)	Birth to 6 years	Child care centers	1,163	18.1	1.3
Nakamura[1]	2002	USA (Nashville)	2 weeks to 21 years	Outpatient Clinic	500	29	0.80
Ogzukaya-Artan[50]	2008	Turkey	5 to 7 years	Day care center	200	18	5.60
Ozguven[26]	2008	Turkey	Not specified	primary school and high school	2,015	14.7	None
Pathak[13]	2010	India	1 month to 5 years	Outpatient clinics	1,562	6.30	16.3% of S.aureus isolates
Ramana[51]	2009	India	5 to 15 years	School	392	16	19% of S.aureus isolates
Rijal[52]	2008	Nepal	less than 15 years	School	184	31	56.1% of S. aureus isolates
Sahr[53]	2010	Sierra Leone	Less than 2 years	Hospital	116	34.50	None
Schlesinger[34]	2003	Israel	0.5 to 17 years	ER, Outpatient Clinics and chronic care institutions	831 healthy 118 chronically institutionalized	23.5 36.4	2.6 21
Shopsin[54]	2000	USA (New York)	1 week to 20 years	Outpatient clinic	275	35	1 patient

to-60-month-old healthy children brought to general health checkup clinics in three teaching hospitals in Taiwan. Two other reports studied similar age groups, but these showed much higher nasal carriage prevalence of 23% and 31.1%[16,17]. The first study was also conducted in Taiwan, on healthy children presenting for well-child visits in three medical centers. The second one was conducted in Brazil, on healthy children less than five years of age attending municipal day care centers. In India, a study conducted on children one-to-59 months old visiting for routine immunizations in outpatient clinics showed a lower carriage rate at 6.3%.[12] This wide range of *S. aureus* colonization rates underscores the importance of geographic differences and the need for local surveillance studies.

Age and gender had no significant association with nasal carriage in this study. Previous studies showed significant variations in *S. aureus* nasal carriage rates with age.[18-20] However, the study population was limited to one-to-five year olds, which could have decreased the variability attributed to unique factors determining nasal colonization in the first year of life and exposure to other factors outside the home after five years of age.

Limiting the study population to children who were between one-to-five years old may also partly explain the lower carriage rates compared to other studies with wider age groups. According to Lee, et al,[18] nasal colonization decreases after one year of age and rises again after five years. In a report by Peacock and associates on newborns, more than 70% had at least one positive nasal culture with *S. aureus* and the mother was thought to be the source of infection .[11] Long-term carriage rarely persists and its incidence drops sharply after the first year of life, probably due to acquired immunity or niche competition with other organisms.[19] A second peak in colonization occurs after five years of age, possibly due to school attendance and increasing number of household inhabitants.[20] These age-associated variations are thus important considerations when interpreting the results of the study.

This study found *Streptococcus pneumoniae* in 5.1% of participants. This could have potentially caused "bacterial interference" to diminish the *S. aureus* nasal carriage rate in the study population. Past epidemiologic data have shown an inverse relationship between *S. aureus* and *S. pneumoniae* colonization.[13,21-22] This may be due to the bactericidal effect of *S. pneumoniae* on *S. aureus* through the former's production of hydrogen peroxide.[21] This phenomenon has been termed "bacterial interference", in which co-existing bacteria of different species affects the survival of other species.[23] In a study done by Bogaert and associates, this natural competition was seen between vaccine-type pneumococci and *S. aureus*. They also found an increase in *S. aureus*-related otitis media after pneumococcal vaccination. In addition, they noted that peak nasal colonization with *S. pneumoniae* and other respiratory pathogens such as *Haemophilus influenza* and *Moraxella catarrhalis* occur between two-to-three years of age.[22] This peak occurs within the age range of our study group, none of whom had received pneumococcal vaccination. Bacterial interference with *S. pneumoniae* may therefore partly explain the low rate of *S. aureus* colonization in this study.

A lower gross monthly income significantly increased the odds of nasal colonization in this study population. There are conflicting findings on the relationship between socioeconomic status and *S. aureus* nasal carriage. Based on a nationwide surveillance in the United States,[24-25] socioeconomic status was not significantly related to the risk of *S. aureus* colonization for MSSA, but it increased the likelihood of carriage of MRSA. On the other hand, in a study conducted by Ozguven and associates in Turkey, children of higher socioeconomic status were found to be more prone to nasal colonization.[26] According to one study by Pathak, et al, in India, resource-rich countries had relatively higher prevalence of *S. aureus*

nasal carriage, probably due to lesser exposure to antigens because of better personal hygiene.[13] Other studies, however, found no association between socioeconomic status and *S. aureus* carriage.[18,27-29] It is difficult to compare the rates between developed and developing countries in literature because the studies involved different age groups or were conducted in different settings (Table 4). In this study, gross monthly income could be a proxy indicator for other factors known to increase nasal colonization such as overcrowding, poor hygiene, a low level of maternal education and limited access to health care.[13,15,17,22,24-25,28-29]

Other variables that were studied were not found to be significantly associated with *S. aureus* nasal carriage. These include recent hospitalization, recent antibiotic use, breastfeeding status, previous or present staphylococcal skin lesions, having a member of the household working in a healthcare institution, and a history of atopic dermatitis, eczema or allergic rhinitis, as seen in other studies.[8,10,12,17-19,27] Cigarette smoking showed a significant association with *S. aureus* nasal carriage on univariate analysis, but did not remain statistically significant on multivariate analysis. Studies show that while active cigarette smoking is protective of *S. aureus* nasal carriage, passive smoking increases colonization. The basis for this observation is unknown.[22,30] Other variables not reported in previous studies were also considered, like nose picking, thumb sucking and nail biting, but our results did not find these to be associated with *S. aureus* nasal carriage.

Aside from epidemiologic factors, successful colonization of *S. aureus* is complicated by other reported determinants, which were not accounted for in this study. These determinants include genetically determined host and bacterial factors which allow *S. aureus* to evade the immune response and propagate in the anterior nares.[10,22] Children continue to be the age group predominantly colonized but the exact reason for this is unknown.[31]

Compared to other studies, CA-MRSA was very low in this study population. In the single subject found to have oxacillin-resistant *S. aureus*, poor socioeconomic conditions as well as overcrowding may have increased the likelihood of CA-MRSA. However, she had no previous hospitalizations nor recent antibiotic use which were also associated with CA-MRSA carriage.[29,31] It has been observed that the prevalence of MRSA has steadily increased, especially among healthy children without the usual predisposing factors. A study in the United States found a 25-fold increase in the number of children admitted to the hospital with an MRSA infection who lacked an identifiable risk factor for prior colonization.[24-25,32] At the Makati Medical Center there have been 15 cases of invasive MRSA infection among pediatric patients between 2005 and 2010, including sepsis, pneumonia and soft tissue and joint infections. Of these 15 cases, ten patients had charts available for review and were described to be previously healthy without co-morbidities.[33] According to Chen, et al, children colonized by MRSA play an important role in its changing epidemiology and could be one of the major forces increasing the incidence of CA-MRSA in previously-healthy individuals.[15]

Unlike hospital acquired-MRSA (HA-MRSA), the oxacillin-resistant isolate in this study was sensitive to clindamycin and other antibiotics tested. Clindamycin therapy, known to suppress exotoxin production, has been successfully used in CA-MRSA.[29] There is growing evidence that CA-MRSA is intrinsically different from that of hospital origin in terms of genotype, phenotype and epidemiologic features. In contrast with HA-MRSA, CA-MRSA are susceptible to non-beta lactam antibiotics.[24,34] These studies suggest that transmission from the hospital does not comprise the main source of colonization in the community[18] and that these strains most likely originate from and circulate in the community.[1] Knowledge of antimicrobial susceptibility patterns at the local level is essential for

selecting appropriate antibiotic therapy for *S. aureus* infections. The findings in this study are reassuring, showing only one subject with CA-MRSA, which was sensitive to other non-beta lactam antibiotics.

One MSSA isolate was found to be multi-drug resistant. Antibiotic use is one of the most important determinants of antibiotic resistance.[35] However, the carrier of this isolate had no previous history of hospitalization nor recent use of antibiotics. He had untreated scalp furunculosis at the time of study, but had no other recent skin infections.

As the results of this study were based on a one-time cross-sectional survey, the results may have underestimated the real prevalence of nasal MRSA carriage that may be obtained if a longitudinal study was done. Longitudinal studies are required to identify three carriage patterns in individuals: persistent carriage, intermittent carriage or non-carriage.[10] Persistent carriers have higher *S. aureus* loads and a higher risk of acquiring *S. aureus* infection. Subjects who were positive for *S. aureus* could either be persistent or intermittent carriers. Those who tested negative may either be non-carriers or intermittent carriers without *S. aureus* carriage at the time of the study. Therefore, several samples at different points in time are required to determine the carrier state of the subjects.

The study population was limited to children who were between one-to-five years old and it is possible that studying a wider range of age groups would result in a higher rate of nasal carriage. A longitudinal study involving multiple samples per subject over time might also reveal a higher rate of colonization. The natural competition for nasal colonization between other pathogens such as *Streptococcus pneumoniae* should also be considered in further studies. The epidemiology and implications of *S. pneumoniae* carriage were not investigated in detail in this study.

CONCLUSIONS

The rate of nasal colonization of *S. aureus* in children who were between one-to-five years old in a community in Makati City was 12.9%. Nasal colonization with *S. pneumoniae* was found in 5.1% of the study population.

A lower gross monthly income was significantly associated with *S. aureus* nasal carriage. Other factors studied did not show significant association with nasal colonization. There was a low rate of CA-MRSA nasal carriage in the study population and the isolate was sensitive to other anti-staphylococcal antibiotics tested.

RECOMMENDATIONS

In clinical practice, this study is useful for the choice of treatment for community-acquired *S. aureus* infections. It shows a low rate of MRSA in the study community with high susceptibility to standard anti-staphylococcal antibiotics. The varying rates of CA-MRSA carriage among different reports emphasize the need for local surveillance studies to guide the clinician in appropriate antibiotic choices in treating *S. aureus* infections. However, the findings in this study may be applied only to children within the same age group and with the same socioeconomic status, and future research should include communities of different socioeconomic classes.

Local surveillance studies are essential in the control of CA-MRSA and in guiding local antibiotic policies for staphylococcal infections. A larger study population involving several communities is needed to identify CA-MRSA rates, antibiotic resistance patterns and the epidemiologic risk factors associated with nasal colonization in the local setting.

REFERENCES

1. Nakamura MM, Rohling KL, Shashaty M et al. Prevalence of methicillin-resistant *Staphylococcus aureus* nasal carriage in the community pediatric population. Pediatr Infect Dis J 2002; 21:917-21.
2. Rao S. Methicillin resistant *Staphylococcus aureus* [Online]. [March 2009]. Available from: www.microrao.com. Accessed: July 29, 2011.
3. We MB, Cruda-Pineda CL, Torres TT et al. Nosocomial acquisition of oxacillin-resistant Staphylococcus aureus (ORSA) at the Philippine General Hospital. Phil J Microbiol Infect Dis 1999; 28(4):128-132.

4. Carlos CC. The 2012 antimicrobial surveillance program: progress report. Available from www.ritm.gov.ph
5. Atilano MAG, Pena AC, Chua JA et al. Prevalence of methicillin-resistant Staphylococcus aureus and methicillin-resistant coagulase negative Staphylococcus in a tertiary hospital. Phil J Microbiol Infect Dis 2001; 30(4):126-32.
6. Makati Medical Center Infection Control Committee. Monthly surveillance of bacterial isolates from admitted patients, 2010-2011.
7. Gordon RJ, Lowy FD. Pathogenesis of methicillin-resistant *Staphylococcus aureus* infection. Clin Inf Dis 2008; 46:S350-9.
8. Kluytmans J, Van Belkum A, Verbrugh H. Nasal carriage of *Staphylococcus aureus*: epidemiology, underlying mechanisms, and associated risks. Clin Mic Rev 1997 Jul; 10(3):505-20.
9. Durupt F, Mayor L, Bes M et al. Prevalence of *Staphylococcus aureus* toxins and nasal carriage in furuncles and impetigo. Brit J Derm 2007; 157:1161-67.
10. Wertheim HFL, Melles DC, Vos MC et al. The role of nasal carriage in Staphylococcus aureus infections. Lancet Infect Dis 2005; 5:751-62.
11. Peacock SJ, Justice A, Griffiths D et al. Determinants of acquisition and carriage of *Staphylococcus aureus* in infancy. J Clin Microbiol Dec 2003; 41(12):5718-25.
12. Safdar N, Bradley EA. The risk of infection after nasal colonization with *Staphylococcus aureus*. Am J Med 2008; 121:310-15.
13. Pathak A, Marothi Y, Iyer RV et al. Nasal carriage and antimicrobial susceptibility of *Staphylococcus aureus* in healthy preschool children in Ujjain, India. BMC Pediatr 2010; 10(100).
14. Halablab MA, Hijazi SM, Fawzi MA et al. Staphylococcus aureus nasal carriage rate and associate risk factors in the community. Epid & Infect 2010; 138:702-6.
15. Chen CJ, Hsu KH, Lin TY et al. Factors associated with nasal colonization of methicillin-resistant Staphylococcus aureus among healthy children in Taiwan. J Clin Microbiol 2011; 9(1):131-7.
16. Huang YC, Hwang KP, Chen PY et al. Prevalence of methicillin-resistant Staphylococcus aureus nasal colonization among Taiwanese children in 2005 and 2006. J Clin Microbiol 2007; 45(12):3992-95.
17. Lamaro-Cardoso J, de Lencastre H, Kipnis A et al. Molecular epidemiology and risk factors for nasal carriage of *Staphylococcus aureus* and methicillin-resistant *S. aureus* in infants attending day care centers in Brazil. J Clin Microbiol 2009 Dec; 47(12):3991-97.
18. Lee GM, Huang SS, Rifas-Shiman SL et al. Epidemiology and risk factors for Staphylococcus aureus colonization in children in the post-PCV7 era. BMC Infect Dis 2009; 9:110.
19. Lebon A, Labout JAM, Verbrugh HA et al. Dynamics and determinants of Staphylococcus aureus carriage in infancy: the generation R study. J Clin Microbiol 2008; 46(10):3517-21.
20. Datta F, Erb T, Heininger U et al. A multicenter, cross-sectional study on the prevalence and risk factors for nasal colonization with *Staphylococcus aureus* in patients admitted to children's hospitals in Switzerland. Clin Inf Dis 2008; 47:923-6.
21. Regev-Yochay G, Dagan R, Raz M et al. Association between carriage of Streptococcus pneumoniae and Staphylococcus aureus in children. JAMA 2004; 292:716–720.
22. Bogaert D, van Belkum A, Sluijter M et al. Colonisation by Streptococcus pneumoniae and Staphylococcus aureus in healthy children. Lancet 2004; 363:1871–1872.
23. Sivaraman K, Venkataraman N, Cole AM. Staphylococcus aureus nasal carriage and its contributing factors. Future Microbiol 2009; 4:999-1008.
24. Graham PL III, Lin SX, Larson EL. A US population-based survey of Staphylococcus aureus colonization. Ann Intern Med 2006; 144:318-325.
25. Gorwitz RJ, Kruszon-Moran D, McAllister SK et al. Changes in the prevalence of nasal colonization with *Staphylococcus aureus* in the United States, 2001-2004. J Infect Dis 2008; 197:1226-34.
26. Ozguven A, Tunger O, Cetin CB et al. Investigation of nasal carriage of community-acquired methicillin resistant Staphylococcus aureus in primary and high school students. Mikrobiyol Bul 2008; 42(4):661-7.
27. Creech CB, Kernodle DS, Alsentzer A et al. Increasing rates of nasal carriage of methicillin-resistant *Staphylococcus aureus* in healthy children. Pediatric Infect Dis J 2005 Jul; 24(7):617-21.
28. Miller MB, Weber DJ, Goodrich JS et al. Prevalence and risk factor analysis for methicillin-resistant *Staphylococcus aureus* nasal colonization in children. J Clin Microbiol 2011; 49(3):1041-47.
29. Chatterjee SS, Ray P, Aggarwal A et al. A community-based study on nasal carriage of *Staphylococcus aureus*. Indian J Med Res 2009; 130:742-748.
30. Immergluck LC, Kanungo S, Schwartz A et al. Prevalence of *Streptococcus pneumonia* and *Staphylococcus aureus* nasopharyngeal colonization in healthy children in the United States. Epidemiol Infect 2004; 132:18-66.
31. Immergluck LC. Community-associated infections in children – update on community associated methicillin-resistant *Staphylococcus aureus* for the practitioner. Ethnicity & Disease 2007:17; S247-9.
32. Chatzakis E, Scoulica E, Papageorgiou N et al. Infant colonization by Staphylococcus: role of maternal carriage. Eur J Clin Microbiol Infect Dis 2011; 30(9):111-7.

33. Caballes MC. A descriptive study on the clinical characteristics and outcomes of methicillin-resistant *Staphylococcus aureus* bacteremia in pediatric patients at the Makati Medical Center. A 5-year review. 2011.
34. Schlesinger Y, Yahalom S, Raveh D et al. Methicillin-resistant *Staphylococcus aureus* nasal colonization in children in Jerusalem: community vs. chronic care institutions. Isr Med Assoc J 2003; 5:847–51.
35. Costelloe C, Metcalfe C, Lovering A et al. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. BMJ 2010; 340:2096.
36. Adler A, Givon-Lavi, Moses AE et al. Carriage of methicillin-resistant *Staphylococcus aureus* in a cohort of infants in southern Israel: risk factors and molecular features. J Clin Microbiol 2010; 48(2): 531–538.
37. Buck JM, Harriman KH, Juni BA et al. No change in methicillin-resistant *Staphylococcus aureus* nasal colonization rates among Minnesota school children during 2 study periods. Infect Dis Clin Pract 2008;16:163-5.
38. Herold BC, Immergluck LC, Maranan MC et al. Community-acquired methicillin-resistant *Staphylococcus aureus* in children with no identified predisposing risk. JAMA 1998; 279:593-8.
39. Ciftci IH, Koken R, Bukulmez A et al. Nasal carriage of *Staphylococcus aureus* in 4-6 age groups in healthy children in Afyonkarahisar, Turkey. Acta Paediatrica 2007; 96:1043-6.
40. Erdenizmenli M, Napar N, Senger SS et al. Investigation of colonization with methicillin-resistant and methicillin-sensitive *Staphylococcus aureus* in an outpatient population in Turkey. Jpn J Infect Dis 2004; 57:172-5.
41. Faden H, Lesse AJ, Trask J et al. Importance of colonization site in the current epidemic of staphylococcal skin abscesses. Pediatrics 2010; 125:e618.
42. Fan J, Zhou W, Shu M et al. Nasal carriage of community-acquired methicillin-resistant *Staphylococcus aureus* in healthy children from Chengdu. Chinese J Contem Ped 2011; 13(1):16-19.
43. Fritz SA, Garbutt J, Elward A et al. Prevalence of and risk factors for community acquired methicillin-resistant and methicillin-sensitive *Staphylococcus aureus* in children seen in a practice-based research network. Pediatrics 2008; 121:1090-98.
44. Hisata K, Kuwahara-Arai K, Yamanoto M et al. Dissemination of methicillin-resistant Staphylococci among healthy Japanese children. J Clin Microbiol 2005 Jul; 43(7):3364-72.
45. Huang YC, Hwang KP, Chen PY et al. Prevalence of methicillin-resistant *Staphylococcus aureus* nasal colonization among Taiwanese children in 2005 to 2006. J Clin Microbiol 2007; 45(12):3992-5.
46. Hussain FM, Boyle-Vavra S, Daum RS. Community-acquired methicillin-resistant *Staphylococcus aureus* colonization in healthy children attending an outpatient pediatric clinic. Pediatr Infect Dis J 2001; 20(8)763-7.
47. Lear A, McCord G, Peiffer J et al. Incidence of *Staphylococcus aureus* nasal colonization and soft tissue infection among high school football players. JABFM 2011; 24(4):429-35.
48. Lo WT, Lin WJ, Tseng MH et al. Risk factors and molecular analysis of panton-valentine leukocidin-positive methicillin-resistant *Staphylococcus aureus* colonization in healthy children. Pediatr Infect Dis J 2008; 27(8):713-8.
49. Lu PL, Chin LC, Peng CF et al. Risk factors and molecular analysis of community methicillin-resistant *Staphylococcus aureus* carriage. J Clin Microbiol 2005; 43(1):132-9.
50. Oguzkaya-Artan M, Baykan Z, Artan C. Nasal carriage of *Staphylococcus aureus* in healthy preschool children. Jpn J Infect Dis 2008; 61:70-72.
51. Ramana KV, Mohanty SK, Wilson CG. *Staphylococcus aureus* colonization of anterior nares of school going children. Indian J Pediatr 2009; 76(8):813-6.
52. Rijal KR, Pahari N, Shrestha BK et al. Prevalence of methicillin resistant *Staphylococcus aureus* in school children of Pokhara. Nepal Med Coll J 2008; 10(3)192-195.
53. Sahr F, Solayide AA, Hanson C et al. Nasal carriage rate of *Staphylococcus aureus* and antimicrobial susceptibility pattern among children in Freetown, Sierra Leone. Sierra Leone J Biomed R 2010; 2(1).
54. Shopsin B, Mathema B, Martinez J et al. Prevalence of methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* in the community. J Infect Dis 2000; 182:359-62.