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NASAL CARRIAGE RATE OF *STAPHYLOCOCCUS AUREUS* AND MRSA AMONG HEALTH CARE WORKERS IN TERTIARY CARE CENTER

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Abstract
*Staphylococcus aureus*is a gram positive bacterium responsible for several bacterial infections. *S. aureus*especially methicillin-resistant *S. aureus*(MRSA),are usually resistant to several antibiotics which is a global public health problem, associated with considerable mortality and morbidity worldwide.This study aimed to determine the frequency of staphylococcal nasal carriage of health care workers (HCWs) and antimicrobial susceptibility profile of the isolates in Gandaki Medical College and Research Centre Pvt. Ltd, Pokhara, Nepal. The study was conducted in altogether 288 samples. Nasal swabs from all hospital care workers were collected. For isolation and identification of MRSA culture and different biochemical tests were performed. Chi-square test was used to analyze data. Out of 58 (20.14%) *S. aureus*isolated 18.97% are MRSA, more MRSA were noticed in female (21.08%) than male (18.18%). However, there was no significant association between gender and MRSA (p=0.723). Overall 3.08% male were carrier of MRSA and 4.04% female were carrier of MRSA. The prevalence of nasal carrier MRSA was 3.82%. Vancomycin and Amikacin were found to be most effective (100%) against Methicillin-Resistant *S. aureus*followed by tetracycline (94.83%). It was concluded that prevalence of MRSA is still emerging. Nasal carriage of *S. aureus*and MRSA among HCWs necessitates the need of control in the frequency of their exposure with the vulnerable patients and need of strict infection control measures to be followed to control the nosocomial infections. The results emphasize the need for high standards of infection control in tertiary care

Key words: Antibiotics, antimicrobial, Health care workers, MRSA, nasal carrier, nosocomial infection, *S. aureus*

Introduction

Staphylococci belong to the family Micrococcaceae. They are gram positive spherical cocci. Micrococcaceae cells may occur singly or as irregular clusters[1]. These are ubiquitous organisms and the primary natural habitat is mammalian body surfaces. Some are members of man and others are the commonest cause of suppuration[2].

The genus *Staphylococcus* has at least 40 species. The three most frequently encountered species of clinical importance are *Staphylococcus aureus, Staphylococcus epidermidis,* and *Staphylococcus saprophyticus.* Among them, *Staphylococcus aureus* is a major pathogen for humans. *Staphylococcus aureus* is coagulase positive which differentiates itself from other species[3].

Staphylococcus aureus is a gram-positive coccus where the round cells, approximately 1 mm in diameter, form grape-like (Greek staphyle) clusters indicative of the ability to divide in more than one plane. They are capable of both aerobic and anaerobic respiration and most strains ferment mannitol aerobically. On nutrient agar they form characteristic golden (Latin aureum) or white colonies. They produce catalase, coagulase and an extracellular cell clumping factor, and some strains produce capsules[4].

The coagulase positive species *Staphylococcus aureus* is well documented as a human opportunistic pathogen. As a nosocomial pathogen, *Staphylococcus aureus*has been a major cause of morbidity and mortality[5].*Staphylococcus aureus* capable of invading intact normal skin are rare, most able to cause infection, only if they enter through breaks in the skin. *Staphylococcus aureus* causes pyogenic infections (breast abscess, post-operative wound infections, folliculitis etc.) and disseminated infections(septicemia, toxin mediated infections etc)[6].

The *S. aureus* transmission occurs by direct or indirect contact, especially the colonization in which the individual becomes the carrier of the microorganism, without necessarily showing characteristic signs and symptoms of infection[7].The staphylococci associated with infections in humans are colonizers of various skin and mucosal surfaces[8].

There are two types of *Staphylococcus aureus*found in nosocomial environments: permanent and transitory. The former can be found on healthcare-workers and in the hospital environment. The latter can be found in infected patients and in carriers, which are in transitory contact with the hospital[9].

Presence of *Staphylococcus aureus* nasal colonization can provide an indication of a higher risk for subsequent infection, including with MRSA[10]. Infections caused by *S. aureus* have a poorer prognosis when the infecting strain is MRSA. Treatment of the infections caused by these strains became more difficult since *S. aureus* became resistant not only to usual penicillin related antibiotics but also most other structurally unrelated antibiotics such as rifampicin, chloramphenicol[11].

Drug resistance is seen mostly in hospital acquired infections than in community acquired infections due to widespread use of antibiotics in the hospital.Those hospital strains are characterized by developing resistance to multiple antibiotics at the same time. Common examples of such strains of bacteria showing drug resistance include *S. aureus, E. coli* etc.[12]

Multi drug resistance (MDR) is a condition enabling a disease causing organism to resist distinct drugs or chemicals of a wide variety of structure and function targeted at eradicating the organism. Multi drug resistant isolates are even more likely to be associated with complications in the therapeutic management of patients with infectious diseases. Multi drug resistance is defined as resistance to two or more antibiotics belonging to different structural classes[13].

Methicillin resistant staphylococci has steadily increased worldwide especially among cases acquired in hospitals[14]. There are several mechanisms of methicillin resistance in staphylococci, including inactivation by the beta lactamase enzymes, penicillin binding proteins with reduced penicillin binding capacity, and acquisition of the mecA gene which encodes new penicillin binding proteins PBP-2a with low affinity for beta lactams. The later mechanism accounts for the majority of resistance to methicillin and other beta lactams[15].

Strains of *Staphylococcus aureus* that carry the *mecA* gene, which encodes for PBP are referred to as methicillin resistant *Staphylococcus aureus* (MRSA) The mecA gene is carried on a mobile DNA element (SCC *mec*) that mediates wide dissemination of the antibiotic resistance[8].

In the 1960s and 1970s MRSA was not feared because several other treatment options existed, including use of tetracyclines, macrolides and aminoglycosides[16]. MRSA isolates are resistant to all currently available β-lactam antimicrobial agents [10]and are not effectively treated by most antibacterial agents which caused a major challenge for chemotherapy[17]. Since the emergence of Methicillin resistant *S. aureus*, the glycopeptidesvancomycin has been the only uniformly effective treatment for staphylococcal infections. In May 1996, the world's first documented clinical infection due to *S.aureus*with intermediate resistance to glycopeptides (glycopeptides-intermediate *S. aureus*) was diagnosed in a patient in Japan. The recommended treatment for multi-drug resistant MRSA is glycopeptides, particularly vancomycin. Since the emergence of vancomycin resistance in enterococci in 1988 and its in vitro demonstration that its resistance genes (Van A and Van B) are transmissible to other bacterial species including *S. aureus*, emergence of vancomycin resistance in clinical staphylococci has become a great concern. Clinicians are continually being challenged by infections caused by *S. aureus*. The treatment of suspected *S. aureus* infections is becoming increasingly more complicated and clinical significance of these strains requires further investigation[18].

Approximately 10 to 40% of people carry *S. aureus*in their anterior nares. Nasal carriage of MRSA can be found among 1 to 2% of the general population but in as many as 10 to 15% of patients admitted to acute-care hospitals and intensive care units[19].

Nasal carriage of *S. aureus* has been identified as a risk factor for community-acquired and nosocomial infections. Healthy hospital personnel may carry pathogenic hospital strains in their nose and skin and may spread these pathogens to the community leading to more dreadful condition[20]. HCWs who are at interface between the hospital and the community may serve as agents of cross contamination of hospital acquired and community acquired MRSA[21].

The prime focus of this study is to determine the nasal carriage rate of *S. aureus* and MRSA among healthcare workers at Gandaki medical college and research centre private limited, Pokhara. The study will also demonstrate the sensitivity pattern of different antibiotics used against it. This study is useful for the healthcare personnel to maintain necessary universal control measures to prevent possible transmission to vulnerable patients.

Materials and methods

Antibiotics disc and culture media used were obtained from the manufacturer; Hi-Media Laboratories Pvt. Limited, Bombay, India.

Sample source

The study was conducted at the Microbiology Laboratory of Gandaki Medical College and Research Centre Pvt. Ltd. Pokhara, Nepal. The duration of the study was from 9th October 2016 to 9th April 2017. Altogether 288 HCWs were enrolled in this study. Nasal swabs from all hospital care workers were collected.

Specimen collection and processing

Sterile cotton swab dipped in sterile physiological saline was used for the collection of samples from anterior nares. All the samples selected for the study was processed using standard protocols. After receiving and labeling the samples, they were inoculated into Mannitol salt agar, MacConkey agar, and Blood agar.

Bacterial identification

The inoculated culture plates were incubated at 37˚C for 24 hours. *S. aureus* colonies were identified and confirmed by studying colony morphology, and gram's stain reaction and biochemical tests. Isolates that were gram-positive cocci, yellow colonies on MSA, pink colonies on MA and β-haemolytic colony on BA were considered as *S. aureus* in this study[22]. Then the cultures were sub cultured on nutrient agar (NA) at 37˚C for 24 hours for further processing. Colony having round, convex, opaque, smooth-glistening surface with colony diameter 2-3 mm were indicative of Staphylococci. Most staphylococci produced soft butyrous colony with golden yellow pigment. For further confirmation of *S. aureus*, various tests like gram staining, catalase test, slide and tube coagulase test were performed from isolated colonies. Standard protocol provided[6][8][25]and was followed by confirmatory identification of *S. aureus*.

Antibiotic susceptibility test

All *S. aureus* isolated from nasal screening process were subjected to in-vitro antimicrobial, susceptibility test by Kirby-Bauer disc diffusion method as recommended[23]. In this study the antibiotics used were Ciprofloxacin (30mcg), Cloxacillin (10mcg), Erythromycin (15mcg), Gentamicin (10mcg), Cefoxitin (30mcg), Oxacillin (1mcg), Penicillin (10 units), Amikacin (30mcg), Vancomycin (30mcg), Tetracycline (30mcg), Ceftriaxone (30mcg) and Cefotaxime (30mcg). The MRSA strains were identified by testing with Oxacillin and resistant strains were also screened against Cefoxitin disc, those strains resistant to both discs were considered as MRSA strains in this study[6][22].

Results

Out of total 288 samples taken from HCWs, 65(22.57%) were male and 223(77.43%) were female. Table 1 shows the gender wise distribution of *S. aureus* carrier. Highest nasal carrier of S. aureus was found in the age group 31-40 years i.e. 23.81% which is illustrated in table 2.

ENT department encountered 40% prevalence of nasal carrier whereas maternity ward has lowest i.e. 4.75% (table 3). Among different professions in the hospital nasal carriage rate of *S. aureus* was found highest in nurses i.e. 24.83% (table 4). Table 5 depicts the antibiotic susceptibility pattern of *S. aureus* isolates where 18.97% (11/58) were methicillin resistant *Staphylococcus aureus*. The most sensitive drugs for *S. aureus* strains are vancomycin (100%) and amikacin(100%).

Figure 1 represents the antibiotic resistance pattern of MRSA strains where all MRSA strains were susceptible towards vancomycin and amikacin whereas resistant to cloxacillin and penicillin.

In table 6 the *S. aureus* are categorized into MSSA (Methicillin Sensitive *S. aureus*) and MRSA (Methicillin Resistant *S. aureus*). Both the group of *S. aureus* showed marked variation in sensitivity pattern to common antibiotics. Table 7 explains the distribution of MRSA in male and female. Though MRSA was found to be more in female than male but

the result was statistically insignificant. MRSA strains were found in the age group of 21-30 and 31-40 which can be observed in the table 8.

The department wise distribution shows that highest percentage of MRSA among HCWs was found in the obtained result was statistically insignificant (table 9). Table 10 shows the distribution of MRSA among different professional group but the results were statistically insignificant.

Table 1: Gender wise distribution of *S. aureus* carrier

Sex	*S. aureus* carrier		Total	*p*- value	*p*- value
	Positive	Negative			
Male	11(16.92%)	54(83.07%)	65	0.000	0.463
Female	47(21.08%)	176(78.92%)	223	0.000	
Total	58(20.14%)	230(79.86%)	288(100%)		

Table 2: Comparative study of nasal carrier of *S. aureus* isolated from different age group

Age group	*S. aureus* carrier	Non carrier	No of sample	*p*-value	*p*-value
≥20	-	6(100%)	6		0.5
21-30	41(20.39%)	160(79.61%)	201	0.000	
31-40	15(23.81%)	48(76.19%)	63	0.000	
41-50	2(14.29%)	12(85.71%)	14	0.000	
51-60	-	4(100%)	4		
Total	58(20.13%)	230(79.86%)	288(100%)		

Table: 3 Distribution of *S. aureus* carrier among different department

Department	*S. aureus* carrier		No of sample	*p*-value
	Positive	Negative		
Emergency	3(18.75%)	13(81.25%)	16	0.365
ENT	8(40%)	12(60%)	20	
Gyane&Obst.	3(11.11%)	24(88.89%)	27	
ICU	7(18.9%)	30(81.08%)	37	
Laboratory	6(20%)	24(80%)	30	
Maternity	1(4.76%)	20(94.24%)	21	
Medicine	6(28.57%)	15(71.43%)	21	
NICU	4(26.67%)	11(73.33%)	15	
Orthopedic	5(15.63%)	27(84.37%)	32	
Paediatric	4(17.39%)	19(82.61%)	23	
PICU	3(20%)	12(80%)	15	
Post-up	4(36.36%)	7(63.64%)	11	
Surgery	4(20%)	16(80%)	20	

ENT: Eye nose throat, ICU: Intensive care unit, **NICU**: Neonatal care unit **PICU**: Paediatric intensive care unit and **Post-up**: Post-operative

Table 4:Comparative Study of Nasal carrier of *S. aureus* among professional group

Profession	*S. aureus* carrier		No of sample	*p*-value
	Positive	Negative		
Doctor	11(16.41%)	56(83.59%)	67	0.220
Nurse	36(24.83%)	109(75.17%)	145	
Lab worker	4(16%)	21(84%)	25	
Attendant	7(13.75%)	44(86.25%)	51	
Total	58(20.14%)	230(79.86%)	288(100%)	

Table 5: Antibiotic susceptibility pattern of *S. aureus* isolates

Antibiotics	Sensitive	Resistant	Total *S. aureus*	*p*-value
Amikacin	58(100%)	-	58	
Cefotaxime	25(43.1%)	33(56.9%)	58	0.358
Cefoxitin	47(81.03%)	11(18.97%)	58	0.000
Ceftriaxone	44(75.86%)	14(24.14%)	58	0.000
Ciprofloxacin	31(53.45%)	27(46.55%)	58	0.347
Cloxacillin	42(72.41%)	16(27.59%)	58	0.001
Erythromycin	29(50%)	29(50%)	58	1.104
Gentamicin	44(75.86%)	14(24.14%)	58	0.000
Oxacillin	18(31.03%)	40(68.97%)	58	0.005
Penicillin	18(31.03%)	40(68.97%)	58	0.005
Tetracycline	55(94.83%)	3(35.17%)	58	0.000
Vancomycin	58(100%)	-	58	

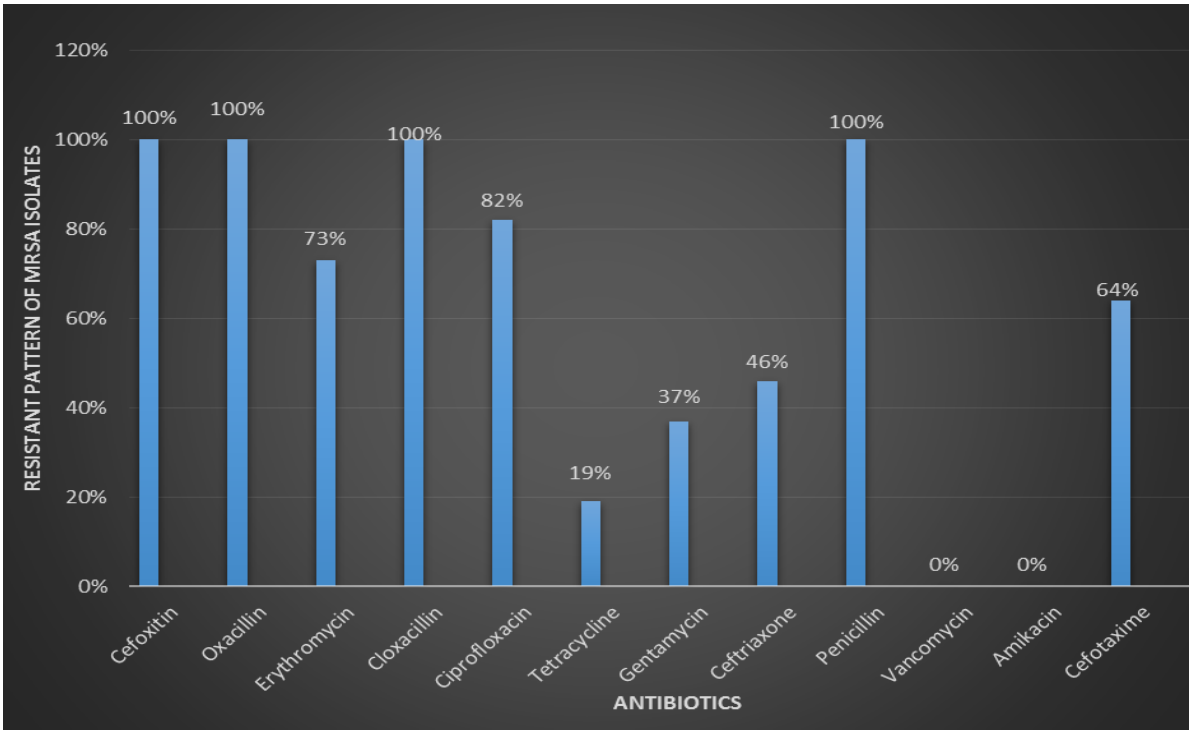

Figure 2: Antibiotic resistance pattern of MRSA

Table 6: Drug susceptibility pattern of MSSA and MRSA

	MSSA	MRSA
Pan Susceptible	4 (8.51%)	-
Mono Resistant	13 (27.66%)	-
Multi Drug Resistant	30 (63.83%)	11(100%)
Total	47	11 (100%)

Table 7: Gender wise distribution of MRSA

Sex	MRSA	MSSA	*S. aureus* carrier	*p*-value
Male	2(18.18%)	9(81.82%)	11(18.97%)	0.723
Female	9(19.15%)	38(80.85%)	47(81.03%)	
Total	11(18.97%)	47(81.03%)	58(100%)	

Table 8: Distribution of MRSA among different age group

Age group	*S. aureus* carrier	MRSA	MSSA	*p*- value	*p*-value
≥ 20	0	-	-		1.261
21-30	41	9(21.95%)	32(78.05%)	0.000	
31-40	15	2(13.33%)	13(86.33%)	0.000	
41-50	2	-	2(100%)		
51-60	0	-	-		

Table 9: Distribution of MRSA in different department

Department	Total *S. aureus* carrier	MRSA	MSSA	*p*-value	*p*-value
Emergency	4	-	4		0.420
ENT	8	2(25%)	6	0.066	
Gyane	3	-	3		
ICU	7	1(14%)	7	0.005	
Laboratory	6	2(33.33%)	4	0.284	
Maternity	1	-	1		
Medicine	6	1(16.67%)	5	0.040	
NICU	4	-	4		
Orthopaedic	4	-	4		
Paediatric	4	2(50%)	2	0.757	
PICU	3	-	3		
Post-up	4	1(25%)	3	0.243	
Surgery	4	2(50%)	2	0.757	

Table 10: Distribution of MRSA among different professional group

Profession	*S. aureus* carrier		Total *S. aureus* carrier	*p*-value	*p*-value
	MRSA	MSSA			
Doctor	2(20%)	8(80%)	10	0.012	0.349
Nurse	8(22.22%)	28(19.31%)	36	0.000	
Lab worker	1(20%)	4(80%)	5	0.103	
Attendant	-	7(100%)	7		
Total	11(18.97%)	47(81.03%)	58(100%)		

Discussion

In this study, nasal carriers of *S. aureus* were 21.08% female and male 16.92%. Similar findings[20] revealed that nasal carriage rate of *S. aureus* in female HCWs were 21.2% and in male 19%. However, in this study, the association between sex and nasal carriage of *S. aureus* was not statistically significant (p=0.463). Other study[24] also found sex is not a risk factor for nasal colonization of *S. aureus* and there is no activity of any of the groups that predisposes them to *S. aureus* colonization or infection.

The nasal carriage rate of *S. aureus* in this study was 20.14% among HCWs which were higher than that 15.7% reported previously[25] from Universal Medical College, Bhairahawa. Similar results have been reported by previous studies[20] about 20.37% nasal carrier *S.aureus*among HCWs at National Medical College. Other studies[24][26][27] revealed higher rate 28.7%,43.8% and 33.3% of nasal carrier *S. aureus* among health care workers respectively.

Highest nasal carrier of *S. aureus* was found in age group 31-40 year (23.82%) and lowest percent of carrier were found in the age group 41-50 year (14.29%). While, no *S. aureus* nasal carrier was found in age group ≥ 20 year and 51-60 year. Similarly, a study[28] conducted in Kathmandu found higher nasal carrier among age group 36-45 year (33.3%) and lowest among the age group of above 46 year (4.8%). This may be due to low number of samples collected from the age group ≥ 20 year and 51-60 year.

Regarding the ward wise distribution of nasal carrier, higher prevalence of nasal carrier *S. aureus* was found in department of ENT 40%. The higher carrier rate among HCWs of ENT department could possibly due to the high frequency of contact with patients of eye, nose and throat andalsodue to poor hygiene. In post-operative department *S. aureus* carrier was 36.36 % and in medicine department was 28.57%. Similar study[28] conducted reported 35.7% of nasal carriage of *S. aureus* in post-operative ward whereas other study[21] observed highest nasal carriage rate of *S. aureus*among medicine (44.8%). *S. aureus* nasal carriage among the staffs from post-operative suggests the possible transmission from wound infection caused by these organisms and also could be due to weak hygiene practice.

Among different profession, highest nasal carriage rate of *S. aureus* was found in nurses 24.83%. Previous studies[9][29]found higher prevalence among nurses. Nurses are regularly in contact with patients which might be the cause for higher carrier number. Staffs in the hospital tend to be colonized while working in the hospital and carrier rate may increase during their prolonged stay and can act as source of infection. It also indicates the need of the control in the frequency of their exposure with the vulnerable patients.

This study showed *S. aureus* were 100% sensitive towards vancomycin and amikacin. Same result was reported by previous studies[25][28][30]. The isolated strains showed highest resistant to penicillin and oxacillin 68.97% which is followed by erythromycin 50%, ciprofloxacin 46.55%. The least effectiveness of penicillin and oxacillin is probably due to indiscriminate and empirical use of these drugs leading to emergence of resistant strains. Furthermore, these drugs are relatively cheaper and easily available all over-the-counter in Nepal[31].

In this study, cefoxitin (81.03%) was more susceptible than oxacillin (31.03%). Recently a number of studies proposed using cefoxitin to be superior in predicting the presence of mecA in *S. aureus* and coagulase negative staphylococci with a high degree of sensitivity and specificity. It is a good inductor of penicillin binding protein 2a production in *S. aureus* isolates that carry the *mecA*gene[21].

All MRSA strain were susceptible towards vancomycin and amikacin and resistant towards cloxacillin and penicillin. Similar results were reported in previous studies[25].

Out of 47 Methicillin sensitive *S. aureus*, 63.83% were MDR, 8.51% were pan susceptible and 27.66% were mono resistant. In case of MRSA 100% isolates were MDR and no isolates were pan susceptible and mono resistant. Similar study has also shown the emergence of MDR *S. aureus* in hospitals[32]. These studies clearly indicate about the appropriate steps to be taken to reduce MRSA and MDR strains in hospital settings to minimize nosocomial infections.

The present study revealed that the total identified MRSA carrier was 3.81%.which correlates with previous studies[25] and was lower than other studies[33][34][35][36]. The observed MRSA is higher than the reports of other studies[10][37]. This may indicate cross-contamination of MRSA between health care personnel and patients.

Out of 288 HCWs, 19.15% female and 18.18 % male was carrier of MRSA which was similar to previous studies[37] where as other studies[25][38] found higher prevalence of MRSA among female HCWs than male HCWs. This could be because more number of sample were collected from female HCWs and female HCWs might lack good hygiene practice along with less immune power.

In this study highest percentage of MRSA was found in age group 21-30 years (21.95%) followed by age group 31-40 years (13.33%) and no MRSA was found in the age group ≥20 year, 41-50 year and 51-60 year. Similar study[38] also observed highest rate of MRSA carriers in the age group 20 to 29 years (5.9%). While on contrary, other study[30] found carriage of MRSA strains higher in the oldest group > 40 year (9.6%) in Argentina. However, there is no association between age and being MRSA carrier (p=1.261). The higher prevalence among the younger HCWs may be due to their lack of knowledge with regard to infection control policies and their missing experience in taking care of MRSA infected patients.

In this study, highest percentage of MRSA was found in paediatric and surgery (50%) which is followed by laboratory (33.33%), ENT and post up (25%). Lowest percentage of MRSA was found in ICU (14%) and medicine (16.67%). Similar results were obtained by previous studies[25][33][38]also found highest rate of MRSA carriers were working in surgical ward. The poor sanitation of the different departments and the poor hygiene practice of the health care workers in different departments may be the reasons behind the higher prevalence of carriage rates in staffs from different departments.

According to their profession, most of the MRSA were isolated from nurses was 22.22% followed by lab workers 20% and doctors 20% and no MRSA was found from attendant. Previous studies[9][21][25][38]] had found MRSA carriage rate was highest among nurses Similarly previous study[28] also reported the higher percentage of MRSA was found among lab personnel (10.5%) followed by nurses (9.9%) and doctors (6.4%). The higher MRSA rate among nurses, doctors and lab workers could possibly be explained by the high frequency of patient contact among these professionals. The nasal carriage of MRSA among HCWs has indicated the chances of transmission of the organism to patients during patient-care.

Conclusion

It is necessary to follow the proper hand washing protocols and other protective measures to protect both the health care worker and patients. Even though this study revealed that the prevalence of nasal carriage *S. aureus* and MRSA among HCWs were comparatively lower than other studies conducted in our country and internationally. But still nasal carriage *S. aureus* and MRSA among HCWs necessitates the need of control in the frequency of their exposure with the vulnerable patients. The basic infection control measures, screening program and treatment of MRSA- positive HCWs can help as an effective measure to control MRSA infections. Multi drug resistance strains are the biggest problem for hospitals because these are usually resistant to most of the common antibiotics. Higher percentage of MDR strain emphasizes the need to discourage antibiotic's abuse. It also supports the need to implement strategies for elimination of nasal carriage of *S. aureus*, so as to prevent severe multi-drug resistant *S. aureus* transmission.

References

[1]. Atlas R (1995). Principles of Microbiology. 1st edition, Mosby-Year Book, Inc; 11830 Westline Industrial Drive, St. Louis, Missouri 63146, pp 681-682.

[2]. Chakrabroty P (2007). A Textbook of Microbiology. 2nd edition, New Central Book Agency (P) Ltd. 8/1 Chintamoni Das Lane, Kolkata 700 009 India. pp 188-210.

[3]. Brooks GF, Butel JS and Morse SA (2004). Medical Microbiology. 23rd edition, New York: McGraw Hill pp 223-247.

[4]. Brown DF, Edwards DI, Hawkey PM, Morrison D, Ridgway GI, Towner KJ and Wren MW (2005). Guidelines for the laboratory diagnosis and susceptibility testing of methicillin resistant *Staphylococcus aureus* (MRSA). J AntimicrobChemother**56**: 1000-1051.

[5]. Murray P, Barron E, Jorgensen J, Pfaller M and Yolkan R (2003). Manual of clinical microbiology. 8thedition, ASM press Washington D.C. USA. pp 383-387.

[6]. Collee JG, Fraser SA, Narmion BP and Simmons (2006). McCartney Practical Medical Microbiology. 14th edition, Churchil Livingstone pp 245-258.

[7]. Carvalho MS, Andrade DF, Sousa AF, Valle AR, Freitas DR, Nascimento GC, Andrade D and Watanabe E (2016). Nasal colonization with *Staphylococcus aureus* in nursing students ground for monitoring. Rev Bras Enferm, **69**:1046-1051.

[8]. Tille P (2014). Bailey and Scott's Diagnostic Microbiology, 13th edition. Elsevier Mos by 3251 Riverport Lin St. Louis, Missouri 63043. pp 223.

[9]. Rashid Z, Farzana K, Satter A and Murtaza G (2012). Prevalence of nasal *Staphylococcus aureus* and methicillin resistant *Staphylococcus aureus* in hospital personnel and associated risk factors. J Acta Pol Pharma**69**: 985-991.
[10]. Gorwitz RJ, Kruszon-Moran D, Mcallister SK, Mcquillan G, Mcdougal LK and Foseim GE (2008). Changes in the prevalence of nasal colonization with *Staphylococcus aureus* in the United States, 2001-2004. J Infect Dis pp**197**. 1226-1234.
[11]. Cosgrove SE, Qi Y and Kaye KS (2005). The impact of methicillin-resistance in *Staphylococcus aureus* bacteremia on patient outcomes: mortality, length of stay and hospital charges. Infect Control HospEpidemiol**26**: 166-174.
[12]. Parija SC (2012). A textbook of microbiology and immunology. 2nd edition, Elsevier publication, India. pp: 181-190.
[13]. Centers for Disease Control (CDC) (2006). Management of multi-drug resistant organisms in Health care settings. CDC, Atlanta USA. pp 1-74..
[14]. Klevens RM, Morrison M, Nadle J, et al. Invasive methicillin-resistant Staphylococcus aureus infections, in the United States. JAMA. 2007; 298: 1763-1571.
[15]. Brumfitt W and Hamilton MJ (1989). Methicillin resistant *Staphylococcus aureus*. New England Journal of Medicine **320**(18): 1188-1196.
[16]. Hugo WB and Russell AD (1993). Pharmaceutical Microbiology. 5th edition, Blackwell Scientific Publication, UK. pp 152-164.
[17]. Niemeyer DM, Pucci MJ, Thanassi JA, Sharma VK and Archer GL (1996). Role of mecA transcriptional regulation in the phenotypic expression of methicillin resistant in *Staphylococcus aureus.* J Bacteriol**178**: 5464-5471.
[18]. Hiramatsu K, Hanaki H, Ino T, Yabuta K, Oguri T and Tenovar FC (1997). Methicillin resistant *Staphylococcus aureus* clinical strain with reduced vancomycin susceptibility. J AntimicrobChemother**40**: 135-139.
[19]. Quezada JNM, Diekema DJ, Perencevich EN, Bailey G, Winokur PL and Schweizer ML (2013). Long term risk for readmission, methicillin resistant *Staphylococcus aureus* (MRSA) infection and death among MRSA colonized veterans. J Antimicrob Agents Chemother**57**: 1169-1172.
[20]. Sah P, Rijal KR, Shakya B, Tiwari BR and Ghimire P (2013). Nasal carriage rate of *Staphylococcus aureus* in hospital personnel of National Medical college and Teaching Hospital and their susceptibility pattern. J Health ApplSci**3**: 21-23.
[21]. Elalia NA, Allaham Na and Ayesh BM (2017). Nasal carriage of methicillin resistant *Staphylococcus aureus* among health care workers at AL Shifa hospital in Gaza Strip. BMC Infect Dis **17**: 28.
[22]. Cheesbrough M (2000). District laboratory practice in tropical countries. Part 2. Cambridge University Press. pp 157-165.
[23]. CLSI (2015). Performance standards for Antimicrobial susceptibility testing. CLSI document M100-S25. Wayne PA: clinical laboratory standard institute.
[24]. Onanuga A and Temedie TC (2011). Nasal carriage of multi- drug resistant *Staphylococcus aureus* in healthy inhabitants of Amassoma in Niger delta region of Nigeria. J African Health Sciences **11**: 176-181.
[25]. Khanal R, Sah P, Lamichhane P, Lamsal A, Upadhaya S and Pahwa VK (2015). Nasal carriage of methicillin resistant *Staphylococcus aureus* among health care workers at a tertiary care hospital in Western Nepal. J Antimicrobial Resistance and Infection Control **4**: 39.
[26]. Pant J and Rai SK (2007). Occurance of *Staphylococcus aureus* in hospital environment and staffs in teaching hospital in Kathmandu, Nepal. NAMLS **8**: 72-73.
[27]. Al-Talib H, Yean CY, Hasan H, NikZuraina NMN and Ravichandran M (2013). Methicillin resistant *Staphylococcus aureus* nasal carriage among patients and healthcare workers in a hospital in Kelatan. Malaysia. J Pol Microbiol**62**: 109-12.
[28]. Khatri S, Pant ND, Bhandari R, Shrestha KL, Shrestha CD, Adhikari N and Poudel A (2017). Nasal carriage rate of methicillin reistant*Staphylococcus aureus* among health care workers at tertiary care hospital in Kathmandu, Nepal. J Nepal Health Res Counc**15**: 26-30.
[29]. Shrestha B, Pokhrel BM and Mohapatra TM (2009). *Staphylococcus aureus* nasal carriage among health care workers in a Nepal hospital. J Brazilian Infect Dis **13**: 322.
[30]. Boncompain CA, Suarez CA and Morbidoni HR (2017). *Staphylococcus aureus* nasal carriage in health care workers: First report from a major public hospital in Argentina. J Rev Argent Microbiol**49**(2): 125-131.

[31]. Kumari N, Malhotra TM and Singh YI (2008). Prevalence of methicillin resistant *Staphylococcus aureus* (MRSA) in a tertiary care hospital in Nepal. Nepal Med Assoc**47**: 53-56.
[32]. Anupurba S, Sen MR, Nath G, Sharma BM, Gulati AK, Mohapatra TM. Prevalence of methicillin resistant Staphulococcusaureusin tertiary referral hospital in eastern Uttar Pradesh. Indian J Med Microbiol 2003;21:49-51
[33]. Askarian M, Zeinalzadeh A, Japoni A, Alborzi A and Memish ZA (2009). Prevalence of nasal carriage of methicillin resistant *Staphylococcus aureus* and its susceptibility pattern in healthcare workers at Namazi Hospital, Shiraz, Iran. J Infect Dis **13**: 241-247
[34]. Shakya B, Shrestha S and Mitra T (2010). Nasal carriage rate of methicillin resistant *Staphylococcus aureus* among at National medical college teaching hospital, Birgunj, Nepal. J Nepal Med Coll**12**: 26-29
[35]. Chen C, Huang Y (2005). Community- acquired methicillin resistant *S. aureus* in Taiwan. J Microbial Immunol Infect **38**: 376-382
[36]. Olonitola OS, Inabo HI, Olayika BO and Bugo ID (2007). Nasal carriage of methicillin resistant *Staphylococcus aureus* by primary school pupils in a University staff school, Zaria, Nigeria. International journal of biological and chemical sciences **1**: 71-75.
[37]. Hogan B, Rakotozandrindrainy R, Al-Emran H, Dekker D, Hahn A, Poppert S, Frickman H, Hagen RM, Michel V, Crusius S, Hernianana JN, Rakotondrainiarivelo JP and Schwarz NG (2016). Prevalence of nasal colonization by methicillin sensitive and methicillin resistant *Staphylococcusaureus* among healthcare workers and students in Madagaskar. J BMC Infect Dis **16**: 016-1733.
[38]. Shibabaw A, Abebe T and Mihret A (2013). Nasal carriage rate of methicillin resisant*Staphylococcus aureus* among Dessie Referral hospital health care workers, Dessie, northest Ethiopia. J Asntimicrob Resist Infect Control **2**: 25.