DOI: 10.7860/JCDR/2019/40473.13054

Original Article

Microbiology Section

Nasal Colonisation of MRSA in Oral Cancer Patients in a Tertiary Care Hospital of Northern India

DEESHA KUMAR[1], ANKUR GOYAL[2], SURABHI GUPTA[3], NIDHI GUPTA[4], ARTI AGRAWAL[5], SAPNA GOYAL[6]

ABSTRACT

Introduction: Methicillin-resistant *Staphylococcus aureus* (MRSA) is a common cause of healthcare-associated infection worldwide. Immunocompromised patients are more susceptible to develop infection from own colonised MRSA.

Aim: To screen oral cancer patients for nasal colonisation of MRSA at two time point during study period.

Materials and Methods: The study was conducted in SN Medical College, Agra for a period of six months. Anterior nares of 50 participants having oral cancer were screened for colonisation of *Staphylococcus aureus*. Isolates were identified as *Staphylococcus aureus* as per standard protocol and were further subjected to see the production of MRSA as per CLSI criteria.

Results: Total 50 patients were enrolled in the study, out of these, 34 were put on chemotherapy while 16 were put on radiotherapy. Before starting any treatment modality 29 (58%) patients were colonised with *Staphylococcus aureus* out of which 16 (32%) were MRSA strains and 13 (26%) were MSSA. Patients who did not show MRSA colonisation in their anterior nares (34/50; 68%) were further screened for MRSA colonisation after three weeks of chemotherapy and four weeks of radiotherapy. 50% patients (7/14) of chemotherapy group demonstrated the conversion of nasal flora in MRSA after three weeks of treatment and 33.3% (3/9) of radiotherapy group showed the conversion in MRSA after four weeks of treatment.

Conclusion: The present study suggests that if a patient is colonised initially with MSSA in oral cancer patient then the patient should not be left as non MRSA producer. As patient might develop MRSA colonisation after chemotherapy and radiotherapy which may further be the reason for resistant infection in immune-compromised cancer patients.

Keywords: Immunocompromised patients, Methicillin resistance, *Staphylococcus*

INTRODUCTION

Staphylococcus aureus is the leading cause of healthcare-associated infection. *S. aureus* is a normal commensal of human being, and nearly 50% of the population are asymptomatic carriers [1]. Although *Staphylococcus aureus* can be cultured from multiple sites of the skin and mucosal surfaces of carriers, the primary reservoir of staphylococci is thought to be the anterior nares [2]. Various studies in India reported MRSA colonisation in various category of patients around 44-46% from multiple body sites [3,4]. Many times with decreasing immunity these commensal can act as pathogen which can cause a subsequent healthcare acquired infection. Several studies have clearly found that about 14-20% of (MRSA) colonisation may progress to MRSA infection [5,6]. Patients infected with MRSA usually show worse clinical outcomes than those with methicillin-sensitive *Staphylococcus aureus* (MSSA) infections. These infections are not only difficult to treat but they can also lead to certain life-threatening complications like pneumonia [7] and bacteremia [8]. Immunosuppressed conditions like cancer are also prone to colonisation and subsequent infection by MRSA.

Despite significant advances in treatment modalities, cancer patients continue to remain at substantial risk for developing serious infections. A study conducted in a palliative care setting found that a considerable proportion of cancer patients are colonised with MRSA [9]. The treatment of malignant condition with cancer therapy has become increasingly effective, but it is associated with significant side effects, including bone marrow suppression. Patients undergoing radiotherapy and chemotherapy for oral cancer are more susceptible to bacterial infections [10]. A retrospective study indicated that 12 out of 27 cancer patients with MRSA colonisation undergoing chemotherapy subsequently developed sepsis [11]. Kang YC et al., performed a study to observe the nasal MRSA colonisation at two time point survey in end stage kidney disease patients receiving haemodialysis [12].

Only limited current MRSA nasal colonisation data in oral cancer patients from India is available. Therefore, in the present study we planned to screen the oral cancer patients for nasal colonisation for MRSA. They would also be assessed for any change in colonisation pattern leading to MRSA colonisation due to chemotherapy and radiotherapy treatment modalities. Therefore, nasal colonisation would be checked at two time point in oral cancer patients.

MATERIALS AND METHODS

The present observational prospective study was conducted in the Department of Microbiology and Department of Radiotherapy and Oncology, SN Medical College and Hospital, Agra, Uttar Pradesh, India, from March to August 2018 for six months after obtaining approval from the institutional ethical committee, SN Medical College, Agra vide letter no: IEC/2018/01 dated 06/03/2018.

A written consent was taken from every patients enrolled for the study. The age of patients varied from 43 to 64 years and male female ratio was 3.8: 1. All patients who presented for the first time in oncology OPD and diagnosed as oral cancer and who gave consent for study were included in the study. Those patients who did not consent for the study and had other immune-compromised condition were excluded from the study. A total of 50 participants having oral cancer were screened for colonisation of *S. aureus* in anterior nare as per standard protocol [4].

First nasal swab sample was collected when patient was enrolled for the study. Based on treatment regimen these patients were divided in to two groups. In chemotherapy group (n=34), second sample was taken after three weeks of chemo treatment and in radiotherapy group (n=16), second sample was taken after 01 cycle (four weeks) of radiotherapy. Nasal swabs were processed as per standard criteria.

Colonies of *Staphylococcus aureus* were identified by colony morphology and were confirmed by Gram stain, catalase test and slide and tube coagulase test. Strains confirmed as *Staphylococcus aureus* were tested for resistance to methicillin by disc diffusion technique as per CLSI M100-S24 2017 guidelines using cefoxitin disc (30 microgram), Himedia Laboratory, India. Data was filled and analysed descriptively on Microsoft excel software.

RESULTS

[Table/Fig-1] shows the organism isolated in nasal flora during first time survey. A total of 29 (58%) cases were having *Staphylococcus aureus* in their nasal cavity out of which 16 (32%) were MRSA [Table/Fig-1]. Fifty patients were divided into two groups according to treatment plan, first group was given chemotherapy (n=34) and second group was given radiotherapy (n=16) [Table/Fig-2].

Organism isolated	Number of patients (n=50)	Percentage
MRSA	16	32%
MSSA	13	26%
NPG	7	14%
MSCONS	6	12%
MRCONS	6	12%
Pseudomonas aeruginosa	2	4%

[Table/Fig-1]: Organisms isolated from nasal cavity in oral cancer patients before starting treatment (n=50).
MRSA: Methicillin resistant *staphylococcus aureus*; MSSA: Methicillin sensitive *staphylococcus aureus*; NPG: Non pathogenic growth; MSCONS: Methicillin Sensitive Coagulase Negative *Staphylococcus*; MRCONS: Methicillin Resistant Coagulase Negative *Staphylococcus*

Organism isolated	Patients going for chemotherapy (n=34)	Patients going for radiotherapy (n=16)
MRSA	12 (35.2%)	4 (25%)
MSSA	11 (32.3%)	2 (12.5%)
NPG	5 (14.7%)	2 (12.5%)
MSCONS	2 (5.8%)	4 (25%)
MRCONS	4 (11.7%)	2 (12.5%)
Pseudomonas aeruginosa	Nil	2 (12.5%)

[Table/Fig-2]: Organisms isolated from nasal cavity in patients before Chemotherapy (n=34) and Radiotherapy (n=16).
MRSA: Methicillin resistant *staphylococcus aureus*; MSSA: Methicillin sensitive *staphylococcus aureus*; NPG: Non pathogenic growth; MSCONS: Methicillin Sensitive Coagulase Negative *Staphylococcus*; MRCONS: Methicillin Resistant Coagulase Negative *Staphylococcus*

We only selected those patients for second sample in whom nasal flora had not shown any MRSA bacteria in their first sample. In chemotherapy group of patients, a second sample was taken after giving three weeks of chemotherapy. With the best of our efforts only 14 out of 22 non MRSA cases could be followed rest 5 were lost to follow-up and 3 died.

In radiotherapy group of patients, a second sample from nasal cavity was taken four weeks after radiotherapy. With the best of our efforts only 9 out of 12 non MRSA cases could be followed. Rest 1 was lost to follow-up and 2 died.

Patients in whom nasal flora were not positive for MRSA before chemotherapy, we found that 7 (50%) out of 14 cases have been converted into MRSA. In those patients whose nasal carriage was non MRSA before radiotherapy we found that 3(33.3%) out 9 cases, flora has converted into MRSA [Table/Fig-3].

[Table/Fig-4] shows the change of nasal flora in MRSA from other flora after chemotherapy and radiotherapy. In the present study, 4 (80%) out of 5 MSSA nasal carriage before chemotherapy has been converted to MRSA nasal carriage after three weeks of chemotherapy and surprisingly all (2) cases MSSA nasal carriage before radiotherapy has been converted to MRSA nasal carriage four weeks after first fraction of radiotherapy.

Organism isolated from Non-MRSA at second time point survey	Number of patients after Chemotherapy (n=14)	Number of patients after Radiotherapy (n=9)
MRSA	7 (50%)	3 (33.3%)
NPG	3 (21%)	1 (11.1%)
MRCONS	2 (14.2%)	1 (11.1%)
MSCONS	1 (7.14%)	2 (22.2%)
MSSA	1 (7.14%)	0 (0%)
Pseudomonas aeruginosa	0 (0%)	2 (22.2%)

[Table/Fig-3]: Organisms isolated from nasal cavity in Non MRSA nasal carriage patients after Chemotherapy (n=14) and after Radiotherapy (n=9).
MRSA: Methicillin Resistant *Staphylococcus aureus*; MSSA: Methicillin Sensitive *Staphylococcus aureus*; NPG: Non Pathogenic Growth; MSCONS: Methicillin Sensitive Coagulase Negative *Staphylococcus*; MRCONS: Methicillin Resistant Coagulase Negative *Staphylococcus*

Patient nasal flora at first time point survey before chemotherapy (n)	After Chemotherapy (n) change in flora to MRSA	Patient nasal flora at first time point survey before radiotherapy (n)	After radiotherapy (n) change in flora to MRSA
NPG (5)	2 (40%)	NPG (2)	0 (0%)
MSSA (5)	4 (80%)	MSSA (2)	2 (100%)
MRCONS (4)	1 (25%)	MSCONS (4)	1 (25%)

[Table/Fig-4]: Percent conversion of various nasal flora to MRSA after chemotherapy and radiotherapy.
MRSA: Methicillin resistant *Staphylococcus aureus*; MSSA: Methicillin sensitive *staphylococcus aureus*; NPG: Non pathogenic growth; MSCONS: Methicillin Sensitive Coagulase Negative *Staphylococcus*; MRCONS: Methicillin Resistant Coagulase Negative *Staphylococcus*

DISCUSSION

Cancer patients are at risk for developing serious infections. Due to immunocompromised status many times these patients may get infected with normal resident flora and ultimately become infected. In the present study, before starting any treatment modality, 29 (58%) cancer patients were colonised with *Staphylococcus aureus* out of which 16 (32%) were MRSA strains and 13 (26%) were MSSA. Worldwide many studies showed various prevalence of nasal colonisation in various categories of patients. O'Brien FG et al., studied the colonisation rate of MRSA in two remote communities in Australia and found colonisation rates of 42% and 24% [13]. Saxena S et al., in their study from East Delhi collected a total of 319 nasal swabs from both anterior nares of healthy parents attending a well-baby clinic. Of these, 94 yielded growth of *S. aureus* (29.4%). Out of these 94 isolates, 17 (18.1%) were MRSA [14].

In a palliative care setting, Ghanem HM et al., found 8.3% prevalence of MRSA [9]. Other studies on palliative care patients found that on admission, 24 of 281 (8.5%) patients tested positive for MRSA [15]. In another study overall prevalence of nasal carriage for MRSA was 4.1% in cancer patients at the time of admission [16]. Srinivasan A et al., in his study in children with cancer found that 0.6% were colonised with MRSA in 2000 and 2.9% in 2006 [17]. Crysandt M et al., in his study on patients with solid or hematological malignancies found that 1.3% were colonised with MRSA in their nasal flora [11]. In a study authors found 6.7% prevalence of MRSA in renal transplant patients [18].

In the present study, we divided our patients into two groups on the basis of therapy given to the patients, one on chemotherapy and another on radiotherapy treatment protocol. In chemotherapy group those patients whose nasal flora were not positive for MRSA before chemotherapy, we found that 7 (50%) out of 14 cases have been converted into MRSA. We also found that 4 (80%) out of 5 MSSA nasal carriage before chemotherapy has been converted to MRSA nasal carriage after three weeks of chemotherapy. Other significant conversions seen were NPG to MRSA in 2 patients and MRCONS to MRSA in 1 case. In radiotherapy group those patients whose nasal carriage was non MRSA before radiotherapy, we found that 3 (33.3%) out 9 cases, flora has converted into MRSA. We also found that 100% of MSSA nasal carriage before radiotherapy has been converted to MRSA nasal carriage four weeks after first

fraction of radiotherapy. Other significant conversions seen were MSCONS to MRSA in 1 patient.

In the present study, conversion of nasal flora to MRSA is much higher after chemotherapy than radiotherapy and the difference is statistically significant. Our study suggests that if a patient is colonised with MSSA then there is a high chance that it will be converted to MRSA colonisation after Chemotherapy or Radiotherapy. This study also emphasises that in patients with chronic diseases like cancer if nasal carriage initially showed MSSA then it must be decolonised to avoid its conversion into MRSA and further life-threatening complications like pneumonia and sepsis. The results indicate the need of a prospective study with follow-up of large number of subjects. Overall, chemotherapy caused more conversion of nasal flora to MRSA in comparison to radiotherapy. Present study emphasises that based on treatment protocol, MRSA conversion of nasal flora may differ.

LIMITATION

The number of patients included in the present study is less therefore a large prospective case control study should be done to see any role of therapy in conversion of nasal flora in MRSA. Another limitation is that study on genetic level may give more significant correlation. Various risk factors may also be analysed to establish any correlation.

CONCLUSION

In the current scenario, healthcare associated infection especially MRSA is a serious threat to mankind especially in immunocompromised patients like cancer. Therefore, these group of patients should be screened for presence of MRSA in their nasal flora, if patients nasal flora is showing MSSA initially, it must be taken seriously and should be treated as there is high chance in MSSA flora for development of MRSA following various treatment strategies.

REFERENCES

[1] Shorr AF. Epidemiology and economic impact of meticillin-resistant *Staphylococcus aureus*: Review and analysis of the literature. Pharmacoeconomics. 2007;25(9):751-68.

[2] Kluytmans J, van Belkum A, Verbrugh H. Nasal carriage of *Staphylococcus aureus*: Epidemiology, underlying mechanisms, and associated risks. Clin Microbiol Rev. 1997;10(3):505-20.

[3] Indian Network for Surveillance of Antimicrobial Resistance (INSAR) group, India, Joshi S, Ray P, et al. Methicillin resistant *Staphylococcus aurous* (MRSA) in India: Prevalence & susceptibility pattern. The Indian Journal of Medical Research. 2013;137(2):363-69.

[4] Singh AK, Agarwal L, Kumar A, Sengupta C, Singh RP. Prevalence of nasal colonization of methicillin-resistant *Staphylococcus aureus* among school children of Barabanki district, Uttar Pradesh, India. J Family Med Prim Care. 2018;7:162-66.

[5] Balm MN, Lover AA, Salmon S, Tambyah PA, Fisher DA. Progression from new methicillin-resistant *Staphylococcus aureus* colonization to infection: An observational study in a hospital cohort. BMC Infectious Diseases. 2013;13(1):1.

[6] Davis KA, Stewart JJ, Crouch HK, Florez CE, Hospenthal DR. Methicillin-resistant *Staphylococcus aureus* (MRSA) nares colonization at hospital admission and its effect on subsequent MRSA infection. Clinical Infectious Diseases. 2004;39(6):776-82.

[7] Haeili M, Ghodousi A, Nomanpour B, Omrani M, Feizabadi MM. Drug resistance patterns of bacteria isolated from patients with nosocomial pneumonia at Tehran hospitals during 2009-2011. The Journal of Infection in Developing Countries. 2013;7(04):312-17.

[8] Keynan Y, Rubinstein E. *Staphylococcus aureus* bacteremia, risk factors, complications, and management. Critical Care Clinics. 2013;29(3):547-62.

[9] Ghanem HM, Abou-Alia AM, Alsirafy SA. Prevalence of methicillin-resistant *Staphylococcus aureus* colonization and infection in hospitalized palliative care patients with cancer. American Journal of Hospice and Palliative Medicine. 2013;30(4):377-79.

[10] Panghal M, Kaushal V, Kadayan S, Yadav JP. Incidence and risk factors for infection in oral cancer patients undergoing different treatments protocols. BMC Oral Health. 2012;12(1):1.

[11] Crysandt M, Lemmen SW, Jost E, Brummendorf TH, Osieka R, Wilop S. Antineoplastic chemotherapy in cancer patients with Methicillin-Resistant *Staphylococcus aureus* (MRSA). Oncology Research and Treatment. 2010;33(11):598-603.

[12] Kang YC, Tai WC, Yu CC, Kang JH, Huang YC. Methicillin-resistant *Staphylococcus aureus* nasal carriage among patients receiving hemodialysis in Taiwan: Prevalence rate, molecular characterization and de-colonization. BMC Infectious Diseases. 2012;12:284.

[13] O'Brien FG, Pearman JW, Gracey M, Riley TV, Grubb WB. Community strain of Methicillin resistant *Staphylococcus aureus* involved in a hospital outbreak. J Clin Microbiol. 1999;37(9):2858-62.

[14] Saxena S, Singh K, Talwar V. Methicillin-resistant *Staphylococcus aureus* prevalence in community in the east Delhi area. Jpn J Infect Dis. 2003;56(2):54-56. PubMed PMID: 12824685.

[15] Schmalz O, Strapatsas T, Alefelder C, Grebe SO. Methicillin-resistant *Staphylococcus aureus* in palliative care: A prospective study of Methicillin-resistant *Staphylococcus aureus* prevalence in a hospital-based palliative care unit. Palliat Med. 2016;30(7):703-06.

[16] Heckel M, Geißdörfer W, Herbst FA, Stiel S, Ostgathe C, Bogdan C. Nasalcarriage of methicillin-resistant *Staphylococcus aureus* (MRSA) at a palliative care unit: A prospective single service analysis. PLoS One. 2017;12(12):e0188940.

[17] Srinivasan A, Seifried SE, Zhu L, et al. Increasing prevalence of nasal and rectal colonization with methicillin-resistant *Staphylococcus aureus* in children with cancer. Pediatric Blood & Cancer. 2010;55(7):1317-22. doi:10.1002/pbc.22815.

[18] Ribeiro LLC, Aparecida BD. Prevalence of *Staphylococcus aureus* colonization in renal transplant patients. Rev. Esc. Enferm. USP [Internet]. 2014 Oct [cited 2018 Sep 28];48(5):827-33.

PARTICULARS OF CONTRIBUTORS:

1. MBBS Student, SN Medical College, Agra, Uttar Pradesh, India.
2. Associate Professor, Department of Microbiology, SN Medical College, Agra, Uttar Pradesh, India.
3. Professor, Department of Radiotherapy, SN Medical College, Agra, Uttar Pradesh, India.
4. Tutor, Department of Microbiology, SN Medical College, Agra, Uttar, Pradesh, India.
5. Lecturer, Department of Microbiology, SN Medical College, Agra, Uttar Pradesh, India.
6. Resident, Department of Microbiology, SN Medical College, Agra, Uttar Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Ankur Goyal,
2/44/1A, Ramnagar Colony, Church Road, Agra, Uttar Pradesh, India.
E-mail: agoyal79@yahoo.co.in

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Dec 05, 2018**
Date of Peer Review: **May 08, 2019**
Date of Acceptance: **Jun 28, 2019**
Date of Publishing: **Aug 01, 2019**