



RESEARCH ARTICLE

A HOSPITAL BASED PROSPECTIVE STUDY OF PREVALENCE OF METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS IN DERMATOLOGY INDOOR PATIENTS BY PHENOTYPIC METHOD

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Abstract

Introduction: Methicillin-Resistant Staphylococcus aureus is a cause of increased morbidity and mortality in debilitated and immunocompromised indoor patients.

Aim: The aim of our study was to see the prevalence of Methicillin - Resistant Staphylococcus aureus infection in dermatology indoor patients by phenotypic method and elucidate its predisposing factors and antibiotic sensitivity pattern.

Methods: This was a hospital based prospective study which included all dermatology indoor patients with primary and secondary bacterial infection.

Results: The study enrolled 110 indoor patients with 57 males and 53 females. The mean age of the study was 39.23 years ranging between 2-90 years. Vesicobullous disorders were the commonest dermatoses with secondary infection. Diabetes mellitus was the most common comorbidity being present in 18 patients. S. aureus was the commonest bacterial isolate grown in culture in 66 patients, accounting for 60% of the total isolate. MRSA isolates accounted for 24.55% (27) of the total isolates. Majority of the MRSA patients (n=23, 85.19%) were having HAMRSA, while only 4 MRSA patients (n=4, 14.81%) were having CAMRSA. All MRSA isolates were sensitive to vancomycin and linezolid, while all the MRSA isolates were resistant to cefoxitin, oxacillin, cloxacillin, ampicillin and ciprofloxacin.

Conclusion: The prevalence of MRSA in our study was high. A high percentage of both MSSA and MRSA isolates were sensitive to gentamicin, which is a cheaper, effective and widely available antibiotic.

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Introduction:-

Normal skin is colonized with resident bacterial flora, usually Staphylococcus epidermidis, other coagulase-negative Staphylococci, Corynebacteria and Propionibacterium acnes. Cutaneous infections arise when there is a break in the continuity of the skin or as a part of systemic infection.[1]

Staphylococcus aureus accounts for 30-50% of skin and soft tissue infections.[2][3] Staphylococcus aureus, gram positive cocci is a common commensal of humans and its primary habitat is the moist squamous epithelium of the

anterior nares. About 20% of the population are always colonized with *S. aureus*, 60% are intermittent carriers, and 20% never carry the organism.[4]

MRSA is classified into Community-Acquired MRSA (CAMRSA) and Hospital-Acquired MRSA (HAMRSA). CAMRSA is defined as a bacterial isolate seen in the outpatient setting or within 48 hours of hospitalization .[5] Risk factors for acquiring HA-MRSA include previous admission to healthcare facilities, impaired immune system, use of multiple antibiotics, use of invasive medical devices and old age.[6]

MRSA has been emerging as one of the most important nosocomial pathogens and MRSA isolates were frequently isolated among inpatients at our tertiary care institute. We therefore decided to conduct this study to determine the prevalence of MRSA infection among our inpatients as primary objective by phenotypic method and its predisposing factors and antibiotic sensitivity pattern of MRSA as secondary objective.

Materials And Methods:-

The study was conducted in the Postgraduate Department of Dermatology, in collaboration with Department of Microbiology in a tertiary care hospital of North India over a period of one year after obtaining approval from institutional ethical committee. This was a hospital based prospective study which included all dermatology indoor patients with suspected bacterial infections, both primary and secondary. A written informed consent was taken from all the patients.

Detailed history was taken in a predesigned proforma which included: age, gender, occupation duration of illness, nature and onset of skin lesions ,presence of comorbidities like diabetes mellitus , duration of hospitalisation , history of previous hospitalisation, use of invasive medical devices ,previous history of treatment with antibiotics and immunosuppressive therapy , history of similar complaints in the family/close contacts , history of hospitalisation of any family member in the past .

Detailed general physical, systemic and cutaneous examination was also performed and investigations like complete blood count , renal function test , liver function test and blood sugar fasting were done. HIV serology was done in high risk patients. MRSA was classified as Community Acquired MRSA (CAMRSA) / Hospital Acquired MRSA (HAMRSA) based on bacterial isolate seen within or after 48 hours of hospitalisation.

After thoroughly cleaning the skin lesions with sterile normal saline, pus samples were drawn with a sterile swab and sent to the microbiology department for gram staining, pus culture and antibiotic sensitivity.

Staphylococcus aureus colonies were identified by a smooth, convex, shiny and opaque appearance with a golden yellow pigment seen on blood agar and lactose fermenting colonies seen on MacConkey agar as well as showing catalase positivity, coagulase positivity and mannitol fermentation.

A direct colony suspension equivalent to 0.5 McFarland standard was inoculated on Muller Hinton agar plate that had antibiotic discs of penicillin, oxacillin, vancomycin, ciprofloxacin/levofloxacin, ofloxacin, clindamycin, azithromycin, linezolid, chloramphenicol, doxycycline, cefoxitin as per Clinical and Laboratory Standards Institute (CLSI) guidelines supplemented with 2% sodium chloride and incubated at 37 degrees for 24 hours.

MRSA was defined as an isolate having inhibition zone of <21mm around 30 microgram disc of cefoxitin by disc diffusion method.

Statistical analysis was done using computer software Microsoft Excel and SPSS version 21.0 for Windows. Data was reported as mean \pm standard deviation and proportions as deemed appropriate for quantitative and qualitative variables, respectively. The qualitative data was compared using Fisher's exact test and Spearman's rank correlation coefficient. A p value of <0.05 was considered as statistically significant.

Results:-

There were a total of 110 patients in the study. The mean age of the study subjects was 39.23 years; ranging between 2 to 90 years. Majority of the cases were in the age group of 31-40 years (27, 24.55 %) (table1). Male to female ratio among study subjects was 1.07:1. Male patients dominated the study constituting 51.82% (57) of the total patients

with female patients constituting 48.18% (53). Among females, housewives accounted for the maximum number of cases (38, 34.54%). Among males, most of the patients were manual workers (34, 30.91%). Vesicobullous disorders were the commonest dermatoses with secondary infection (32, 29.09%) followed by eczema (18, 16.36%) (table2)

Comorbidities were present in 34 patients. Diabetes mellitus was the most common comorbidity being present in 18 (16.36%) of the total patients .91 (82.73%) patients were tested for HIV status but all were found to be negative.

Gram-positive cocci was seen on gram staining in 81(73.64%) of the patients followed by Gram-negative cocci in 25 patients (22.73%) and no organism was seen in 4 (3.64%) patients.

S.aureus (MSSA, MRSA) was the commonest bacterial isolate grown in culture in 66 patients (60%).MRSA was isolated from 27 patients accounting for 24.55% of the total bacterial isolates. (table3). 23 MRSA patients (85.19%) were having HAMRSA, while only 4 MRSA patients (14.81%) were having CAMRSA.

Majority of the MRSA patients (13, 48.15%) had duration of illness of more than ≥ 40 weeks with a mean duration of illness of 99.48 weeks and duration of hospitalization was ≤ 7 days in 21 (77.78%) MRSA patients. Diabetes as a comorbidity was present in 5 (18.52%) of the MRSA patients.

MRSA was most commonly isolated from vesicobullous disorders (9, 33.33%) followed by eczema and pyoderma (4, 14.81% each) (table4). All MRSA patients (100%) had history of antibiotics prior to hospitalisation while 15 (55.56%) MRSA patients were on immunosuppressants.

20 (74.07%) MRSA patients had history of previous hospitalisation and 18(66.67%) MRSA patients had history of invasive medical devices in the form of intravenous cannulas.

All the MSSA strains (100%) were sensitive to cefoxitin, linezolid, doxycycline, chloramphenicol and vancomycin. 16 out of the 17MSSA patients (94.12%) tested for the gentamicin were sensitive to the antibiotic. All MRSA isolates (100%) were sensitive to vancomycin and linezolid. 16 out of the 18 MRSA patients (88.89%) who were tested for gentamicin were sensitive to the antibiotic.

Among the MSSA strains tested for ampicillin, 100% resistance was there. 95.65% of the MSSA strains were resistant to penicillin G and 81.25% to oxacillin. All the MRSA isolates were resistant to cefoxitin, oxacillin, cloxacillin, ampicillin and ciprofloxacin. Of the 9 MRSA patients tested for penicillin G, 88.89% were resistant to the antibiotic.

Table1:- Distribution of patients according to age.

AGE (IN YEARS)	NO. OF PATIENTS	PERCENTAGE (%)
≤ 10	8	7.27
11-20	11	10.0
21-30	19	17.27
31-40	27	24.55
41-50	20	18.18
51-60	12	10.91
>61	13	11.82
TOTAL	110	100.00

Table2:- Distribution of patients according to the type of dermatoses.

TYPE OF DERMATOSES	NO. OF PATIENTS	PERCENTAGE (%)
VESICOBULLOUS	32	29.09
ARTHROPOD INFESTATION	3	2.73
CONNECTIVE TISSUE DISORDERS	7	6.36
DISORDER OF APOCRINE GLAND	3	2.73
DEEP FUNGAL INFECTIONS	3	2.73

DISORDER OF PILOSEBACEOUS UNIT	1	0.91
ECZEMA	18	16.36
LEPROSY	5	4.55
MYCOBACTERIAL INFECTION	2	1.82
NEUTROPHILIC DERMATOSIS	3	2.73
NON HEALING ULCER	6	5.45
PAPULOSQAMOUS	3	2.73
PARASITIC INFESTATION	11	10
PYODERMA	9	8.18
SCAR	2	1.82
SKIN TUMOUR	2	1.82
TOTAL	110	100.00

Tab3:- Distribution Of Patients According To Bacterial Isolate In Culture.

BACTERIAL ISOLATE	NO. OF PATIENTS	PERCENTAGE (%)
ACINETOBACTER	2	1.82
E.COLI	1	0.91
KLEBSIELLA	3	2.73
METHICILLIN SENSITIVE STAPHYLOCOCCUS AUREUS	39	35.45
METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS	27	24.55
NO GROWTH	19	17.27
PROTEUS	1	0.91
PSEUDOMONAS AERUGINOSA	18	16.36
TOTAL	110	100.00

Table4:- Distribution of MRSA patients according to type of dermatoses.

TYPE OF DERMATOSES	NO. OF PATIENTS	PERCENTAGE (%)
VESICOBULLOUS	9	33.33
ARTHROPOD INFESTATION	1	3.7
DISORDER OF APOCRINE GLAND	1	3.7
DEEP FUNGAL INFECTION	1	3.7
ECZEMA	4	14.81
LEPROSY	3	11.11
MYCOBACTERIAL INFECTION	1	3.7
NEUTROPHILIC DERMATOSIS	1	3.7
NON HEALING ULCER	1	3.7
PARASITIC INFESTATION	1	3.7
PYODERMA	4	14.81
TOTAL	27	100.00



Figure1:- Golden Yellow Colonies of *S. aureus* on Blood Agar.



Figure 2:- Methicillin-sensitive *S. aureus* (MSSA) on Muller Hinton Agar Plate.



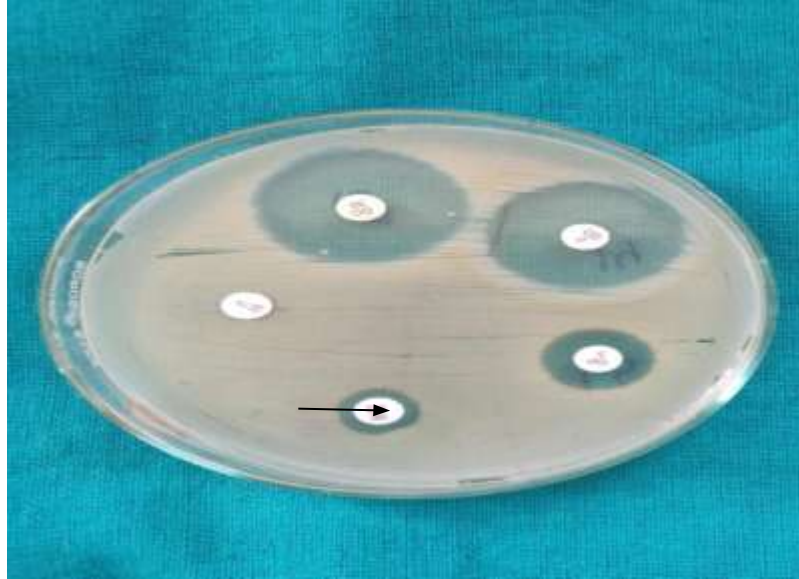


Figure 3:- Crusted Plaque of Pemphigus Patient with Methicillin Resistant Staphylococcus Aureus Culture (Zone of Inhibition of <21mm around Cefoxitin Disc).



Figure4:- Patient Of Hidradenitis Suppurativa With Positive Methicillin- Resistant Staphylococcus Aureus Culture (Zone Of Inhibition Of <21mm Around Cefoxitin Disc).

Discussion:-

Sepsis in dermatology indoor patients is one of the most dreaded complication especially in patients with pemphigus and Toxic Epidermal Necrolysis/Stevens-Johnson syndrome patients and contributes significantly to mortality. High dose of corticosteroids and immunosuppressives add to their susceptibility to develop sepsis.

MRSA infections in hospitals have imposed a high burden on healthcare resources as well as to significant morbidity and mortality.

A total of 110 indoor patients of all age groups and either gender having primary or secondary bacterial infection were studied. The mean age of cases was 39.23 years and the age group 31-40 accounted for the maximum number of cases (24.55%) followed by age group 41-50 years (18.18%).

In a similar previous study, the age group 41-50 accounted for the maximum number of cases (21.6%). [7] The earlier age group in our study could be due to more number of pemphigus patients in our study as pemphigus occurs in a younger age group in Indian population as compared to western countries.

The males (57 cases) outnumbered the females (53 cases) in our study with the ratio being 1.07:1. This is in accordance with the previous studies in the literature. [7,8]. The male preponderance in this study could be due to the fact that the majority of the cases in the study were manual workers who are prone to trauma, as well as the risk of close physical contact among themselves. The role of close physical contact in MRSA acquisition has been presented in previous studies. [9]

Among males, manual workers (30.91%) accounted for the maximum number of cases in our study. Among females, housewives (34.54%) constituted maximum number of the cases. This could be due to the reason that both manual workers and housewives are subjected to frequent trauma.

Similar findings were observed in the previous study. [7]

Vesicobullous disorders were the commonest disorder to be secondarily infected (29.09%) followed by eczema (16.36%). Most of the previous Indian studies have also found vesicobullous disorders to be the most commonly secondarily infected with bacteria. [7][8] [10][11][12]

MRSA was most commonly isolated from vesicobullous disorders (33.33%) followed by eczema (14.81%) and pyoderma (14.81%). In a similar previous study, prevalence of MRSA in dermatology inpatients with vesicobullous disorder was found to be 32.6%. [13]

Pemphigus vulgaris (100%) was the most common disorder among the vesicobullous group of disorders to be infected by MRSA in our study. This could probably be due to the non healing erosions persisting for longer duration acting as a nidus for bacterial colonization. Moreover, these patients are admitted in the general wards along with other patients, requiring a prolonged hospital stay and immunosuppressive drugs, which contributes to bacterial infection, especially MRSA. Similar finding has been reported in the previous literature. [13]

Among the MRSA isolates, mean duration of illness was 99.48 weeks with duration of illness of ≥ 40 weeks seen among the vesicobullous MRSA isolates and statistically, there was a highly significant association between duration of illness and MRSA acquisition ($p=0.0001$). Longer duration of illness was also seen in leprosy and eczema patients. Duration of illness was found to correlate with the risk of MRSA infection, especially among autoimmune vesicobullous disorders in previous studies. [14]

Majority of the MRSA patients (77.88%) had duration of hospitalisation of ≤ 7 days with mean duration of hospitalisation of 14.65 days. This could be due to the reason that majority of these patients were old pemphigus patients who were on pulse therapy and in phase 1, leprosy patients of recurrent erythema nodosum leprosum with frequent hospitalisation. All MRSA patients (100%) had history of antibiotics use prior to hospitalization with a positive correlation ($\text{corr}=1$) and statistically highly significant association between history of antibiotics and MRSA acquisition ($p=0.00001$). 55.56% of the MRSA patients were on immunosuppressives, mainly oral/ injectable corticosteroids and cyclophosphamide with a statistically significant association between history of immunosuppressants and MRSA acquisition ($p=0.024$). Many previous studies have shown a positive correlation

with prolonged hospital stay, indiscriminate use of antibiotics, intake of antibiotics before coming to the hospital and corticosteroid therapy with MRSA emergence.[15][16][7]

66.67% of the MRSA isolates had history of invasive medical devices in the form of intravenous cannula with a statistically, significant association between history of invasive medical devices and MRSA acquisition ($p=0.037$). Previous studies have also reported that *S. aureus* is the most common cause of infections on indwelling medical devices. [17][18]

81 patients in the present study (73.64%) showed presence of gram positive cocci on gram staining and *S. aureus* were grown in 66 of these cases accounting for 60% of the cases. This is in accordance with a previous study conducted in which *S. aureus* was isolated in 59.01% cases. [8] However a higher percentage of *S. aureus* (85.5%) was isolated in a similar previous study. [7]

In the present study, 59.1 % of the *S. aureus* was MSSA, while 40.9% of the *S. aureus* was MRSA. MRSA accounted for 24.5% of the total bacterial isolates which comparable to a previous study in which prevalence was found to be 22.2%. [7] However in another previous study, MRSA accounted for only 9.845 % [8] 85.19% of MRSA patients were having HAMRSA while only 14.81% patients were having CAMRSA which is comparable to previous study in which 87.5% of the MRSA isolates were HAMRSA. [7] The other isolates grown were acinetobacter, *E. coli*, klebsiella, proteus and pseudomonas aeruginosa .

No growth in culture was obtained in 17.27% of the cases. These were the cases who had already taken antibiotics prior to hospitalisation and the organism may have been sensitive to the antibiotic taken.

The antibiotic sensitivity pattern in our study showed that 100% of the MSSA isolates were sensitive to ceftazidime, linezolid, doxycycline, vancomycin and chloramphenicol; 94.12% of MSSA strains were sensitive to gentamicin while 90.91% were sensitive to clindamycin. Only 30.77% of the MSSA showed sensitivity to cloxacillin and 18.75% percent to oxacillin in our study. However, in a similar previous study, 100% MSSA strains were sensitive to cloxacillin. [7]

Among the MRSA isolates, all MRSA isolates were sensitive to linezolid, doxycycline, vancomycin; similar to that seen in previous study. [7] 91.67% of MRSA isolates were sensitive to clindamycin; 88.89% were sensitive to gentamicin and 77.78% were sensitive to chloramphenicol while in previous study higher (93.5%) number were sensitive to amikacin, clindamycin and rifampicin. [7] However in a similar previous study , sensitivity of MRSA to amikacin was only 41.2%. [11] Thus, in our study both MSSA and MRSA showed high sensitivity to gentamicin which is a cheap, effective and widely available antibiotic than vancomycin and linezolid and thus can be considered as first line antibiotic for both MSSA and MRSA in resource poor situations.

100% of the MSSA strains tested for ampicillin were resistant, 95.65% of the MSSA strains were resistant to penicillin G, 86.67% to ciprofloxacin, 81.25% to oxacillin and 69.23% to cloxacillin while in a similar previous study, 87.5% of the MSSA strains were resistant to penicillin while all strains were sensitive to cloxacillin. [7] Thus in our study, MSSA isolates showed higher resistance to penicillin and cloxacillin.

Among the MRSA isolates, 100 % of the strains tested for ceftazidime, oxacillin, cloxacillin and ciprofloxacin were resistant. 88.89% of the MRSA isolates showed resistance to penicillin G; more than half of the MRSA (55.56%, 54.55%) strains showed resistance to azithromycin and erythromycin respectively which similar to previous study in which all MRSA strains were resistant to penicillin, cloxacillin and erythromycin. [7]

Conclusion:-

It was found that prevalence of MRSA in our study (24.5%) was high compared to other studies. Risk factors for MRSA acquisition identified in our study were prolonged duration of illness, history of antibiotics, history of previous hospitalisation, and history of invasive medical devices. It was found that a high percentage of both MSSA and MRSA isolates were sensitive to gentamicin which is a cheaper ,effective and widely available antibiotic and can be considered as first line antibiotic for both MSSA and MRSA in our setup.

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