Original Research Article

A study on community associated *Staphylococcus aureus* and its susceptibility pattern to Mupirocin and Fusidic acid in primary pyoderma patients

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Abstract

Background: Primary pyodermas are one of the most common dermatological diseases. *Staphylococcus aureus* (*S. aureus*) is frequently isolated. It has developed resistance to many antimicrobials and Methicillin Resistant *Staphylococcus aureus* (MRSA) is a major problem. The precipitous usage of topical antimicrobials especially Mupirocin and Fusidic acid has increased the development of multi-resistant strains of *S. aureus* and in India, few studies have shown susceptibility profile to these drugs.

Aim: This study aimed at the clinical and bacteriological profile in primary pyoderma patients, prevalence of MRSA and the resistance pattern of *S. aureus* to Mupirocin and Fusidic acid.

Materials and methods: Patients with primary pyodermas from community were recruited. Gram stain and culture sensitivity was done with swabs taken from the lesions. Antibiotic susceptibility for

S. aureus was tested using VITEK- 2. Mupirocin and Fusidic acid susceptibility was determined by E-strip method.

Observations: A total of 107 patients of primary pyodermas were included. Pyoderma were common in young age group (P = 0.001). Poor hygiene was the main predisposing factor. Furunculosis (45.8%) was the most common pyoderma followed by impetigo and folliculitis (16.8% each). Culture was positive in all except 3. *S. aureus* was isolated in 61.7% and polymicrobial flora in 13.1%. Prevalence of MRSA was 39.5% (P= 0.066). All strains of *S. aureus* demonstrated 100% susceptibility to Mupirocin and Fusidic acid.

Conclusions: Furunculosis still has the highest incidence in adult population with a high prevalence of MRSA (39.5%). Despite extensive usage of Mupirocin and Fusidic acid, no resistance was found in this part of India.

Key words

Pyodermas, *Staphylococcus aureus*, Antibiotic susceptibility, Mupirocin, Fusidic acid.

Introduction

Cutaneous bacterial infections are one of the many common infections in humans with 17% incidence in the community [1]. Folliculitis and furunculosis are the common primary pyodermas. *Staphylococcus aureus* (*S. aureus)* and β-hemolytic Streptococcus are frequently associated [2, 3], but, Proteus, Pseudomonas species and Coliform bacilli have been implicated [2]. *S. aureus* has developed resistance to many antibiotics, most commonly penicillin, probably due to the ability of the bacteria to produce β-lactamase enzyme. Moreover they show cross resistance to other penicillins like ampicillin, amoxicillin, carbenicillin and piperacillin [4]. The first β-lactamase stable semi synthetic penicillin-Methicillin was introduced in 1960 and within year resistant organisms were detected [5].

Based on the susceptibility to methicillin, *S. aureus* was divided into two major subtypes- Methicillin- resistant (MRSA) and Methicillin-sensitive *Staphylococcus aureus* (MSSA). Further, MRSA strains have been categorized as community- acquired MRSA (CA- MRSA) and nosocomial/ healthcare- associated MRSA (HA-MRSA). Unlike HA- MRSA, CA- MRSA is frequently susceptible to non- β-lactam antibiotics, but they may develop multidrug resistance due to inappropriate and injudicious use of antibiotics [6]. Data from National Staphylococcal Phage Typing Centre, New Delhi shows that the prevalence of MRSA had increased from 9.8% in 1992 to 45.4% in 1998 in India [7].

Many topical antimicrobials have been used in past, namely: povidone-iodine, framycetin ointment and neomycin/polymyxin B-bacitracin cream. However, the evidence of efficacy of these agents, compared to Mupirocin and Fusidic acid, is not very supportive [8]. Mupirocin and Fusidic acid are the most commonly used topical antimicrobials for primary pyodermas. Along with treatment of skin infections, they are also used for eradication of nasal carriage of MRSA [1].

The usage of these topical antimicrobials has increased the likelihood of development or transfer of antibiotic resistance. Studies outside India have shown Mupirocin and Fusidic acid resistance to be 14.1% [9] and 11% to 18% [10], respectively.

There has been a frequent change in the trend of antibacterial susceptibility pattern of *S. aureus* and this poses a challenge in the successful treatment of pyodermas [11]. Therefore, it is important to know the common organisms which are responsible for primary pyodermas, prevalence of MRSA in them and their profile of resistance to mupirocin and fusidic acid.

Materials and methods

It was a hospital based, descriptive study, conducted from November 2013 to May 2015 in a tertiary care hospital, Mysore, Karnataka, India. An informed consent was taken and recorded on a standard performa after approval by the ethical committee of the institution. One hundred and seven cases of primary pyodermas were included and sample size was selected on the basis of frequency of primary pyodermas in the outpatient department.

Inclusion criteria

All primary pyoderma cases irrespective of age were included.

Exclusion criteria

- Refusal, denial of consent
- H/O receiving topical antibiotic therapy within previous 1 week
- H/O receiving systemic antibiotic therapy within last 15 days
- H/O hospitalization within last 3 months
- H/O other infectious diseases Secondary pyoderma
- Pregnant, lactating mothers

History and examination

A detailed history regarding age, sex, occupation, nutrition, hygiene, duration of disease, any aggravating factors and history of any other systemic disease was taken. Hygiene was graded on the basis of frequency of changing clothes and bathing habits. It was 'Good' if the patient changed clothes twice daily and took bath daily with application of soap, and 'Poor' if change of clothes were once daily or once in two days or more and bathed without soap application, once in two days or more.

A complete general, physical and systemic examination was conducted. Cutaneous lesions were examined in detail and the description including site, size, shape, number, distribution and regional lymph nodes was noted. Lesions were classified as: impetigo, folliculitis, furunculosis, ecthyma, carbuncle, cellulitis, abscess and sycosis barbae.

Collection of specimen

Intact pustules were cleaned with spirit and then ruptured with a sterile needle. Pus was expressed and collected on to two sterile cotton swabs. In crusted lesions, normal saline was used to clean the wound. Two swabs were rubbed over the pus or the edge of the ulcer. The swabs were then immediately transported to the microbiology laboratory for further processing.

Microbiological examination

Pus from the first swab for used to prepare smears and were stained by Gram's Method. The pus from the second swab was inoculated on blood agar and McConkey's agar. The culture plates were inoculated at 37°C for 24- 48 hours, aerobically. The following tests were carried out on the colonies to identify S. aureus:

- Catalase test
- Coagulase test- Slide coagulase test, Tube coagulase test
- Oxidation fermentation (OF) test- Hugh Leifson's method
- Mannitol fermentation test
- Urease test

All *S. aureus* isolated were tested for the antibiotic susceptibility by Vitek-2 compact system for Penicillin, Oxacillin, Amoxicillin/Clavulanic acid, Erythromycin, Ciprofloxacin, Gentamicin, Cefadroxil. Mupirocin and Fusidic acid susceptibility was determined by commercially available antibiotic E- test strips (Himedia, Bombay) using European Committee on Antimicrobial Susceptibility Testing (EUCAST) recommendations.

Methicillin resistance was detected using oxacillin. The strains having minimum inhibitory concentration (MIC) > 4 mcg/ml for oxacillin were considered MRSA.

Statistical analysis was done using SPSS for Windows version 18. Chi- square test was used to test significance of clinical spectrum and antibiotic susceptibility pattern of *S. aureus*. Cross tabulates were applied to calculate mean,

median, standard deviation. P<0.05 was considered significant.

Figure - 1: Furuncle over right forearm.

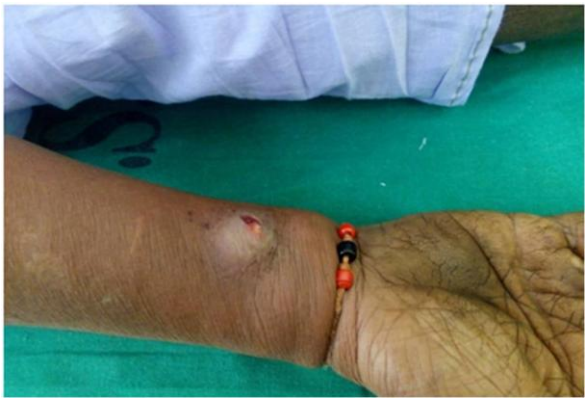


Figure - 2: Impetigo contagiosa.

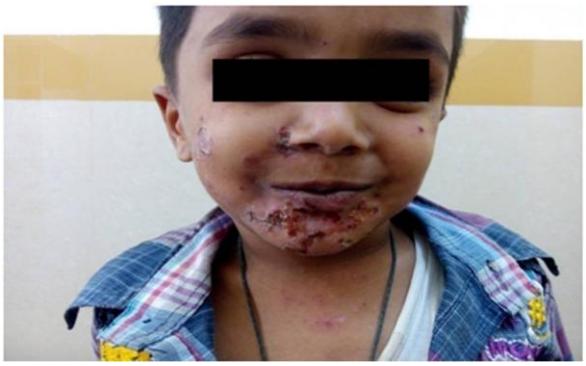
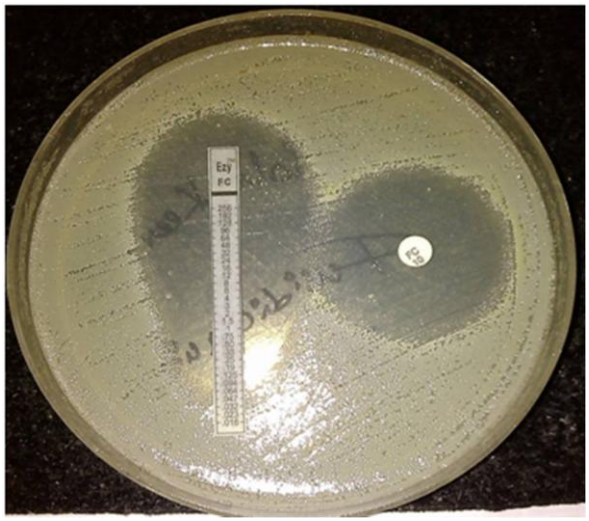


Figure - 3: *S. aureus* colonies on blood agar.

Results

A total of 107 primary pyoderma cases were recruited. The ages of 107 subjects ranged from 1 to 79 years with a mean age of 29.25 ± 19 and median 27 years. Maximum numbers of patients were young adults (20- 40 years) with incidence of 36.5% **(Table – 1)**. There were 77 (72%) males and 30 (28%) females. The female to male ratio was 1:7. Students (31.7%), homemakers (14%) and preschoolers (10.2%) presented more with the disease **(Table – 2)**. Poor personal hygiene was seen in 11 (10%) cases (P= 0.01).

Figure - 4: Fusidic acid E- test strip and Disc showing zone of sensitivity.



The most common diagnosis was found to be furunculosis in 49 (45.8%), followed by impetigo (**Figure – 1, 2**) and folliculitis each in 18 (16.8%). Lesser incidence of abscess (5.6%), ecthyma (4.6%) and carbuncle (1.9%) were observed (P= 0.00) **(Table – 3)**. Most of the cases of pyoderma involved the lower extremities (30.8%), followed by face (22.4%), neck and trunk (11.2%) (P= 0.00).

On culture, *S. aureus* was the most common organism isolated (61.7%) from the positive cultures, followed by other Staphylococci- *S. epidermidis* (7.5%) and *S. hominis* (3.7%). Non-haemolytic Streptococci were cultured in only 2 (1.9%) of the patients. Polymicrobial flora was seen in 13.1% of the cultures, but 2.8% of the cases showed no growth (P= 0.06) **(Table – 4)**.

Incidence of MRSA was 39.50% in patients with *S. aureus* pyodermas (P= 0.06). All strains of the organism were sensitive to both mupirocin and

fusidic acid (P= 0.00). The MIC values for both the antimicrobials were low. The range was 0.19-0.38 for Mupirocin and 0.047- 0.125 for Fusidic acid (**Figure – 3, 4**).

Table - 1: Pyoderma cases in relation to age.

Age (Yrs)	Males (%)	Females (%)	Total (%)
< 20	26 (24.3)	12 (11.2)	38 (35.5)
21- 40	33 (30.9)	6 (5.6)	39 (36.5)
41- 60	13 (12.1)	8 (7.5)	21 (19.6)
61- 80	5 (4.7)	4 (3.7)	9 (8.4)
Total	77	30	107

Discussion

Pyodermas have become a significant cause of skin infection. The bacteria can gain entry in to the skin when the natural defence of the skin breaks down due to various factors- trauma, after invasive procedures, or normal flora can cause the infection. Changing trends are being noted in the etiological aspects of primary pyoderma, and the problem of emergence of drug resistant strains is increasing [12]. Knowledge of prevalence of MRSA and their current anti-microbial profile becomes necessary for the selection of appropriate treatment of these infections [6]. Hence, the present study was conducted to find out the clinical and bacteriological profile of primary pyodermas and the susceptibility profile of *S. aureus* to Mupirocin and Fusidic acid in this part of India.

Table - 2: Occupation.

Occupation	Cases (%)
Student	34 (31.7)
Infant	0 (0)
Pre- school	11 (10.2)
Homemaker	15 (14.0)
Skilled worker	17 (15.8)
Unskilled worker	9 (8.4)
Agriculturist	8 (7.4)
Businessman	6 (5.6)
Retired personnel	4 (3.7)
Others	3 (2.8)

The age group of our cases ranged from 1 to 79 years, mean age being 29.25 years. Maximum numbers of patients were young adults (20- 40 years) with incidence of 36.5%. This is consistent with the results reported by Ghadge and Sali [13] and Bhaskaran and team [14]. However, Chopra and colleagues [2] reported increased incidence in the paediatric age group, attributing it to poorly developed epidermal barrier in children. The increased involvement in our study may be due to the sheer volume of people in this age bracket in the community.

Table - 3: Classification of pyodermas.

Diagnosis	Cases (%)
Furuncle	49 (45.8)
Impetigo	18 (16.8)
Folliculitis	18 (16.8)
Pyoderma	6 (5.6)
Abscess	6 (5.6)
Ecthyma	5 (4.6)
Cellulitis	3 (2.8)
Carbuncle	2 (1.9)

Males (72%) outnumbered females (28%). A Female to male ratio of 1:7 in our study correlates well with the other published studies by Sajna and team [15] and Patil, et al. [16]. Male preponderance could be due to the evidence that males carry higher numbers of bacteria than females [17] and more number of males attending the O.P.D.

The increased incidence of pyoderma was seen in pre- schoolers and students (42%). A low incidence was found among businessmen and

officials. Ramani and Jayakar [18] too reported similar findings. Out of 107 patients of primary pyodermas, furunculosis constituted 49 (45.8%), folliculitis and impetigo in 18 (16.8%) each of the cases. Lesser incidence of abscess in 6 (5.6%), ecthyma in 5 (4.6%) and carbuncle in 2 (1.9%) patients were observed. Patil and co-workers [16] have reported folliculitis (59%) and furunculosis (33.3%) as the commonest pyodermas, impetigo in 33% and ecthyma in 3.3% of the cases. These findings are consistent with our study. Since adults constituted a majority of the group, it explains the increased incidence of furunculosis and folliculitis. Thind P, et al. [19] had more cases of impetigo (55.2%). This was attributed to more number of children in their study.

Table - 4: Organisms isolated.

Organism	Cases (%)
No growth	3 (2.8)
S. aureus	66 (61.7)
S. epidermidis	8 (7.5)
S. hominis spp hominis	4 (3.7)
Coagulase negative S. aureus	3 (2.8)
P. aeruginosa	3 (2.8)
Non- haemolytic Streptococci	2 (1.9)
Acinetobacter	1 (0.9)
Leuconostoc	1 (0.9)
Klebsiella	1 (0.9)
Proteus	1 (0.9)
Polymicrobial flora	14 (13.1)

Majority of the patients had good hygiene constituting up to 90% which was highly significant (P= 0.010). However, this is in contrast to previous studies which have demonstrated poor hygiene as a factor associated with bacterial infections [12]. We observed that the lower extremities were involved in 30.8% cases followed by face, neck (22.4%) and trunk (14%), whereas, Gandhi S, et al. [12] have reported similar results where lower limbs were involved in 60%, and head and neck in 47.5% of their cases. Clusturing of lesions to the extremities were also seen in other studies [16].

S. aureus is the most common bacteria causing primary pyoderma and has a high incidence of MRSA leading to multiresistant strains. In our study, *S. aureus* was the most common organism isolated in 66 (61.7%) pyoderma lesions, followed by other Staphylococci- *S. epidermidis* (7.5%) and *S. hominis* (3.7%). These results are similar to results reported by Patil R, et al. (81.4%) [16] and Thind P, et al. (79%) [19]. Moreover, there was low incidence of Streptococci which was cultured in 2 (1.9%) patients. Beta- hemolytic Streptococci have been isolated in 2.3% to 9% by many others [20].

Three cases (2.8%) demonstrated sterile cultures. This is significantly lower than the observation of Baslas, et al. [21] and Gandhi S [12] who have reported no growth in 14.9% and 9.5% of their cases, respectively. However, polymicrobial flora has been found in 5-16% [21] which is in consistant with our study (13.1%).

Many reports from India and Asia have highlighted the prevalence of MRSA. According to National Staphylococcal Phage Typing Centre, there was an increase in the occurrence of MRSA from 9.83% in 1992 to 45.44% in 1998 [7]. But MRSA was seen to be more common in southern part of India [22] than in the west (20.33%) or north (18.88%) [23]. Our findings corroborate this as we had a prevalence of MRSA of 39.5%. But, our observations are in concurrence with studies reported by Senthilkumar [22] and Venniyil, et al. [24] from south India with prevalence of MRSA of 46% and 78%, respectively. Though in our study, there was no statistical difference in MRSA and MSSA, thus indicating that high percentage of MRSA is a problem. The reason for the difference in prevalence in various parts of the country could be the different strains of *S. aureus* causing the disease. The generous use of antibiotics in current times could be the cause for the increased rate [12].

Topical antibiotics are used alone more effectively and are preferable to oral antibiotics for the treatment of limited disease. The most commonly used antimicrobials presently- Mupirocin and Fusidic acid were previously associated with low incidence of resistance. However, the resistance is being increasingly reported as per various studies [9, 10]. In India, as shown by Thind P, et al. [19] in 2010 and Kumaraswamy, et al. [25] there was no resistance to Mupirocin in CA- MRSA and the MIC values were considerably low (0.064- 0.125). We too observed that all strains of *S. aureus* were sensitive to Mupirocin with low MIC values (0.18- 0.38). But, reports from various hospitals all over the world have shown Mupirocin resistant *S. aureus*. Resistance rates for HA- MRSA was 2% in Kerala [26], 5% in North India with high MIC values (512- 1024) [27] and 14% in Korea [9]. This implies that resistance to Mupirocin has developed in HA-MRSA but community associated strains are still sensitive.

As in our study, no resistance to Fusidic acid has been found by Thind P, et al. [19]. All *S. aureus* strains were sensitive to Fusidic acid with MIC values of 0.047- 0.125. However, 2.63% of CA-MRSA strains were found to be resistant to Fusidic acid in Sikkim [28]. Variable resistance to Fusidic acid has been identified in Pakistan ranging from 2% to 66.66% [29]. In United Kingdom, Fusidic acid resistance rates among MRSA doubled between 1990 and 2001 and was 7.7% in 2012 [30]. This implies that resistant strains of Fusidic acid are slowly increasing.

Primary pyodermas still remains a common problem to the community with highest incidence of furunculosis (54.8%) and folliculitis (16.8%) in adult population. *S. aureus* is the most common bacteria causing the infection (61.7%) with a high prevalence of MRSA (39.5%). Though usage of Mupirocin and Fusidic acid has become extensive, there is no resistance to these antimicrobials in this part of India. These drugs can be used, though cautiously, for the treatment of pyodermas.

Conclusion

MRSA is a challenging organism on many fronts. Given the current scenario, emergence of antibacterial resistance and increase in the CA-MRSA is making the treatment difficult. There is paucity of susceptibility pattern of S. *aureus* to Mupirocin and Fusidic acid. As the situation is not new; the use of a single antibiotic at therapeutic or sub- therapeutic levels is known to induce resistance by bacteria. The future therapeutic potential of valuable topical agents has been threatened by the emergence of resistance, although at present this does not appear to be significant.

Hence, it is important to monitor the changing trends of antibiotic sensitivity and mandatory to survey and screen clinical isolates for resistance to reduce the problem of antibiotic resistance.

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