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INCIDENCE AND TREND OF ANTIMICROBIAL SUSCEPTIBILITY AND RESISTANCE OF METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS IN DIABETIC FOOT ULCERS

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ABSTRACT

Introduction: The present study attempts to examine the microbial profile and antibiotic susceptibility of diabetic foot infections in patients admitted in surgical wards of a tertiary care centre for diabetic foot ulcers. **Methodology:** A prospective study was performed on 100 diabetic patients with foot ulcers admitted in surgical wards of a tertiary healthcare centre over a period of 24 months. **Results:** A total of 300 tissue samples were obtained from 100 patients during the study duration and evaluated for culture and antimicrobial susceptibility. Both Multimicrobial and unimicrobial infections are seen in culture. Gram positive cocci 'Staphylococcus aureus' was commonest isolate seen in culture. Other common isolates were coagulase negative staphylococcus(CoNS), acinetobacter, gram negative bacilli, anaerobes, mixed growth. In the wound culture sensitivity report, 31% cases were Staphylococcus aureus. 6% cases of which were sensitive to commonly used antibiotics called Methicillin sensitive staphylococcus aureus (MSSA) and the other 25% cases were Methicillin resistant staphylococcus aureus (MRSA). These were resistant to the commonly used antibiotics and sensitive only to higher antibiotics like meropenem, imipenem, tigecycline. Post higher antibiotics administration rendered the wound better and subsequent wound swab samples were culture negative and free of these superbugs MRSA.

KEYWORDS: Diabetic foot ulcer, MRSA, antimicrobial susceptibility.

INTRODUCTION

Diabetes is a group of metabolic syndromes characterized by a hyperglycemic state which may either occur due to a decrease in insulin secretion, defective insulin activity, or both.[1] Foot ulcers and other foot problems are a major cause of morbidity and mortality in people with Diabetes mellitus. Diabetic foot infections (DFIs) are the leading cause of hospitalization for diabetic patients worldwide. In developing countries like India, it accounts for 20% of hospital admissions.[2-3] DFI is a multifactorial process and three factors predispose to tissue damage, namely neuropathy, peripheral vascular disease, and susceptibility to infection in case of a direct injury to the foot.[4-6] A patient suffering from Diabetic infection may present with a wide variety of complaints like cellulitis, infected ulcer, abscess myositis, necrotizing fasciitis, gangrene, septic arthritis, carbuncle, osteomyelitis and so on. Careful inspection and examination, controlling sugars are essential so that the treatment can be tailored accordingly. The patient undergoes incision and drainage, thorough debridement sos amputation as per the clinical condition of the patient After that patient is managed in the wards with cleaning and dressing and with antibiotics as per the culture and sensitivity.

DFIs are usually polymicrobial, caused by aerobic gram positive cocci like Staphylococcus aureus, gram negative bacilli (Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa), and anaerobes. Proper management of these infections needs appropriate antibiotic selection.[7] Empirical treatment is based on the pathogens and the susceptibility pattern seen in the community where the hospital is located[15] (Fig. 1 and 2). Beta-lactam antibiotics are the most commonly used antibiotics for bacterial infections.[8] However, the accelerated emergence of antibiotic resistance to these groups of drugs among the prevalent pathogens is the

most serious threat to the management of such infections. These isolates are usually multidrug resistant which further complicate the scenario.

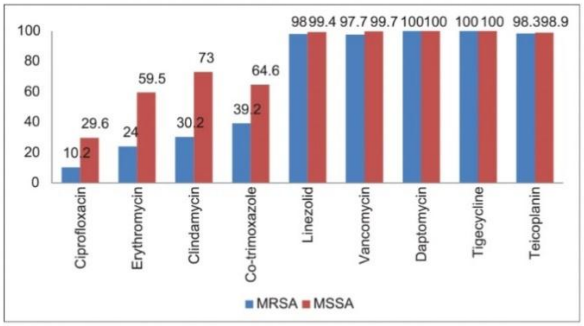

Figure 1: Antibiotic sensitivity pattern in methicillin-resistant *Staphylococcus aureus* and methicillin-sensitive *Staphylococcus aureus* isolates

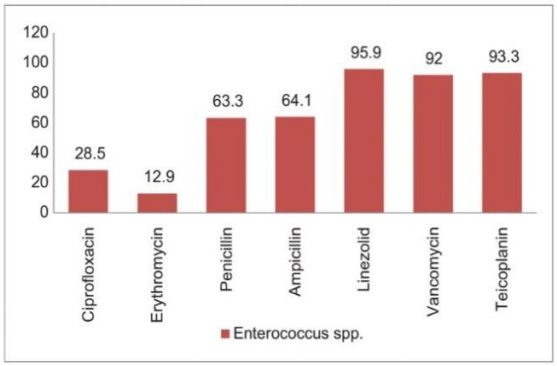

Figure 2: Antibiotic sensitivity pattern of *Enterococcus* species

MATERIALS AND METHODS

Study type- A prospective study was performed on 100 diabetic patients with foot ulcers admitted in surgical wards of a tertiary healthcare centre over a period of 24 months.

Study population- Patients with Type 1 or Type 2 Diabetes mellitus in the age group of 13 to 70 years who were hospitalized for the management of lower extremity wounds and not meeting any exclusion criterion who gave consent for participation in the study were included in study Patients in the Age group less than 13 years and above 70 years immunocompromised patient patient on long term systemic steroid therapy, patients denying participation and patients with malignant ulcer were excluded from the study.

Specimen collection - After surgical debridement of the slough and necrotic tissue over the wound, the wound was washed thoroughly with normal saline and a wound swab was collected from the floor of the ulcer for Gram staining and culture and sensitivity. The specimen was collected in a sterile container soaked with normal saline and was transported to our microbiology laboratory for further processing. Subsequently two more wound swabs were collected at a weekly interval and processed in similar manner.

Specimen processing – Wound swab was first smeared over a glass slide for gram staining after which it was streaked over Nutrient agar McConkey agar and blood agar and kept in an incubator at 37^{o} C.

MRSA screening - Staphylococcus species was tested for Methicillin resistance with 30 microgram cefoxitin disc by Kirby Bauer disc diffusion method. Quality control was performed using Escherichia coli ATCC 25922 for ESBL detection. Staphylococcus aureus 43300 was used for MRSA detection, according to National Committee for Clinical Laboratory Standard guidelines[10] a zone of inhibition which was equal to or more than 21mm was considered susceptible to cefoxitin and the organism was reported as Methicillin Sensitive Staphylococcus aureus. Those isolates that produced zone of inhibition less than 21mm with cefoxitin was considered as Methicillin Resistant Staphylococcus aureus (MRSA) and then these category of bacterial isolates were further tested for higher antibiotics like piperacillin/tazobactam meropenem, imipenem.

RESULTS

A total of 100 diabetic patients with foot ulcers admitted to our hospital were studied during the 24 months study period. Out of the 100 patients, 77 were males and 23 females with maximum patients in age group of 51-60 years. The culture swabs of all diabetic patients under study were collected and processed in microbiology for the organisms which were further analyzed.

First culture swab report: In our study from the first culture swab we isolated 5 swabs positive for Acinetobacter species 11 swabs positive for anaerobes, 2 swabs positive for Mixed growth 13 swabs were positive for CONS 31 swabs were found positive for Staphylococcus aureus Rest of the swabs showed no growth on culture.

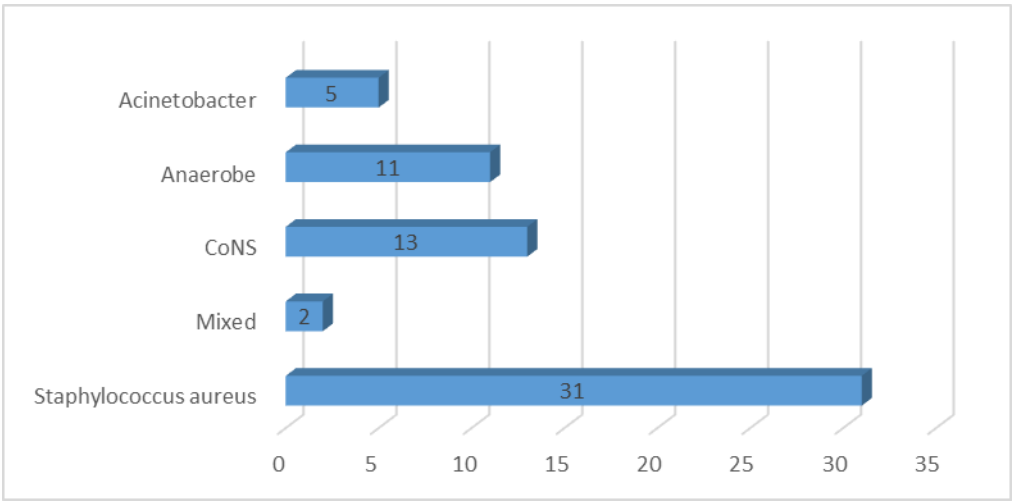

Figure 3: First wound swab culture report.

Combined study of microbiological spectrum of all 3 swab culture reports taken on 3 different occasions from each patient in study: Analyzing the swab reports from all 3 cultures done per patient and for 100 cases in total Most predominant organism in 1st culture was Staphylococcus aureus Acinetobacter spp in 2nd cultures and negative growth in 3rd series of cultures.

Staphylococcus aureus was present totally in 31 cases in 1st culture 10 cases positive in 2nd culture and 3 cases in 3rd culture Acinetobacter spp was present in 5 cases in 1st culture 14 were positive in 2nd culture and 11 cases in in 3rd culture Anaerobes were present in 11 cases in 1st culture 8 cases positive in 2nd culture and 2 cases in 3rd culture CONS were present in 13 cases in 1st culture 12 cases positive in 2nd culture and 5 cases in 3rd culture. Mixed growth was present in 2 cases in 1st culture 5 cases in 2nd culture and 9 cases in 3rd culture 38 swabs out of 100 were negative in 1st culture, 51 swabs negative in 2nd culture and 70 were negative in 3rd culture.

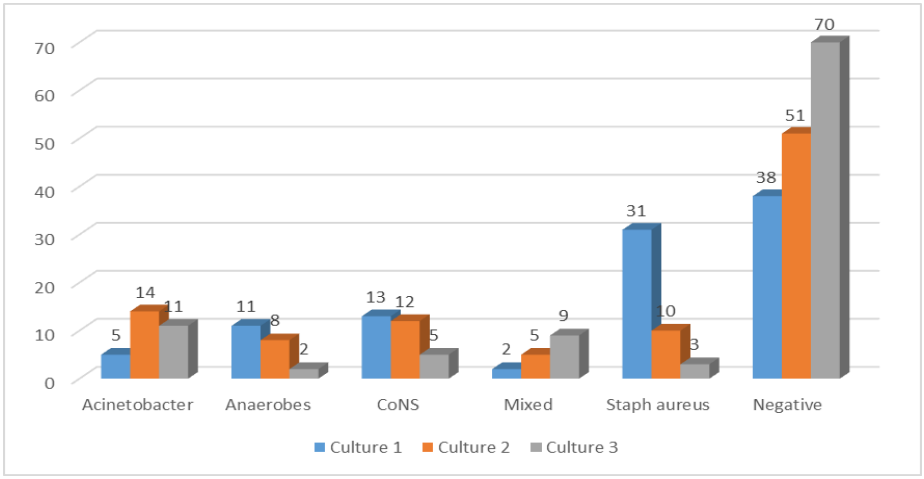

Figure 4: Serial wound swab cultures report.

On analysis of culture sensitivity pattern of these microorganisms it was found that 61% of culture positive cases were resistant to commonly used antimicrobials like penicillin, ciprofloxacin and gentamicin.

Only 39% cases were found sensitive to these commonly used antibiotics demonstrating that there is a high frequency of resistance to these commonly used antimicrobials. This warranted the need to introduce and discover newer antimicrobial drugs and judicious use of available antimicrobials.

It was found that among the 100 diabetic foot ulcers, all culture positive cases were sensitive to higher antibiotics like imipenem, meropenem, tigecycline There is a cautious role of these higher antibiotics in diabetic foot ulcer management. It should be used judiciously as there is no significant resistance noted against these yet Hence in order to avoid resistance these antibiotics should not be used in all cases empirically which might lead to the early development of resistance.

The above data says that all cases of acinetobacter spp anaerobes and mixed growths were sensitive to commonly used antibiotics like penicillin, ciprofloxacin, gentamicin and higher antibiotics Almost no resistance was noted by these organisms to the above antibiotics.

15% cases of CONS(6 Cultures) were resistant to commonly used antibiotics that is penicillin(PEN) cipro(CIPR), genta(GEN) and showed no resistance to higher antibiotics like meropenem(MERO), imipenem(IMI) tigecycline(TIGE)

Among 31 cases of Staphylococcus aureus in culture swab reports, 6 were sensitive to penicillin cipro and genta which means they were MSSA (6% cases) and were sensitive to higher antibiotics as well 25 cases in culture swab reports were resistant to penicillin cipro and genta means they were MRSA(25% cases) and of these all 25 cases(100% cases) were sensitive to higher antiobiotics like meropenem, imipenem.

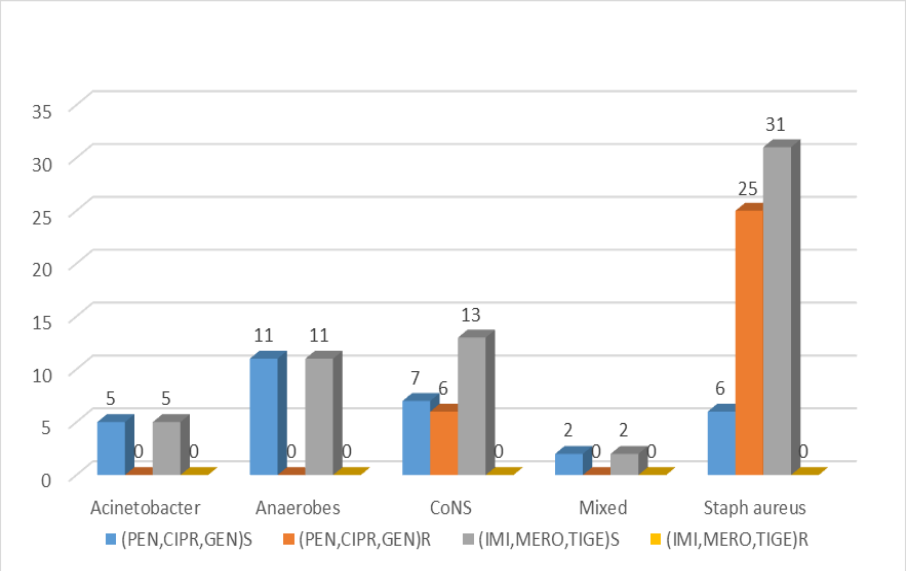

Figure 5: Antibiogram of serial wound swab culture.

DISCUSSION

Foot ulcers are the major complication of diabetes which affects quality of life. It has a poor tendency to heal which results in long duration of stay in hospital for treatment. Diabetics should take proper care of their feet so that they will not suffer from these consequences. They should receive proper medical care at the earliest once even minor trauma occurs, so that the continuous further chain of events could be broken. The primary goal in the treatment of diabetic foot ulcers is to obtain wound closure. Management of the foot ulcer is largely determined by its severity (grade) and vascularity, and the presence of infection. A systematic approach to treatment should be undertaken for all diabetic foot lesions. A multidisciplinary approach should be employed because of the multifaceted nature of foot ulcers and the numerous comorbidities that can occur in these patients. Rest, elevation of the affected foot, and relief of pressure are essential components of treatment and should be initiated at the very first presentation. Ill-fitting footwear should be replaced with a postoperative shoe or another type of pressure-relieving footwear for example Microcellular rubber footwear. A mainstay of ulcer therapy is adequate debridement of all necrotic, callus, and fibrous tissue followed by regular cleaning and dressing of the wound. Treatment of the underlying ischemia is critical in achieving a successful outcome, regardless of topical therapies. Vascular surgical consultation should be obtained when a patient presents with an ischemic wound and when ulcers show no sign of progress despite appropriate management. For patients presenting with diabetic foot ulcers, aerobic and anaerobic cultures should be obtained, followed by initiation of appropriate broad spectrum antibiotic therapy. Antibiotic coverage should subsequently be tailored according to the clinical response of the patient, culture results, and sensitivity testing. Underlying osteomyelitis is frequently present in patients with moderate to severe infections and requires aggressive bony resection of infected bone and joints followed by four to six weeks of culture-directed antibiotic therapy. Among the isolates usually Gram positive cocci and Gram negative bacilli predominate. Staphylococcus aureus is the predominant cocci and there is a growing trend of these isolates to be resistant to commonly used penicillins termed MRSA(Methicillin Resistant Staphylococcus Aureus) which requires use of higher antibiotics like tigecycline, imipenem and meropenem. Overall incidence of these highly resistant MRSA infection in diabetic foot ulcers is 15-30% in most studies.[12,13] Therefore knowledge about the wound culture sensitivity is an essential part of wound management which minimizes the use of empirical therapy in order to identify these highly resistant MRSA.

CONCLUSION

Prevention of diabetic foot infection begins with identifying patients at risk. The severity of infection and identifying the pathogenic cause are the most important factors in determining the appropriate treatment. Mild to

moderate infections can usually be treated in the outpatient setting with oral antibiotics, while severe infections require hospitalization and parenteral therapy. Identification of clinically-related bacteria is vital for the treating clinician. As the effects of different systemic antibiotics for the treatment of diabetic foot infection is very heterogeneous, appropriate antibiotic therapy is dependent on culture results and the clinical response. Once MRSA is detected on culture, one should start higher antibiotics at earliest which helps in both early improvement in wound and discharge from hospital. It also increases chances of limb preservations, thereby increasing the quality of life and reducing further threat of development of resistance to various antibiotics.

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