PRINT ISSN 1119-8362
Electronic ISSN 2659-1499

Full-text Available Online at
https://www.ajol.info/index.php/jasem
https://www.bioline.org.br/ja

J. Appl. Sci. Environ. Manage.
Vol. 28 (12) 4033-4039, Dec. 2024

Occurrence and Antibiotics susceptibility profile of *Staphylococcus aureus* in Chronic skin Ulcer patients attending a Specialist Public healthcare Hospital at Chanchaga Local Government Area, Minna, Niger state, Nigeria.

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ABSTRACT: *Staphylococcus aureus* is a non-motile gram positive bacterium that is responsible for a large amount of disease in humans and animals. The objective of this paper is to evaluate the occurrence and antibiotics susceptibility profile of *Staphylococcus aureus* in Chronic skin Ulcer patients attending a Specialist Public healthcare Hospital at Chanchaga Local Government Area, Minna, Niger state, Nigeria using appropriate standard methods. The results obtained indicated that *Staphylococcus aureus* predominates with thirty- four (34)(89.5%) isolates, while *Staphylococcus epidermidis* was found to be four (4)(10.5 %) isolates. Antibiotic sensitivity testing revealed high resistance of *S. aureus* isolates to Zinacef (91%), Amoxacillin (94%), while *S. epidermidis* isolates showed total resistance to Ampiclox (100%), Amoxacillin (100%),Zinacef (100%) and Rocephine(100%). *Staphylococcus aureus* and *Staphylococcus epidermidis* isolates showed total (100%) susceptibility to Pefloxacin, Gentamicin and Ciprofloxacin antibiotics. Multi-drug resistant (MDR) patterns were also detected among the isolates of *Staphylococcus aureus* and *Staphylococcus epidermidis*. This study concludes that understanding the resistance patterns is critical for guiding effective treatment strategies and warrant continual surveillance to reduce the escalating threat of antibiotic resistant Staphylococcus infection in chronic skin ulcer among patients. It was recommended that the overuse and misuse of antimicrobial agent should be stopped.

DOI: https://dx.doi.org/10.4314/jasem.v28i12.11

Cite this Article as: DANASABE, D; BABA, J; MUHAMMAD, I. L; MIKAIL, T. (2024). Occurrence and Antibiotics susceptibility profile of *Staphylococcus aureus* in Chronic skin Ulcer patients attending a Specialist Public healthcare Hospital at Chanchaga Local Government Area, Minna, Niger state, Nigeria. *J. Appl. Sci. Environ. Manage.* 28 (12) 4033-4039

Dates: Received: 22 October 2024; Revised: 20 November 2024; Accepted: 08 December 2024; Published: 18 December 2024

Key words: Antibiotics susceptibility; *Staphylococcus aureus*; Ulcer

Staphylococcus aureus is a non-motile, gram-positive bacterium that is responsible for a large amount of diseases in humans and animals. "It is a major pathogen that colonizes and infects both immune-compromised hospital patients and healthy immune-competent people in the community (Gilbert *et al.*, 2022). These bacteria are found naturally on the skin and in the nasopharynx of the human body. If there is a break in the skin due to injury or surgery, or if a person's immune system is suppressed, the presence of *Staphylococcus aureus* on the skin can cause an infection (Cruz *et al.*, 2021). *S. aureus* occurs mainly on mucosal surfaces (Deyno *et al.*, 2017), and is often involved in many nosocomial infections (Cruz *et al.*, 2021). *S. aureus* been a versatile pathogen is capable of infecting humans with a broad spectrum of illnesses causing both infection and soft tissue infection (Oladipo *et al.*, 2019). Skin and soft tissue infections caused by *S. aureus*, as life-threatening systemic illnesses, are a significant hospital-acquired

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and community-acquired infections (Oladipo *et al.,* 2019). Human skin serves as an effective barrier to infection, protecting the underlying tissues, bones, and organs (Bamigboye *et al.,* 2018; Nguyen and Soulika, 2019). Wounds are defined as a breach in the skin or tissues' structural integrity that affects the skin's ability to defend itself (Herman and Bordoni, 2022). As one the most common causes of death and morbidity in surgical patients, wound infection accounts for 70% to 80% of deaths after burn injuries (Cruz *et al.,* 2021). Out of all surgical deaths, around 70–80% deaths are caused by wound infection (Geriak *et al.,* 2019). Bacteria that cause pus production or wound infection includes, *S. aureus*, *Clostridium* spp., *Actinomyces* spp., *E. coli, Proteus* spp., *Neisseria* spp., *Vibrio vulnificus* and *Candida* spp. (Nguyen and Soulika, 2019). Healthy skin forms a formidable obstacle against microorganisms and many other bacteria, but once this defence process is tampered with, creating a wound, bacteria have an ideal environment for growth and reproduction. Wound contamination occurs because of dynamic host-pathogen interplay such that the sum of the pathogen load is greater than the host's immune defences, resulting in a systemic immune response (Nakatsuji, 2017).

Wound infection happens because of a unique interaction between humans and disease causing microbes (Nakatsuji, 2017). Wound contamination is defined as the appearance of the organism on the wound area (Matard *et al.,* 2020). When the number of bacteria in a wound is low (contamination), there is no problem with wound healing. However, as the number of bacteria in the wound increases, the chance of infection increases. In critical colonization, the bacterial load in the wound becomes unbalanced; leading to infection if the amount of bacteria is not managed fervently (Hadi *et al.,* 2022).Infection can occur in acute wounds, such as surgical wounds (surgery site infections), and in chronic wounds, such as pressure ulcers, diabetic foot ulcers, and leg ulcers, which are more likely to be colonized by bacteria due to infection (Maier and Benoit, 2019). Infection will complicate surgical wound healing and is significantly more common (Duplessis and Biswas, 2020). ‟Wound infections can be superficial (skin only), deep (muscle and tissue), or spread to the organ or site where the surgery was performed (Ngo *et al.,* 2022). Wound infection and wound healing is influenced by several factors. Bacterial colonization and the pathogenic potentials of the colonizing bacterial agent is one of such factors that determine wound healing. Hence, the objective of this paper is to evaluate the occurrence and antibiotics susceptibility profile of *Staphylococcus aureus* in chronic skin Ulcer patients attending a Specialist Public healthcare Hospital at Chanchaga Local Government Area, Minna, Niger state, Nigeria.

MATERIALS AND METHODS

Study area: A prospective cross-sectional study design was conducted to determine the incidence of *Staphylococcus aureus* associated with wound infection among patients presenting at Ibrahim Badamasi Babangida (IBB) specialist Hospital, Minna, Niger state, Nigeria. IBB Specialist Hospital is a health clinic and a Public healthcare organization situated in Chanchaga Local Government Area, Minna, Niger state, Nigeria. Chanchaga Local Government Area is one of the 25 local government areas in Niger State with its headquarters in Minna, the state capital as shown in Fig. 1 below. It lies between latitude 9°35‟ 00” to 9° 41‟ 00” and longitude 6° 25‟ 00” to 6° 37‟ 00”. It covers an area of 72km² with a total population of 201,429 at the 2006 census.

Sample collection: One hundred (100) samples were collected randomly from patients with different wound types in the hospital using sterile swab sticks. The subjects of this investigation were both males and females ranging from children to adults who presents at the study area with wounds of different types. Aseptic swab samples were taken from skin lesions by swabbing the surface of an infected wound with the moistened sterile swab stick. Soon after the sample was collected, the swap stick was then recapped immediately to prevent dryness of the sample and placed on Amies transport media (Collee *et al.,* 1992; Cheesbrough, 2010). During the whole process of sample collection, the use of protective hand gloves was a working habit so as to avoid cross contamination. The samples were properly labeled before being transferred to the Microbiology Laboratory where they were quickly processed, cultured, and examined for significant growth.

Isolation of Staphylococcus aureus: Culture plates of Mannitol salt agar (Hi Media, India) were used. The swab sticks used for the collection of the samples were streaked directly on the labeled agar plates and incubated at 37°C for 24 hrs. After incubation, cultures were examined for significant growth. The distinct tentative *Staphylococcus* colonies on the MSA plates were further purified on freshly prepared Nutrient Agar (NA) plates by repeated sub-culturing until pure colonies (isolates) was obtained. Obtained pure isolates were inoculated aseptically into nutrient agar slants in Bijou bottles and incubated for 24 hours at 37ºC. After incubation, agar slants were then

refrigerated at 4^{o}C to preserve the isolates (Cheesbrough, 2010).

*Characterization and Identification of the Staphylococci Isolates:*The primary identification of the isolates was made based on colony appearance and pigmentation. Biochemical tests were performed to identify the isolates. All the recovering isolates that showed golden yellow colonies on mannitol salt agar plates were confirmed by series of biochemical tests using standard bacteriological procedure. Biochemical tests that were conducted includes, catalase test, citrate utilization, coagulase, oxidase, methyl red, Voges-Proskauer, indole production, motility, Sugar fermentation tests using glucose, sucrose, maltose and lactose. Characterization and identification of the isolates were done using the methods of Cheesbrough (2010), and Senthilkumar *et al.* (2012).

Antibiotic susceptibility testing: Susceptibility pattern was carried out using disk diffusion method. All the pure isolates were kept in the slant nutrient agar containing bottles for antibiotic susceptibility test by Kirby-Bauer disk diffusion technique. Disk diffusion test was performed and interpreted according to the recommendations of the Clinical Laboratory Standards Institute (CLSI, 2020). All tests were performed on Muller-Hinton agar plates. The surface of the sterile Muller- Hinton agar plates were slightly and uniformly inoculated using a sterile cotton swab dipped into the bacterial suspension. Single or multi-disc antibiotics were gently placed on the inoculated agar plates. The antibiotics used includes, Streptomycin, Septrin, Pefloxacin, Erythromycin, Gentamycin, Ampiclox, Zinnacef, Amoxacillin, Rocephin, and Ciprofloxacin. The inoculated plates containing the antibiotics were incubated at the temperature of 37^{o}C for 24 hours. The zone of inhibition in diameter(s) were determined, recorded and interpreted using the standard medical antibiotic breakpoints, and the rates of the susceptibility/ resistance of the isolates were interpreted as either Sensitive (S) or Resistance (R) by measuring their respective inhibition zone diameter (IZD). (Cheesbrough, 2010).

RESULTS AND DISCUSSION

Table 1 above described the distribution of *Staphylococcus aureus* and *Staphylococcus epidermidis* in the clinical samples from the study area. *Staphylococcus aureus* was isolated most from wound swabs of the skin (34 isolates (89.5%), followed by *Staphylococcus epidermidis* (4 isolates (10.5%), to make the total of the isolates to be 38.

This study reports the occurrence and antibiotic susceptibility of *Staphylococcus aureus* and *Staphylococcus epidermidis*. In this study, a total of 38 *Staphylococcus* species from different types of wound swab samples were isolated and identified. *S. aureus* (89.5%) was the most isolated bacteria followed by *S. epidermidis* (10.5%). This contrasts with a study done in India where among 102 isolates, *S. epidermidis* (65%) was the predominant bacteria isolated (Ali *et al.*, 2019).

Table 1: Distribution of *Staphylococcus* species across the wound of patients

Bacteria	Number of isolates	Percentage incidence (%)
Staphylococcus aureus	34	89.5
Staphylococcus epidermidis	4	10.5
Total	**38**	**100%**

Table 2: Percentage susceptibility of the isolates to the antibiotics

Antibiotics (µg)	***Staphylococcus aureus*** **n=34 Percentage (%)**	***Staphylococcus epidermidis*** **n=4 Percentage (%)**
Streptomycin 30µg	85 (15)	50 (50)
Septrin 30µg	71 (29)	75 (25)
Pefloxacin 10µg	100 (0)	100 (0)
Erythromycin 10µg	71 (29)	75 (25)
Gentamycin 10µg	100 (0)	100 (0)
Ampiclox 30µg	50 (50)	0 (100)
Zinnacef 20µg	9 (91)	0 (100)
Amoxacillin 30µg	6 (94)	0 (100)
Rocephin 25µg	62 (38)	0 (100)
Ciprofloxacin 10µg	100 (0)	100 (0)

Numbers outside the bracket = Susceptible percentage; Numbers inside the bracket = Resistance percentage

However, in another study in Korea, *S. aureus* was the most common bacteria found which is in agreement with the present study (Onanuga *et al.*, 2019). Interestingly, similar findings was recorded in Indonesia where out of 93 swab samples studied, 7.7% were found to be *S. aureus* and 50.5% being *S. epidermidis* (Shrestha *et al.*, 2018). This difference in microbial profile in this study could be explained by variation in geographical location, host factor and antibiotic usage. The high incidence of *Staphylococcus aureus* (89.5%) observed among the clinical isolates shows the versatility of this organism amongst other *Staphylococci* which makes it the most endemic pathogen in clinical settings. The highest incidence of *S. aureus* (89.5%) was in wound samples collected from Accident and emergency ward, a finding consistent with reports elsewhere (Lakhundi *et al.*, 2018) and in contrast with reports from other studies. (Kim *et al.*, 2021).The high incidence of the *Staphylococcus aureus* isolates in wound could be attributed to poor personal hygiene

and exposure of the wounds, which might have made it more prone to contamination and infection. Furthermore, most people in this area tend to treat their wounds on their own or employ services of ill-trained quacks before seeking medical attention which could account for the level of colonization by *Staphylococcus aureus* and other *Staphylococcus* species in wounds in this study. The non-coagulase staphylococci identified amongst these isolates might have been contaminants (McArdle *et al.*, 2018) or opportunistic pathogens. Maier and Benoit (2019), had reported the isolation of coagulase negative staphylococci and catalase negative organisms in the wound samples of high school children in Abakaliki. It is well known that other *Staphylococci* though normal commensals, are opportunistic pathogen of man (Eyerich *et al.*, 2018; Ikuta *et al.*, 2022).

Table 2 above indicated that both *Staphylococcus aureus* and *Staphylococcus epidermidis*isolates were100% susceptible to Ciprofloxacin, Pefloxacin and Gentamicin. Susceptibility of the bacterial isolates was also shown towards Septrin and Erythromycin. *Staphylococcus aureus* isolates were highly resistant Amoxacillin and Zinnacef, but moderately resistant to Ampiclox, while *Staphylococcus epidermidis* isolates were 100% resistant to Ampiclox, Zinnacef, Amoxacillin, and Rocephin. Antimicrobial resistance is assuming a centre stage as one of the most important public health problems worldwide. The importance of investigating and understanding the antimicrobial resistance profile of bacterial organisms incriminated in wounds is because wound is the most common skin ulceration worldwide (Haggerty *et al.*, 2019). In this study, all the *S. aureus* isolates obtained were found to be susceptible to Pefloxacin 34 (100%), Gentamycin 34 (100%) and Ciprofloxacin 34 (100%). In contrast, among 100 isolates investigated in Korea, resistance to doxycycline and clindamycin was found to be 12.5%, and 25% respectively (Jordan, 2019). In another study in India, among 65 *S. aureus* isolates investigated 39.7% and 59% were found to exhibit resistance to clindamycin and erythromycin respectively (Thapaliya *et al.*, 2018). Meanwhile, in this study *S. aureus* were resistant to Amoxacillin with 32 (94.1%) %. Moreover, in a related study conducted among 93 isolates in Indonesian 42.9% were resistant to Amoxacillin and 71.4% were susceptible to ciprofloxacin (Tom *et al.*, 2019). In addition, *S. aureus* was also observed to be susceptible to Ciprofloxacin (100%), Streptomycin (85.29%), Gentamycin (100%) and Pefloxacin (100%) in the present study. A similar finding was reported in Indonesian study (100%) (Towell *et al.*, 2020). Findings were reported in India where 25% were resistant to tetracycline (Cruz *et al.*, 2022). On the other hand, in the present study *S. epidermidis* shows high resistance to Ampiclox (100%), Zinnacef (100%), Amoxacillin (100%) and Rocephin (100%). Similar findings were reported among 93 isolates in Indonesia, where resistance to tetracycline (32.6%), erythromycin (65.2%) and clindamycin (52.2%) were reported (Cruz *et al.*, 2021). It is not surprising that the emergence of antimicrobial resistance among bacterial organisms associated with wounds coincided with the introduction of topical antibiotic formulations (Gilbert *et al.*, 2022). This emergence can also be attributed to the extensive use of topical antibiotics including topical clindamycin and topical erythromycin (Gilbert *et al.*, 2022). Unfortunately, one of the persistent driving forces for resistance development in acne is because the condition is routinely treated at the outpatient setting, hence, prescription patterns and regulation of sale of drugs should be considered critical target for antibiotic stewardship efforts.

Table 3: Antibiotic Resistance patterns of the isolates to the antibiotics

Isolates	Resistance Patterns	Multiple Antibiotic Resistance Index
1.	SXT, APX, Z, AM	0.4
2.	Z, AM	0.2
3.	SXT, Z, AM, R	0.4
4.	S, E, APX, AM	0.4
5.	E, APX, Z, AM, R	0.5
6.	Z, AM, R	0.3
7.	SXT, Z, R	0.3
8.	APX, Z, AM, R	0.4
9.	AM	0.1
10.	E, Z, AM	0.3
11.	APX	0.1
12.	APX, Z, AM	0.3
13.	S, SXT, E, APX, Z, AM	0.6
14.	SXT, APX, Z, E, AM, R	0.6
15.	SXT, APX, Z, AM, R	0.5
16.	Z, AM	0.2
17.	Z, AM	0.2
18.	E, Z, AM, R	0.4
19.	S, APX, Z, AM	0.4
20.	S, SXT, APX, Z, R, AM	0.6
21.	E, Z, R	0.3
22.	Z, AM	0.2
23.	APX, AM	0.2
24.	E, Z, AM	0.3
25.	E, Z, AM, R	0.4
26.	S, SXT, Z, AM, R	0.5
27.	APX, Z, AM	0.3
28.	APX, Z, AM, R	0.4
29.	SXT, APX, Z, AM	0.4
30.	APX, Z, AM	0.3
31.	Z, AM, R	0.3
32.	Z, AM	0.2
33.	S, APX, Z, AM	0.4
34.	E, APX, Z, AM, R	0.5
35.	Z, AM, R	0.3
36.	E, Z, AM, R	0.4
37.	S, Z, R, AM	0.4
38.	S, SXT, APX, Z, AM, R	0.6

***Keys:1-34** = Staphylococcus aureus isolates; **35-38** = Staphylococcus epidermidis isolates; **APX** = Ampiclox, **Z** = Zinnacef, **AM** = Amoxacillin, **R** = Rocephin, **E** = Erythromycin, **SXT** = Septrin, **S** = Streptomycin*

The *Staphylococcus* species isolates were tested against ten (10) different antibiotics such as Streptomycin,Septrin, Pefloxacin, Erythromycin,

Gentamycin, Ampiclox, Zinnacef, Amoxacillin, Rocephin, and Ciprofloxacin. The study revealed that the commonest pattern in the resistance of the isolates to the antibiotics include, Amoxacillin (AM), Ampiclox (APX), and Zinnacef (Z). The multiple antibiotics resistance index (MARI) ranges from 0.1 to 0.6 across the isolates as shown in Table 3 above. The average MARI of the *S. aureus* and *S.epidermidis* isolates was calculated to be 0.4. The implication of this is that most of the isolates are resistant to at least four (4) antibiotics, which makes them Multiple Drug resistant (MDR) isolates.

In this study, most of the isolated bacteria were resistant to most of the tested antibiotics. The high levels of resistance to these antibiotics were associated with the antibiotics that are most frequently used in empirical, and serious problems can be encountered while prescribing those antibiotics. Providing updated information through guidelines for prescribing antibiotics becomes a necessity. Our results were comparable with those of the studies conducted elsewhere such as from Zimbabwe (Geraci *et al.* 2017) (ampicillin 80% to 84.6%), and India (Azeredo*et al.,* 2017) (cotrimoxazole 83.3% and ceftazidime 83.3%).For *Staphylococcus aureus,* Pefloxacin, Gentamycin and Streptomycin was the antibiotic that has effecicacy against most of the isolates in this study (100%), (100%) and (85.29) respectively, which makes it a drug of choice for treating multi-drug resistance (MDR) (Diekema *et al.,* 2019).

Conclusion: Staphylococcus aureus and *Staphylococcus epidermidis* are both implicated in the colonization of chronic wounds of the skin as discovered in this study. The bacterial isolates are multidrug resistant (MDR) as reflected by the MARI ratio. Indiscriminate use of drugs could be the cause of the multidrug resistance by the bacteria.

Acknowledgements: The authors extend their appreciation to TETFund for providing funds to carry out this research : Batch 8 (merged), 2022.

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Declaration of Conflict of Interest: The authors declare no conflict of interest.

Data Availability Statement: Data are available upon request from the corresponding author.

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