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Nasal Carriage Prevalence of MRSA in People Living with HIV/AIDS Undertaking Antiretroviral Therapy in a Tertiary Hospital in Port Harcourt

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ABSTRACT

Methicillin resistant *Staphylococcus aureus* (MRSA) is a bacterium which is known globally to cause several difficult to treat infections in humans both in the hospital and community settings. It is also referred to as Oxacillin Resistant *Staphylococcus aureus* (ORSA). Staphylococci are members of the family Micrococcaceae. They are Gram-positive, non motile spherical bacteria, catalase-positive, do not form spores, facultatively anaerobic and occur singly and in irregular grapelike clusters. This study was aimed at determining the prevalence of MRSA nasal colonization of HIV positive patients in a Tertiary Hospital in Rivers State. A total of 217 study participants were recruited. From each participant, specimen for *Staphylococcus aureus* culture was collected from the anterior nares, using sterile swabs moistened with distilled water. Moistened sterile swab sticks were inserted into the nostrils 1-2 cm inside, swabbing it in clockwise direction for 3-4 times. The swabs were immediately transported to the Medical Microbiology and Parasitology Laboratory of the University of Port Harcourt Teaching Hospital for culture on Mannitol salt agar .Biochemical tests and antimicrobial testing was carried out on isolates. Blood samples were also collected from the participants from their median cubital vein using a sterile ethylene diamine tetra acetic acid vacutainer needle and tube. The blood samples were sent to the HIV Research Laboratory, where CD4 cell counts were done using a flow cytometer. However, nasal screening in this study identified 82(37.79%) *S. aureus* carriers. Out of these, 82(37.79%) *Staphylococcus aureus* isolates, 54(24.88%) isolates were Methicillin Resistant based on Oxacillin (1µg) disc and 35 isolates were methicillin resistant based on cefoxitin (30µg) disc giving a prevalence of 16.13% in the studied population. Conclusively, it is critical to note that, *Staphylococcus aureus* that are MRSA continue to evolve as an important agent of infection in HIV positive subjects attending the University of Port Harcourt Teaching Hospital. This study also established that there was an equal likelihood of isolation of MRSA from people living with HIV/AIDS irrespective of their CD4+ count or the stage of their disease progression.

Keywords: MRSA, Infection, Prevalence, CD4+, HIV/AIDS,

INTRODUCTION

In the world of the microscopic, *Staphylococcus aureus* is one of the most versatile organisms. It is found worldwide and is a leading cause of many diseases. Even though it is not classified as a true pathogen (an organism that is expected to always cause disease in humans), but as an opportunistic pathogen, it has a diverse repertoire of possible infections. Normally, it is a transient colonizer of the skin and body entry portals (ears, eyes, nasal passages, etc.), and an estimated 20% of humans are carriers (asymptomatic permanent colonization), 60% are intermittent carriers and approximately 20% almost never carried *S. aureus (*Kluytmans, 1997). However, any break in the skin, or colonization of individuals with compromised immune systems can provide an opportunity for this organisms to cause infection. However, the emergence of vancomycin resistant staphylococci was as a result of increase in use of vancomycin to treat infections caused by methicillin resistant staphylococci, *Clostridium difficile* and enterococcal infections (Kirst *et al*., 1998).

Vancomycin intermediate-resistant *Staphylococcus aureus* (VISA) also has been reported. In contrast to the chromosomally mediated resistance for VISA strains, the VISA strains acquire resistance by conjugal transfer of the Van A operon from an *Enterococcus faecalis*, raising the specter of a far more efficient means for dissemination of the resistance among strains of *Staphylococci* (Lowy, 2003).This bug comes naturally armed with a long list of virulence factors, and becoming resistant to antimicrobial drugs is just an added bonus. *Staphylococcus aureus* has long been recognized as an important pathogen in human disease. Due to an increasing number of infections caused by methicillin-resistant *S. aureus* (MRSA) strains, therapy has become problematic. MRSA has thus established itself as a heterogeneous group of organisms with different epidemic potentials resulting in its constantly evolving epidemiology. This heterogeneity is also represented by different virulence potentials and complex interactions with susceptible hosts. HIV-infected patients are now recognized as one of these higher risk groups due to increased rates of both MRSA colonization and infections over the past decade (Wertheim *et al*., 2005).

Therefore, prevention of staphylococcal infections has become more important. Carriage of *S. aureus* appears to play a key role in the epidemiology and pathogenesis of infection. The ecological niches of *S. aureus* are the anterior nares. Since its first appearance in 1960, methicillin resistance in *S. aureus* strains has become widespread in hospitals and intensive care units (ICUs) (Diekema *et al.,* 2004). For MRSA, specifically, colonization rates of 0%–17% have been reported for HIV- Positive outpatients' and 17%–31% for inpatients. HIV has been identified as an independent risk factor for determining colonization with MRSA (Hidron *et al*., 2005). The reason for the higher colonization rates observed are unclear, but could include factors such as frequent contact with persons in healthcare and community related settings, and frequent exposure to antibiotics, leading to a greater likelihood of becoming colonized with resistant strains of different organisms (Aaron *et al*., 2017). This study was aimed at determining the prevalence of MRSA nasal colonization of HIV positive patients in a Tertiary Hospital in Rivers State.

MATERIALS AND METHODS

This study was carried out at HIV clinic at the University of Port Harcourt Teaching Hospital located at Alakahia in Obio/Akpor Local Government Area of Rivers State. Consented subjects were enrolled for this cross sectional study. This study was conducted for a duration of six months. Adult male and female HIV positive patients (18 years and above) on antiretroviral drugs for up to six months and above were enrolled for this study. However, Children (under 18 years), Adults HIV positive subjects who are not on antiretroviral drugs, patients who were on antibiotic treatment for any bacterial infection during the time of data collection were excluded from this study.

Sample Collection: Nasal Swab samples were collected from the anterior nares of consenting HIV positive patients who reported at the University of Port Harcourt Teaching Hospital, HIV Clinic. Samples were collected from Adults. Any consenting participant who visited the clinic from January 2016 through June 2016 was enrolled in the study. A total of 217 study participants were recruited. From each participant, specimen for *Staphylococcus aureus* culture was collected from the anterior nares, using sterile distilled water aseptically moistened sterile swab. Moistened sterile swab sticks were inserted into the nostrils 1-2 cm inside, swabbing it in clockwise direction for 3-4 times. The swabs were immediately transported to the Medical Microbiology and Parasitology Laboratory of the University of Port Harcourt Teaching Hospital for microbiological analysis. Blood samples were also collected from the participants from their median cubital vein using a sterile ethylene diamine tetra acetic acid vacutainer needle and tube. The blood samples were sent to the HIV Research Laboratory, where CD4 cell counts were done using a flow cytometer.

Sample Size Calculation

The sample size was calculated by considering a 95% confidence level d=0.05 and an expected prevalence of 17%. According to this, a minimum sample size of 217 was needed for this study.
To calculate the sample size using (Daniel, 1999): $N= \frac{Z^2 P(1-P)}{d^2} = \frac{Z^2 Pq}{d^2}$

$N= \frac{(1.96)^2 \times 0.17 \times 0.83}{(0.05)^2} = \frac{3.8416 \times 0.17 \times 0.83}{(0.05)^2} = 216.81$

Then, N=217, therefore the minimum sample size for this study will be 217.

Ethical Clearance

An informed, written consent was obtained from all participants after explanation of the purpose of the study. They were given the option of not to participate in the study if they wanted. Ethical approval was also obtained from the ethics committee of the University of Port Harcourt Teaching Hospital where this study was carried out.

RESULTS

Table 1: Occurrence of *Staphylococcus aureus* in HIV Population Studied

	Sensitivity Based on	
***Staphylococcus aureus* Isolates**	**Ox (%)**	**Fox (%)**
MRSA	54 (24.88)	35 (16.13)
MSSA	21 (9.68)	47 (21.66)
Intermediate-Oxacillin-Resistant *Staphylococcus aureus*	7 (3.23)	0
Total	82 (37.79)	82 (37.79)

P=0.49 (P<0.05, Significant, while P>0.05, Not significant)

KEY:

OX = Oxacillin MRSA = Methicillin Resistant *Staphylococcus aureus*

FOX = Cefoxitin MSSA = Methicillin Susceptible *Staphylococcus aureus*

Table 2: Sex Distribution of MRSA Among the Studied Population

Sex	Total Tested	Positive Subjects	MRSA(Fox)	MRSA(Ox)	Negative
Male	65(29.95	22(33.85)	11(16.92)	13(20)	43(66.15)
Female	152(70.05)	60(39.47)	24(15.79)	41(26.97)	92(60.53)
Total	217(100)	82(37.79)	35(42.68)	54(24.88)	135(62.21)

P=0.59 (P<0.05, Significant, while P>0.05, Not significant)

This current study, showed the existence of 24.88% and 16.1% MRSA prevalence out of 82 *S. aureus* (Plate 1) isolates using oxacillin (OX)(Plate 2) and cefoxitin (FOX)(Plate 2) respectively. Overall, there is no significant difference in the determination of MRSA using Oxacillin and Cefoxitin amongst HIV subjects from this study p = 0.49 (Table 1). Based on the 65 HIV Positive adult males enrolled in this study, 22 (33.85%) were *Staphylococcus aureus* carriers and 11(16.92%) were MRSA positive using cefoxitin and 13(20.0%) using oxacillin while out of the 152 HIV Positive females enrolled in this study, 60(39.47%) were *Staphylococcus aureus* carriers and 24(15.79%) were MRSA positive for Cefoxitin and 41(26.97%) for oxacillin (Table 2). This study showed a varying distribution in the isolation of *Staphylococcus aureus* and MRSA along the various age groups using oxacillin and cefoxitn. There is significant difference in the distribution of MRSA amongst HIV subjects of the various age groups p = 0.003. The isolation MRSA was highest in age group 31 – 40 years and there was no isolation of MRSA from age group 11 – 20 years (Table 3). In this study, the HIV positive patients were grouped into three stages of HIV infection based on their $CD4^+$ count (both previous i.e. $CD4^+$ count before they were placed on Anti-retroviral drugs) and the current $CD4^+$ count, it was further shown that 37.79% of patients, who underwent this study, were in stage 1 of their HIV/AIDS disease progression, while 38.71% were in stage 2 and 23.5% were already in stage 3. However, there was observed 5.07% incidence of MRSA among those in stage 1, while 6.45% and 4.61% among those in stage 2 and 3 respectively (P=0.085) (Table 4).The mean of the previous $CD4^+$ cell count of the MRSA positive population was 401cells/µl (Table 5) while that of the recent $CD4^+$ count was 379 cells/µl (Table 6) indicating a reduction. The median of the recent $CD4^+$ count amongst the MRSA positive HIV patients was 332cells/µl.

Table 3: Age Distribution of MRSA in the Study

Age Group	No Tested	No Positive (%)	MRSA(OX)	MRSA(Fox)
11 - 20	3	0(0)	0	0
21 - 30	41	16(7.37)	11	5
31 - 40	86	33(15.21)	24	16
41 - 50	65	25(11.52)	14	9
51 - 60	18	6(2.76)	4	3
61 - 70	4	2(0.92)	1	2
Total	217	82(37.79)	54	35

P=0.003

Table 4: Distribution of MRSA among Patients at Different HIV/AIDS Clinical Stages

Stages	No. of Patients Based on Previous CD4 Count	No. of PT Based on Current CD4 Count	No. of MRSA Positive PT
Stage 1 $CD4^+ \geq 500$ cells/µl	82(37.79%)	78(35.94%)	11(5.07%)
Stage 2 $CD4^+$ 200 – 499 cells/µl	84(38.71%)	90(41.47%)	14(6.45%)
Stage 3 $CD4^+$<200 cells/µl	51(23.50%)	49(22.58%)	10(4.61%)
Total	217(100%)	217(99.99%)	35(16.13%)

P=0.085

Table 5: Current Mean CD4+ Count of MRSA Positive Patients

Intervals	X	F	cf	fx	$d = {}^{x-A}/_{h}$	fd
0 – 100	50	7	0	350	-6.0	-42.0
100 – 200	150	3	10	450	-5.0	-15.0
200 – 300	250	4	14	1000	-4.0	-16.0
300 – 400	350	8	22	2800	-3.0	-24.0
400 – 500	450	2	24	900	-2.0	-4.0
500 – 600	550	5	29	2750	-1.0	-5.0
600 – 700	650	3	32	1950	0	0
700 – 800	750	1	33	750	1.0	1
800 – 900	850	0	33	0	2.0	0
900 – 1000	950	0	33	0	3.0	0
1000 – 1100	1050	1	34	1050	4.0	4
1100 – 1200	1150	0	34	0	5.0	0
1200 – 1300	1250	1	35	1250	6.0	6
						$\sum fd = -95$

Using $x = a + h(\frac{\sum fd}{N})$

A =650

N =35

h =100

x =650 + 100 (-95/35)

$= 650 - \frac{9500}{35}$

= 650-271.43

= 378.57

X = 379

The mean of current $CD4^+$ count of MRSA positive patients is 379cells/µl

Table 6: Previous CD4+ Mean Calculations of the HIV Patients

Intervals	x	f	Cf	Fx	d = $x - A/h$	fd
0 – 100	50	5	0	250	-6.5	-32.5
100 – 200	150	5	10	750	-5.5	-27.5
200 – 300	250	4	14	1000	-4.5	-18
300 – 400	350	7	21	2450	-3.5	-24.5
400 – 500	450	3	24	1350	-2.5	-7.5
500 – 600	550	3	27	1650	-1.5	-4.5
600 – 700	650	4	31	2600	-0.5	-2.0
600 – 700	650	4	31	2600	-0.5	-2.0
700 – 800	750	0	31	0	0.5	0
800 – 900	850	2	33	1700	1.5	3.0
900 – 1000	950	1	34	950	2.5	2.5
1000 – 1100	1050	0	34	0	3.5	0
1100 – 1200	1150	0	34	0	4.5	0
1200 – 1300	1250	0	34	0	5.5	0
1300 – 1400	1350	1	35	1350	6.5	6.5
						∑fd = -104.5

Using x = a + h (∑fd/N)

Where x = mean
A = Assumed mean = 700
N = Population size
h = width = 100

x = 700 + 100 (-104.5/35)
= 700 –10450/35
700 – 298.57
x = 401.43
x ≈ 401cells/µl.

Therefore, the mean of previous CD4+ count of MRSA positive patients was 401cells/µl.

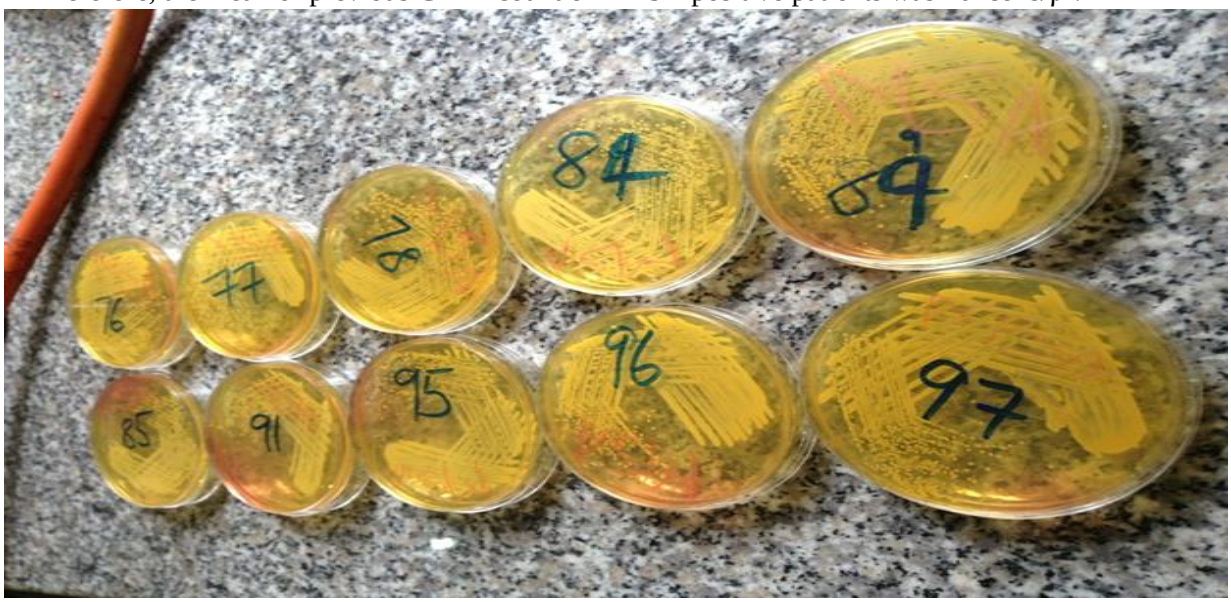

Plate 1: Cross Section of *Staphylococcus aureus* Isolates on Mannitol Salt Agar

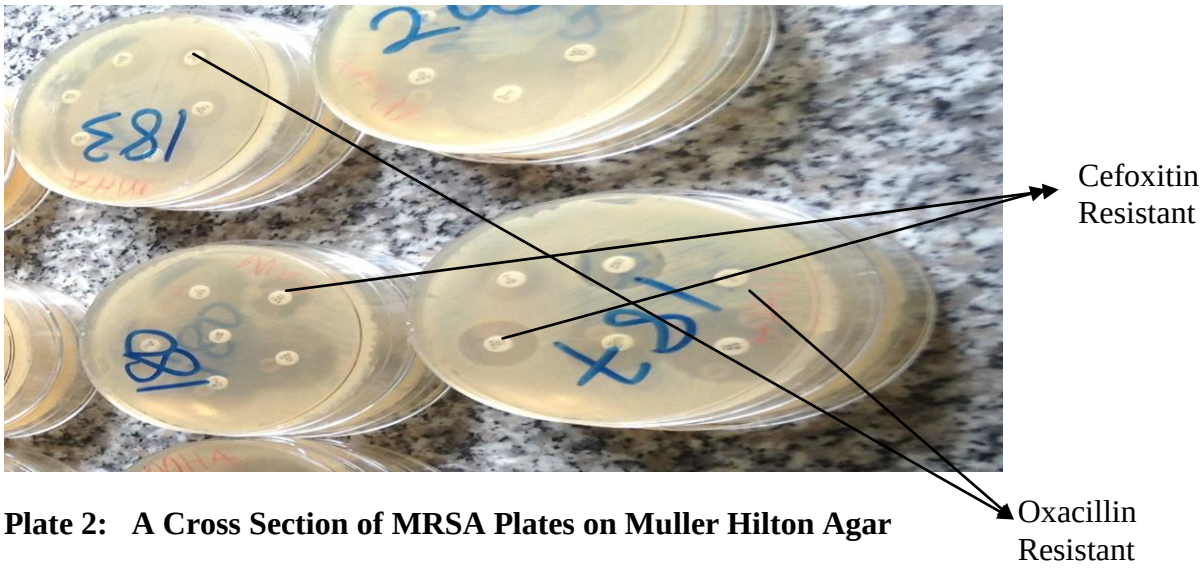

Plate 2: A Cross Section of MRSA Plates on Muller Hilton Agar

DISCUSSION

The result obtained in this study was consistent with that obtained by Olakekan *et al*., (2016) which gave 33% prevalence of *S. aureus* among the study population. HIV has been reported as an independent factor leading to the colonization with MRSA. The reason for this high prevalence or rates of colonization is not clear but could be as a result of frequent contact with health care workers. Nevertheless, in this study, *Staphylococcus aureus* percentage colonization among HIV patients was higher than the 19.67% reported by Eiff *et al*., (2001) among patients undergoing dialysis in an Iranian health facility but it was similar to what Hekmat *et al*., (2008), Ghazvini and Hekmat, (2007) had observed from different studies at different times which summarily puts *Staphylococcus aureus* nasal carriage range to be between 36.9% to 45.8% which agreed with the study's *Staphylococcus aureus* nasal carriage prevalence rate. Kluytmans *et al.,* (1997) reported that, 60% of healthy individuals are intermittent carriers and approximately 20% almost never carry *Staphylococcus aureus* with all prevalence of *Staphylococcus aureus* isolation being between 20-45%. Overall, the rate of MRSA identified from the nasal specimen of HIV patients in this study (16.13%) was consistent with that of Taiwo *et al*.,(2005) (17%), the 0-17% reported by Hidron *et al*.,(2010), 16% by Olakekan *et al*.,(2012).

The MRSA rates obtained from this study can also be compared favourably with that obtained from Austria and Germany hospitals, which were between 10% and 20% but higher than that obtained in Nertherlands, Sweden, and Denmark which had prevalence below 10%. MRSA rates of 24-30% and 40% were obtained from France and Italy respectively (NIPH, 2003; Wannet *et al*., 2004; Nester *et al*., 2004). It was lower than that obtained by Adesida *et al*., (2016) (20%) and Lemma *et al*., (2015) (26%). Also, it can be noted that MRSA colonization is generally lower in resource poor countries than you could find in resource rich countries with inadequate health facilities and poor societal attitude towards medical treatment. For instance, the prevalence of MRSA in some countries like the Netherlands is still very low, as low as 1.0% (El- Jalil *et al*., 2008), while the prevalence of MRSA was reported to be 10% in Tunisia, Malta, and Algeria and about 15% in Kenya, as compared to the high prevalence of 21 to 30% in Cameroon and Nigeria (Emeka-Nwabunnia *et al.,* 2015).

Similarly, the level of hygiene disposition of a populace or society, according to Pathak *et al.,* (2010) could be a factor determining the rate of nasal carriage of MRSA among HIV patients. Perhaps, one possible explanation for the high nasal carriage of *S. aureus* in resource rich countries could be low rates of exposure to antigens due to better personal hygiene. For example, the national nosocomial infection surveillance network (USA), had shown that over 50% of *S. aureus are* MRSA among those in the United States of America, mega rich Asia, with very high

prevalence observed in Hong Kong (75%) and Japan (70%) and in some part of Europe like Portugal and Italy. While in some other countries, who are not as rich as the aforementioned countries but have a rich culture of hygiene and adhere seriously to infection control measures, records of extremely low prevalence of 2% in Switzerland and 1.0% in Netherlands were observed (Emeka-Nwabunnia *et al.,* 2015).

Nevertheless, this study showed a decline in the mean CD4+ (401cells/µl – 379 cells/µl) among the population of subjects living with HIV/AIDS, using their previous and current $CD4^+$ count at the time of the collection of samples, indicating a slight reduction in their ability to defend themselves from systemic invaders. This Study further deduced that 37.79% of patients, who underwent this study, were in stage 1 of their HIV/AIDS disease progression, while 38.71% were in stage 2 and 23.5% were already in stage 3. Although, study subjects in stage 2 of their HIV/AIDS disease progression had the highest nasal carriage of MRSA, 6.45%, there was no identifiable explanation as to why it was that way. However, there was observed no significant difference in the number of patients in the stages of HIV infection using their previous and current $CD4^+$ count, which showed MRSA infection. This implies that, there was an equal probability or likelihood of isolating MRSA from persons living with HIV/AIDS irrespective of the level/stage of their disease progression.

Comparatively, the above observation was in line with the position of Shet *et al*., (2009) that, association between HIV infected patients with MRSA colonization, might not be dependent on CD4+ T lymphocyte count. Also, this study's mean $CD4^+$ count, supports the findings of Kluytmans (1997), since the mean $CD4^+$ count of the HIV patients used in this study were within the range obtainable in healthy patients. Therefore, This study's $CD4^+$ results explains the position of Aaron *et al*., (2017) and Nester *et al*., (2004) that, progression from asymptomatic infection to AIDS do not come suddenly but in fact occurs as a continuum of clinical stages with symptoms of active HIV infection being non-specific to include fatigue, rash, headache, nausea and night sweats. Nevertheless, the result do not contradict the position of Azuonwu *et al*., (2010) who suggested that, the clinical stage of AIDS, which is characterized by pronounced suppression of the immune system and development of a wide variety of severe opportunistic infections, is the most predisposed stage to suffering from underlining infections.

CONCLUSION

Staphylococcus aureus that are MRSA continue to evolve in their epidemiology which have led to an increase in colonization and infection of HIV positive population with this organism. This results obtained from this study indicate that MRSA exists in HIV positive subjects attending the University of Port Harcourt Teaching Hospital. Its prevalence is not as high as reported in other studies in this region of Africa but there is need for close monitoring to prevent its trajectory incidence. More MRSA were detected from female subjects than males which was not different from the published report of other researchers in Nigeria, Africa and other parts of the world. This study also established that there was an equal likelihood of isolation of MRSA from people living with HIV/AIDS irrespective of their CD4+ count or the stage of their disease progression.

Authors Contributions

Study design and conception (JPA, NEG and AUU): Sample collection, processing and data collation (JPA): Manuscript write up (AUU and JPA): Data Analysis (AUU): Oversight on all stages of the research (NEG and AM): All authors read and approved the final manuscript.

Conflict of Interest

All authors declared no conflict of interest.

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REFERENCES

Aaron, U. U., Azuonwu, O., and Ayodele, M. O. (2017). Public Health Implications of HIV Incidence in Orashi Communities of Niger Delta, Nigeria. *EPRA International Journal of Multidisciplinary Research*, 3(4), 80-87.

Adesida, S., Boelens, H., Babajide, B., Kehinde, A., Snijders, S. (2005) Major epidemic clones of *Staphylococcus aureus* in Nigeria. *Microbiology Drug Resistance*, 11, 115–121.

Adesida, A. S Okeyide, O. A., Abioye, A., Omolopo, I., Egwuatu, O. T., Amisu, O. K., Coker, O. A. (2016). Nasal Carriage of Methicillin Resistant *Staphylococcus aureus* among Elderly people in Lagos, Nigewria. *Avicenna Journal of Clinical Microbiology and Infection.* 3(4), e39272. Retrieved from Dio:10.17795/ajcmi-39272 on 15th of April, 2016.

Azuonwu, O. Obire, O., Ramesh, P. and Nwankwo, E. M. (2010). Prevalence and Risk Factors of HIV in Ndoki Communities of Nigeria. Journal of Pharmacy Research, 3(7), 1607-1611.

Borg, M.A., de Kraker, M., Scicluna, E., van de Sande-Bruinsma, N., Tiemersma, E., (2007). Prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) in invasive isolates from southern and eastern Mediterranean countries. *Journal of Antimicrobiology Chemotherapy*, 60, 1310–1315.

Breurec, S., Zriouil, S. B., Fall, C., Boisier, P., Brisse, S. (2011). Epidemiology of methicillin-resistant Staphylococcus aureus lineages in five major African towns: emergence and spread of atypical clones. *Clinical Microbiology Infection*, *17*, 160–165.

Centers for Disease Control and Prevention (CDC). (2013). General Information About MRSA in the Community. Retrieved from www.cdc.com on 10th April, *2016).*

Chacko, J., Kuruvila, M., and Bhat, A. K., (2009). Factors affecting the nasal carriage of MRSA in human immunodeficiency Virus- infected patients, *Indian Journal of Medical Microbiology*, 25, 146–148.

Cheesbrough, M. (2006). District Laboratory Practice in Tropical Countries (Part 2). Low Price Edition. Cambridge: Cambridge University Press.

Cheung, A. L., Eberhardt, K.. J, and Chung, E. (1994). Diminished virulence of a sar$^-$/agr$^-$ mutant of *Staphylococcus aureus* in the rabbit model of endocarditis. *Journal of Clinical Investigation, 94, 1815-22.*

Crisostomo, M. I., Westh, H., Tomasz, A., Chung, M., Oliveira, D. C., and Lencastre, H. (2001). The evolution of methicillin resistance in *Staphylococcus aureus*: similarity of genetic backgrounds in historically early methicillin-susceptible and resistant isolates and contemporary epidemic clones. *Proceedings of the National Academy of Science*, 98, 9865-9870.

David, M. Z., and Daum, R. S. (2010). Community-Associated Methicillin-Resistant *Staphylococcus aureus*: Epidemiology and Clinical Consequences of an Emerging Epidemic. *Clinical Microbiology Reviews (American Society for Microbiology)*, 23(6), 616–687.

Deureuberg, R. H., and Stobberinyh, E. E. (2008). The evolution of *Staphylococcus aureus*. *Infection Genetics and Evololution*, 8, 747 –7 63.

Diekema, D. J., BootsMiller, B. J. and Vaughn, T. E. (2004). Antimicrobial resistance trends and outbreak frequency in United States hospitals. *Clinical Infectious Diseases*, 38, 78-85.

60(10), 1204-1209.

El-Jalil, H. A., Jallad, M., and Thwaini, A.. J. (2008). Nasal Carriage of Methicillin Resistant *Staphylococcus aureus* in Individuals Exposed and Not Exposed to Hospital Environments. *European Journal of Scientific Research*, 22(4), 570-574.

Emeka-Nwabunnia, I., Chiegboka, N. A., Udensi, U. J., and Nwaokorie, F. O. (2015). Vancomycin-Resistant *Staphylococcus aureus* Isolates from HIV Positive Patients in Imo State, Nigeria. Science *Journal of Public Health. Special Issue: Who Is Afraid of the Microbes*, 3, 5-1, 1-7.

Emele, F. E., Izomoh, M. I., and Alufohai, E. (1999). Microorganisms Associated with wound infections in Ekpoma, Nigeria. *West African Journal of Medicine,* 18(2), 97-100.

Enright, M. C., Robinson, D. A, Randle, G., Feil, E. J., Grundmann, H. and Spratt, B. G. (2002). *The evolutionary history of methicillin-resistant Staphylococcus aureus (MRSA). Proceedings of the National Academy of Science USA, 99, 7687-7692.*

Fournier, B., and Hooper, D.C. (2000). A new two-component regulatory system involved in adhesion, autolysis, and extracellular proteolytic activity of *Staphylococcus aureus. Journal of Bacteriology, 182, 3955-3964.*

Francois, P., and Schrenzel, J. (2008). Rapid Diagnosis and Typing of *Staphylococcus aureus*. *Staphylococcus: Molecular Genetics*. Caister Academic Press.

Ghamba, E., Mangoro, Z., and Waza, D. (2012). Reoccurrence and distribution of methicillin-resistant *Staphylococcus aureus* (MRSA) in clinical specimens in Bauchi, North eastern Nigeria. *Journal of Medicine and Medical Sciences*, 3, 506–511.

Ghazvini, K. and Hekmat, R. (2007). Nasal and skin colonization of *Staphylococcus aureus* in hemodialysis patients in Northeast of Iran. Iran J Kidney Dis.;1:21–24. pmid:19357439.

Gray, J. W. (2004). MRSA: the problem reaches paediatrics. *Archives of Diseases in Children, 89(4), 297–298.*

Grundmann, H., Aires-de-Sousa, M., Boyce, J., and Tiemersma, E. (2006). Emergence and resurgence of Methicillin-resistant *Staphylococcus aureus* as a public-health threat. *Lancet*, 368(9538), 874-885.

Hekmat, F., Mamani, M., Hajia, M., Sharifi,, M. A. (2008). Prevalence of *Staphylococcus aureus* carriage in patients on hemodialysis and their correlation to infections. 8th International Congress on Infections Diseases, Tehran, Iran.

Hidon, A., Kempker, R., Moanna, A., and Rimland, D. (2010). Methicillin Resistant Staphylococcus aureus in HIV infected patients. *Dove Press Journal: Infection and Drug Resistance*, 3, 73 - 86

Hidron, A. I., Edwards, J. R., Patel J. (2008). NHSN annual update: antimicrobial-resistant pathogens associated with healthcare-associated infections: annual summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2006–2007. *Infectious Control Hospital Epidemiology,* 29(11), 996–1011.

Hidron, A. I., Kourbatova, E. V., and Halvosa, J. S. (2005). Risk factors for colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) in patients admitted to an urban hospital: emergence of community associated MRSA nasal carriage. *Clinical Infectous Dis*eases, 41(2),159–166.

Hidron, A., Kempker, R., Moanna, A., and Rimland, D. (2010). Methicillin resistant *Staphylococcus aureus* in HIV-infected patients. *Infection and Drug Research*, 3, 73–86.

Jason , E. F., Matthew , J. H., Paul, L. S., Tracy, R., and Karen, C. (2015). Prevalence and risk factors for methicillin resistance *staphylococcus aureus* in an HIV-positive cohort. *American Journal of Infection Control*. 43(4), 329-335.

Microbiology Review, 10(3), 505-520.

Kirst, H. A., Thompson, D. G. and Nicas, I. T. (1998). Historical yearly us-age of vancomycin. *Antimicrobial Agent Chemotherapy*, 42, 1303-1304.

Lemma, M. T., Zenebe, Y., Tulu, B., Mekonnen, D., and Mekonnen, Z. (2015). Methicillin Resistant Staphylococcus aureus among HIV infected Pediatric Patients in Northwest Ethiopia: Carriage Rates and Antibiotic Co-Resistance Profiles. *PLoS One*, 10(9), e0137254.

Liang, X., Yu, C. and Sun, J. (2006) Inactivation of a two-component signal transduction system, SaeRS, eliminates adherence and attenuates virulence of *Staphylococcus aureus*. *Infection and Immununity, 74, 4655-4665.*

Lowy, F. D. (1998). *Staphylococcus aureus* infections. *New England Journal of Medicine*, 339(8), 520-532.

Luong, T. T., Newell, S. W., and Lee, C.Y. (2003). Mgr, a novel global regulator in *Staphylococcus aureus. Journal of Bacteriology,* 185, 3703-3710.

Marmot M. (2001).Economic and Social Determinants of Disease. *WHO Bulletin,* 79,906-1004.

Nester, E. W., Anderson, D. G., Roberts, C. E., Pearsall, N. N. and Nester, M. T. (2004). *Microbiology: A Human Perspective* 4th (Edn), McGraw Hill, New York. Pp 509 – 528.

Norwegian Institute of Public Health. epidemiologyDoid Infections caused by methicillinresistant *Staphylococcus aureus* (MRSA) Surveillance of Communicable Diseases in Norway. 2003. p. 23.

Odu, N. N., and Okonko, I. O. (2012). Nasal carriage and antibiotics susceptibility of *Staphylococcus aureus* in healthy students of University of Port Harcourt, Rivers State, Nigeria. *New York Science Journal* , 5 (7),56-63.

Odusanya., O. O. (2002). Antibiotic susceptibility of Microorganisms at a general hospital in Lagos, Nigeria. *Journal of National Medical Association*, 94(11): 994-998.

Ojulong, J., Mwambu, T. P., Jolobo, M., Agwu, E, Bwanga, F., Najjuka, C., and Kaddu-Mulindwa, M. (2009). Relative prevalence of Methicillin resistant Staphylococcus aureus (MRSA) and its susceptibility pattern in Mulago hospital- Kampala, Uganda. *International Journal of Infectious Disease*, 11, 87-89.

Olakekan, A. O., Schaumburg, F., Nurjadi, D., Dike, A. E., Ojurongbe, O., Kolawole, D. O., and Kun, T. F. (2012). Clonal expression accounts for an excess of antimicrobial resistance in *Staphylococcus aureus* colonosing HIV-Positive individuals in Lagos, Nigeria. *International Journal of Antimicrobial Agents*, 40(3), 268-272.

Onanuga, A. and Temedia,T. C., (2011). Nasal carriage of healthy in habitants of Amassoma in Niger Delta region of Nigeria. *African Health Sciences*, 11(2), 176–181.

Pathak, A., Marothi, Y., Iyer,, R.V., Singh, B., Sharma, M., Eriksson, B., Macaden, R. and Lundborg, B. (2010). Nasal Carriage and Antimicrobial Susceptibility of *Staphylococcus aureus* in healthy preschool children in Ujjain, India. *BMC Pediatriatics*, 10, 100.

Patti, J. M., Allen, B. L., McGavin, M. J. and Hook, M. (1994). MSCRAMM-Mediated adherence of microorganisms to host tissues. *Annual Review of Microbiology*, 48, 585-617.

Peacock, S. J, Moore, C. E. and Justice, A. (2002). Virulent combinations of adhesin and toxin genes in natural populations of *Staphylococcus aureus. Infection and Immunity,70, 4987-96.*

Peacock, S. J., Justice,A., Griffiths, D., de Silva, G.D., Kantzanou, M. N., Crook, D., Sleeman, K. and Day, N.P. (2003):Determinants of acquisition and carriage of Staphylococcus aureus in infancy. *Journal of Clinical Microbiology*, 41(12):5718- 5725.

Shittu, A. O., Okon, K., Adesida, S., Oyedara, O., Witte, W., Strommenger, B., Layer, F. and Nubel, U. (2011). Antibiotic resistance and molecular epidemiology of *Staphylococcus aureus* in Nigeria. *BMC Microbiology*, 11, 92–99.

Taiwo, S. S., Bamidele, M., Omonigbehin, E. A., Akinsinde, K. A. and Smith, S. I. (2005). Molecular epidemiology of methicillin-resistant Staphylococcus aureus in Ilorin, Nigeria. *West African Journal of Medicine*, 24, 100–106.

Terry, A. O. A., Ogbolu, D.O., Mustapha, J. O., Akinbami, R., and Ajayi, A.O. (2012). The non-association of Panton-Valentine leukocidin and mecA genes in the genome of Staphylococcus aureus from hospitals in South Western Nigeria. *Indian Journal of Medical Microbiology*, 30, 159–164.

UNAIDS. Report on the global AIDS epidemic 2013. (2013). Available at: http://www.unaids.org/en/HIV_data/2006GlobalReport/default.asp. (Accessed on 10 June 2016).

Von Eiff, C., Becker, K., Machka, K., Stammer, H. and Peters, G. (2001). Nasal carriage as a source of *Staphylococcus aureus* bacteremia. *North England Journal Medical, 344, 11-16.*

Wertheim, H.F., Melles, D.C,, Vos, M.C., van Leeuwen, W., van Belkum, A., Verbrugh, H.A. and Nouwen, J.L. (2005). The role of nasal carriage in *Staphylococcus aureus* infections. *Lancet Infect Dis*. 5:751–762. doi: 10.1016/S1473-3099(05)70295-4. [PubMed] [Cross Ref].

Wannet WJB, de Neeling AJ, Heck MEOC, Pluister GN, Spalburg E, Tiemersma EW. MRSA in Nederlandse ziekenhuizen: Surveillanceresultaten 2003 en recente ontwikkelingen. Infectieziekten Bulletin. 2004;15:167–170.

Zinderman, C.E., Conner, B., Malakooti, M.A., LaMar, J.E., Armstrong,A.and Bohnker, B. K. (2004). Community-Acquired Methicillin-Resistant *Staphylococcus aureus* Among Military Recruits. *Emerging Infectious Diseases*, 10 (5), 941–944.