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Review

Prevalence and genetic lineages of *Staphylococcus aureus* nasal colonization and urinary tract infection among people living with HIV/AIDS in Nigeria: A systematic review

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ABSTRACT

To provide an empirical insight on *Staphylococcus aureus (S. aureus)* nasal colonization and urinary tract infection (UTI) among people living with HIV/AIDS (PLWHA) in Nigeria, a quantitative synthesis and systematic review were executed. A comprehensive bibliometric search was conducted for published articles using the keywords 'nasal *S. aureus* carriage', 'Urinary *S. aureus'*, 'nasal MRSA', 'staphylococci-HIV coinfection', 'urinary MRSA' and 'all states of Nigeria'. Eligible studies and the number of subjects (n) were analysed according to the PRISMA criteria. Out of the 79 examined studies, only 6 (n=1181) and 6 (n= 1350) on nasal and urine samples, respectively, were eligible. The pooled prevalence of nasal carriage and UTI of *S. aureus* were 29.6% and 6.8%, respectively. However, the pooled nasal MRSA carriage was 13.4%. The pooled prevalence of *luk-F/S-PV*-carrying *S. aureus* among nasal samples was 13.0%. Molecular typing from 3 studies showed MRSA-ST8-t064 and MSSA-ST15-t084 as the predominant genetic lineages. The *S. aureus* isolates from both sample types had the highest (>50%) resistance to penicillin, sulfamethoxazole-trimethoprim, erythromycin, and tetracycline. Multi-drug resistance was not significantly higher among *S. aureus* isolates from urine than nasal samples (60% versus 40.0% of eligible studies) (p= 0.5271). A moderate and high pooled prevalence of genetically diverse MRSA and *luk-F/S-PV*-carrying *S. aureus* were obtained from PLWHA, respectively. These findings emphasize the importance of routine screening for MRSA among PLWHA in Nigeria and other HIV endemic countries.

Introduction

Staphylococcus aureus (*S. aureus*) is one of the most prevalent opportunistic bacteria in the healthcare setting and community and has been a serious public health concern due to its swift tendency to acquire antimicrobial resistance (AMR) and elaborate relevant virulent toxins, enzymes and other macromolecules such as the pore-forming toxins, superantigens, phagocytosis inhibitors, and biofilm-forming capacity (Oliveira et al., 2018). *S. aureus*, especially the methicillin-resistant *S. aureus* (MRSA) strain, has been responsible for various infectious diseases that ranged from folliculitis to food poisoning (Aung et al., 2017). Particularly, it could be responsible for certain life-threatening conditions such as endocarditis, urethritis, necrotizing pneumonitis, and osteomyelitis (Siddiqui and Koirala, 2021). These conditions are predominantly prevalent among the immunocompromised hosts, such as those living with human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS).

Among the HIV-infected patients, *S. aureus* colonization and subsequent infection are considered to be a major cause of significant morbidity and mortality (Hsu et al., 2020). Previous studies suggest that the prevalence of nasal colonization with MRSA is higher in HIV-infected individuals than in the general population (Popovich et al., 2013). HIV infection has also been related to persistent colonization. The higher colonization burden may be associated with a higher incidence of subsequent infections (Olalekan et al., 2016). MRSA colonization in HIV-infected patients may vary widely in different geographical regions (Sabbagh et al., 2019), the time point of the survey (Delorenze et al., 2013), and the coverage of antiretroviral therapy in the population (Cenizal et al., 2008).

Because MRSA strains are often nosocomial pathogens, they are referred to as healthcare-associated MRSA (HA-MRSA) (Choo, 2017). Besides HA-MRSA strains, MRSA strains that are transmitted in the community, referred to as community-associated MRSA (CA-MRSA) are also often reported (Loeffler et al., 2013). CA-MRSA infections could also be caused by livestock-associated MRSA (LA-MRSA) (Quitoco et al., 2013).

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LA-MRSA is initially associated with livestock and genetically differs from HA-MRSA and CA-MRSA. The definition of CA- and HA- strains is no longer a strict one, as either strain has been described to be responsible for outbreaks in both hospital and community settings (Bal *et al.* 2016). However, it is relevant to delineate the pattern of predominant transmission.

A high nasal carriage rate of MRSA in HIV infected persons may require early chemotherapeutic interventions. It was inferred that hospitalized HIV-infected patients are about seventeen times more likely to contract *S. aureus* infection in comparison to non-HIV patients (Senthilkumar et al., 2001). Also, the increasing prevalence of staphylococcal infections caused by MRSA has been difficult to treat due to the high rate of AMR. The determination of *S. aureus* nasal carriage rate and AMR profiles along with their genetic lineages of nasal *S. aureus* isolates in healthy populations is necessary to identify risk factors that could predispose people living with HIV/AIDS (PLWHA) to infection (Chen et al., 2015).

Although some instances, HIV-associated immunosuppression could mask symptoms of *S. aureus* UTI to asymptomatic disease (Ngowi et al., 2021); it is considered an important health problem that could complicate the course of HIV infection and AIDS in sub-Saharan Africa (Tessema et al., 2020; Haile Hantalo et al., 2020). This is because PLWHA are at an increased risk of acquiring urinary tract *S. aureus* infection (asymptomatic and asymptomatic) due to immune system suppression (Barnie et al., 2019).

PLWHA who had *S. aureus*-associated bacteremia could have these pathogens translocated to urine in quite a high proportion. Therefore, the detection of *S. aureus* in the urine (bacteriuria) does not necessarily represent a primary UTI, but could point towards an *S. aureus* bloodstream infection (Schuler et al. 2021). Hence, hematogenous translocation of *S. aureus* from blood to urine is possible (Schuler et al. 2021). To provide a relatively faster microbiological test turnaround time (TAT) for *S. aureus* bacteraemia (Hassoun et al., 2017) in resource-limited settings, positive bacteriuria could suggest bacteraemia, especially when patients had a concurrent high fever (Saran et al., 2018). Urinary tract catheterization has been recognized as a major risk factor for *S aureus* bacteriuria in bacteremic patients (Walker et al., 2017; Kramer et al., 2020).

Among HIV infected individuals, asymptomatic UTI can progress to symptomatic UTI characterized by mild irritation during voiding to bacteremia, sepsis, and death (Tessema et al., 2020). HIV infected persons whose CD4+ cell T cell count is less than 500 cells/mm^3 are commonly affected by UTIs including those caused by *S. aureus* (Febta et al., 2016). According to a study from Tanzania, a CD4$^+$ cell count <200 per microliter was significantly associated with UTI among HIV positive individuals (Chaula et al., 2017). Also, it is complicated by the emergence of AMR, making UTI chemotherapeutics very challenging. In this regard, *S. aureus* and HIV co-infection are becoming a major challenge and lead to additional healthcare costs (Frank-Peterside et al., 2013). Since *S. aureus* could pose a significant risk of life-threatening infections when translocated from various anatomic sites in PLWHA. This study aims to determine the pooled prevalence and antimicrobial resistance pattern of *S. aureus* nasal colonization and UTI, genetic lineages and PVL producing strains from PLWHA in Nigeria.

Methodology

Study Design

This is a systematic and synthesized review of the distribution pattern and prevalence of *S. aureus*, MRSA, their genetic lineages, antimicrobial resistance phenotypes and genotypes, and *luk-F/S-PV* gene in the nasal cavity and UTI of PLWHA, that was conducted using the best available evidence in Nigeria. This systematic review was based on the guidelines of Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) (http://prisma-statement.org/PRISMAstatement/checklist.aspx, accessed on 16 September 2021). This review was submitted for registration with PROSPERO (No.: 301550)

Articles Search

A thorough review of suitable and eligible full-text articles was conducted from 'PubMed', 'Scopus', 'Hinari', 'Google Scholar', and 'Web of Science' on peer-reviewed articles published between January 2012 to January 2021 on *S. aureus* nasal carriages and UTI among PLWHA in Nigeria. Specifically, keywords were carefully selected from the Medical Subjects Headings (MeSH) of the US National Library of Medicine (https://www.ncbi.nlm.nih.gov/mesh/, accessed on 24 December 2021).

Selection of Studies

Studies identified in the literature search were checked by title and abstract. The papers with relevant abstracts were examined in detail. The criteria for the inclusion and exclusion of the studies were established by authors before the literature were reviewed. The inclusion criteria for this systematic review included: (1) studies that were original articles, short communications, correspondence, or letters that provided sufficient original data about the prevalence of '*Staphylococcus aureus* nasal carriage', *Staphylococcus aureus* UTI', 'MRSA nasal carriage', 'Methicillin-resistant *Staphylococcus aureus*'; (2) studies in which all MRSA strains were adequately presented; and (3) studies that were published in English. The exclusion criteria were: (1) studies that contained duplicate data or were overlapping articles; (2) reviews and conference abstracts; (3) articles that included fewer than 10 subjects; (4) studies performed on healthy humans or other non-HIV diseases such as diabetics; (5) articles published before the year 2012; (6) longitudinal studies with no specific nasal staphylococci prevalence at the initial sampling; (7) studies that were solely on staphylococci isolates with no or full information of the number of persons colonized or infected; and (8) studies on other human samples.

Data Extraction

Authors independently ascertained the characteristics of each study, including the first author's surname, year of publication, continent, country, study years, detection method, staphylococci prevalence, antimicrobial resistance phenotypes and genotypes, virulence factors, and molecular typing reports. When there was disagreement, the relevant paper was reviewed, and the differences were resolved by consensus.

Statistical Analysis

The pooled prevalence of nasal carriage of *S. aureus*, MRSA and PVL carrying-*S. aureus* was calculated. MetaXL Version 5.3 (EpiGear International, Queensland, Australia) was used for all statistical analyses. Where possible, an analysis of pooled prevalence was carried out using the random-effects model.

Results

Out of the 79 examined studies, only 6 (n=1181) and 6 (n= 1350) on nasal and urine samples, respectively, were eligible (Figure 1 and Table 1). The pooled nasal carriage of *S. aureus* and MRSA were 29.6% (range: 20.0-60.9%) and 13.4% (range: 6.1-40.0%), respectively (Table 2). However, the pooled urinary *S. aureus* was 6.8% (range: 0.0-42.5%) with significant heterogeneity (Table 2). In relation to urinary MRSA, only a single study reported a high prevalence of 40.0% (Table 1). The pooled prevalence of *lukS/F-PV* carrying *S. aureus* among nasal samples was 13.0% (Figure 2). High-level and diverse AMR were reported in the MRSA and MSSA strains, including those belonging to

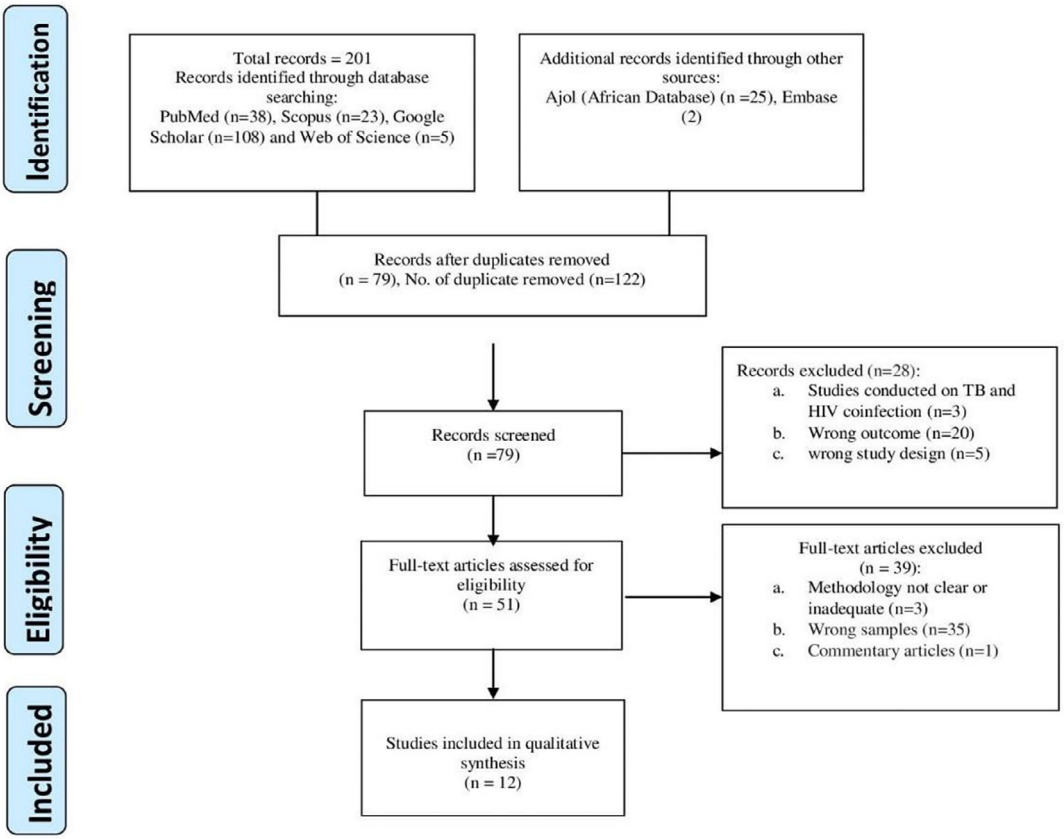

Figure 1. Identification and selection flowchart of articles on *Staphylococcus aureus* nasal colonization and urinary tract infection among PLWHA

genetic lineages commonly found in animals. The *S. aureus* isolates from both sample types from 10 studies had the highest (>50%) resistance to penicillin (and derivative), sulfamethoxazole-trimethoprim, erythromycin, and tetracycline. According to the European centre for disease control, multidrug resistance phenotype is defined as acquired AMR to at least one agent in ≥ 3 classes of antimicrobial agents (ECDC, 2014). Multi-drug resistance was not significantly higher among *S. aureus* isolates from urine than nasal samples (60% versus 40.0% of eligible studies) (p= 0.5271) (Table 3). Molecular typing from 3 studies showed MSSA and MRSA of the *spa* types t064 and t084 is the predominant (Table 4). However, other genetic lineages such as those with *spa* types t774, t7806, t084, t355, and t127 were reported (Table 4).

Discussion

Studies on the *Staphylococcus aureus* (*S. aureus*) and its methicillin-resistant strain, Methicilin-Resistant *S. aureus* (MRSA) nasal carriage among PLWHA could provide a good understanding of their transmission to other parts of the body and their role in the persistence of AMR, especially in invasive infection such as those found in the urinary tract. To the best of our knowledge, this is the first comprehensive synthetic and systematic review on the *S. aureus* and MRSA nasal carriage and UTI in Nigeria, a country with about 1.9 million people living with HIV (prevalence rate of 1.4%) in adults aged 15 to 49 years in 2019 (UNAIDS, 2019).

With a pooled prevalence of 29.6% *S. aureus* nasal carriage in PLWHA, it can be inferred that this value is within the normal range of 25 to 30% of healthy adults (Sakr et al., 2018). However, it is higher than the pooled reported prevalence in a systematic review of healthy humans without occupational risk of colonisation (15.9%) (Abdullahi et al., 2021a). The difference in pooled prevalence from this study with other individual or meta-analytical studies could be attributed to variation among the laboratory methodologies used, specific characteristics of the individuals tested (eg. age), pattern of antimicrobial use, status of antiretroviral therapy, and living conditions such as large family sizes and lower sanitary standards.

Few eligible cross-sectional studies on MRSA nasal carriage in PLWHA have been published (n=6) (Table 1), *S aureus* is among the most common pathogens in hospital-acquired infections and also in patients with a suppressed immune system. From our study, the pooled prevalence of nasal MRSA carriage was 13.4%. Antimicrobial-resistant *S. aureus* colonization is considered a major threat to public health, especially when they are MRSA strains. For instance, a higher mortality rate (OR: 1.93, 95%CI: 1.54-2.42) was reported to be associated with MRSA strains than with methicillin-sensitive *S. aureus* strains (Cosgrove and Sakoulas, 2003). The results of our analysis were higher than the 7% global MRSA nasal colonization in PLWHA (Sabbagh et al., 2019), and also significantly higher than in healthy persons (0.2%-3.5%) (Brasel and Weigelt, 2016). It is important to remark that previous systematic reviews on PLWHA by Ferreira et al (2014) and Sabbagh et al (2019) were on risk factors determinants and burden, respectively, of MRSA colonization and infection. Also, both dwelled on all types of samples (such as skin, faecal, aspirates, pus, etc.) and no clear distinction was made between colonization and infection. Conversely, the pooled *S. aureus* UTI among PLWHA was 6.8%. This is contrary to the findings of most studies that showed a much higher individual prevalence of *S. aureus* UTI among PLWHA (Table 1). A possible explanation for this variation could be due to the zero *S. aureus* UTI recorded by a large sample-sized and relatively recent study by Ya'aba et al (2019). Perhaps the absence of *S. aureus* UTI in the subjects could be caused by the influence of antiretroviral therapy (ART), as most newly diagnosed HIV patients were immediately placed on ART as of 2019 through the

Table 1
Study characteristics, antimicrobial resistance, and virulence genes of *Staphylococcal aureus* nasal carriage and UTI among PLWHA in Nigeria (n=12)

Reference	City/ State	Type of sample	Number of Persons tested	No. of *S. aureus* positive (%)	Total number of MRSA phenotypically positive (%)	Laboratory detection methods	Antimicrobial resistance phenotypes (aside from MRSA)	AMR genes	Virulence gene detected
Olowe et al (2015)	Osun/ SW	Urine	242	13 (25.5)	NT	C	AMX (100.0), COT (69.2), ERY (46.2), CXM (92.3)	NT	NT
Olalekan et al (2012)	Lagos/ SW	Nasal	374	125 (33.0)	60 (16.0)	C/P/M	CHL (47), SXT (90.0)	*mecA* (60, 10.7)	*lukS/F-PV* (in all *S. aureus:* 50, 10.7)
Olalekan et al (2016)	Osogbo/ SW	Nasal	187	51 (27.3)	20 (10.7)	C/P/M	COT (92.0), CHL (53.0), CIP (25.0), ERY (65.0), TET (71.0), and PEN (100.0).	*mecA* (20, 10.7)	*lukS/F-PV* (in all *S. aureus*: 21, 11.2)
O'Malley et al (2015)	Lagos/ SW	Nasal	23	14 (60.9)	5 (21.7)	C/P/M	TET (82.0), LEV (14.3), SXT (76.0)	*mecA* (4, 28.6)	*lukS/F-PV* (In all *S. aureus*: 5, 21.7)
Frank-Peterside et al (2013)	Port Harcourt/ SS	Urine	46	7 (15.2)	NT	C	PEN (100.0), ERY (100.0), SXT (100.0), TET (100.0), AMP (100.0)	NT	NT
Ifeanyichukw et al (2013)	Abakaliki/SE	Urine	80	34 (42.5)	32 (40.0)	C	AMP (38.9), GEN (47.2), CIP (55.6)	NT	NT
Zakka et al (2018)	Jos/ NC	Urine	220	30 (13.6)	NT	C	AMX (100.0), STR (96.7), CHL (96.7), ERY (93.3), GEN (93.3)	NT	NT
Okechukwu and Thairu (2019)	Abuja/ NC	Urine	166	8 (14.8)	NT	C	TET (100.0), GEN (62.5), ERY (12.4)		
Ya'aba et al (2019)	Abuja/ NC	Urine	596	0 (0.0)	NT	C	NT	NT	NT
Abiye et al (2018)	Port Harcourt/ SS	Nasal	217	82 (37.8)	35 (16.1)	C	OXA (24.9), FOX (16.1)	NT	NT
Babatunde et al (2019)	Lagos / SW	Nasal	180	36 (20.0)	12 (6.7)	C/P	SXT (91.0), CIP (77.0), GEN (64.0), ERY (44.0)	*mecA* (12, 6.7)	*lukS/F-PV* (in MRSA: 5 41.7%)
Okwori et al (2014)	Maiduguri/ NE	Nasal	200	42 (21.0)	NT	C	NT	NT	NT

Key
Detection method: C//P/M: Culture / PCR / Molecular typing
NT: Not tested
PEN: Penicillin; AMX: Amoxicillin; ERY: Erythromycin; CHL: Chloramphenicol; CLI: Clindamycin; STR: Streptomycin; TET: Tetracycline; OXA: Oxacillin; FOX: Cefoxitin; LEV: levofloxacin; CIP: Ciprofloxacin; GEN; Gentamycin; SXT: Trimethoprim/sulfamethoxazole; AMP: Ampicillin; AZM; COT: co-trimoxazole

WHO test and treat initiative (90-90-90). However, it is important to remark that nasal colonization with S. aureus has been reported to be a risk factor for subsequent clinical infection in HIV/AIDS patients.

In the studies included in our review, both MRSA and MSSA displayed resistance to beta-lactam and some non–beta-lactam antimicrobials, such as fluoroquinolones, aminoglycosides, tetracyclines, sulfonamides, macrolides, and/or lincosamides (Table 3). Regarding methicillin resistance, out of the 12 studies on *S. aureus* nasal carriage and UTI on PLWHA, only 4 detected the *mecA* gene. Also, some of these studies reported non-congruence results between phenotypic (cefoxitin and/or oxacillin) and the *mecA* positivity rate (Table 1). Although methicillin resistance in some *S. aureus* isolates may be mediated by the novel methicillin resistance gene, the *mecC* gene, rather than the initially reported *mecA* gene. The *mecC*-mediated methicillin resistance is emerging and has been widely reported in wild animals (Abdullahi et al., 2021b).

Nevertheless, it is important to also mention that a previous study that compared the results of oxacillin, cefoxitin disk diffusion and oxacillin screen agar test with *mecA* gene PCR showed dissimilar positivity rates. From the study, oxacillin and cefoxitin disk diffusion tests showed similar sensitivity results, but specificity was higher in the cefoxitin disk diffusion test (96.9% vs. 97.5%) (Demir et al., 2016). Moreover, other studies have indicated that oxacillin often failed to detect low-level heterogeneous MRSA populations and also should not be used in methicillin resistance detection due to lower specificity test results of 56–62% (Matthews et al., 2010; Broekema et al., 2009; Louie et al., 2000).

Furthermore, discrepancies could be explained by a technical problem in PCR such as false colony selection for DNA extraction because of the mixture of MRSA and methicillin-sensitive *S. aureus* isolates instead of a single colony in the first culture plate, loss or mutation in the gene. A technical problem could not be the reason due to using positive and negative control in each run, repeated DNA extraction and retesting. In some instances, the *mecA* gene can be detected, while phenotypically as methicillin-susceptible, representing heteroresistance (Adaleti et al., 2009). This strain also showed growth on the oxacillin screen test, probably due to hyperproduction of β-lactamase or altered ability to bind penicillin-binding proteins (Adaleti et al., 2009). It is reported that these strains have the potential to become highly resistant if exposed to antistaphylococcal penicillins (Adaleti et al., 2009).

A high-level prevalence of AMR was observed in certain classes of antibiotics tested in the eligible studies included in this systematic review. Aside from the cefoxitin/oxacillin resistance detected in MSSA and MRSA, penicillin, sulfamethoxazole-trimethoprim, erythromycin, tetra-

Table 2
Summary of the pooled global prevalence of *Staphylococcus aureus* and MRSA carriages in people living with HIV/AIDS in Nigeria

Samples	Number of studies included	Pooled *S. aureus* carriage rate (%) (range)	OR (95% CI)	*p* value	Number of *S. aureus* studies included	Total number Subjects	*S. aureus*	Pooled MRSA carriage rate (%) (range)	OR (95% CI)	*p* value	Number of MRSA studies included	Total number Subjects	MRSA
Nasal	6	29.6 (20.0-60.9)	5.6 (4.4-7.2)	<0.0001	6	1181	350	13.4 (6.1-40.0)	0.23 (0.24-0.37)	<0.0001	5	981	132
Urine	6	6.8 (6.0-42.5)	Referent	Referent[a]	6	1350	92	NA	Referent	Referent	1	80	32

Key: NA = not available because it's only a single study.

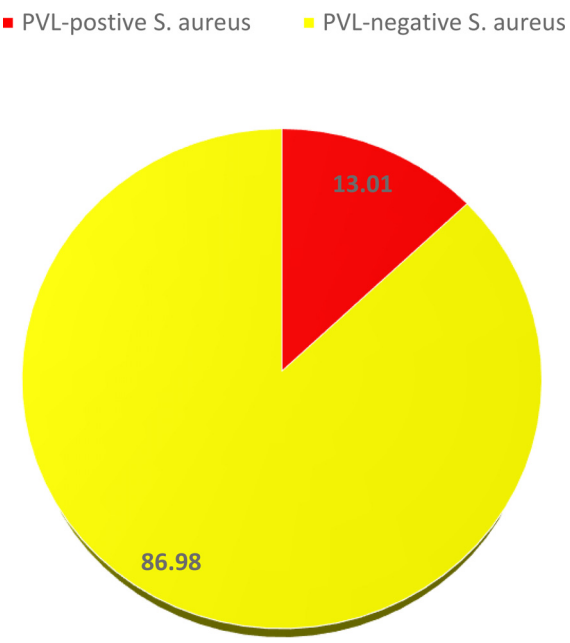

Figure 2. Pooled prevalence of *luk S/F-PV* positive *S. aureus* isolates from PLWHA in Nigeria
NB:
All the three eligible studies were on nasal samples (O'Malley et al., 2015; Olalekan et al., 2012; Olalekan et al., 2016).

cycline and chloramphenicol resistance were the most predominant in *S. aureus* nasal colonization and UTI studies in PLWHA.

Out of the 12 eligible studies, MDR of at least 70% of all *S. aureus* isolates was reported in 5 studies (3 and 2 in nasal colonization and UTI studies, respectively). This is within the range of 30–84.6% reported in other HIV-infected cohorts (Egyir et al., 2016), but higher than what has been recorded by studies on the general population (6–35.7%) (Egyir et al., 2013; Dekkar et al., 2016; Egyir et al., 2014). The prevalence of MDR observed in our systematic review is alarming. In Nigeria and many other developing countries, antibiotics may be acquired without any prescriptions (Donkor et al., 2019). Also, self-medication with antibiotics is common practice, with the prevalence reportedly high. Furthermore, antibiotic misuse is high in livestock and hospital settings in Nigeria (Alhaji, et al., 2018; Abubakar, 2020). These factors contribute to the high prevalence of MDR observed in the current systematic review. The high prevalence and rates of self-medication among the general public in Nigeria could explain the higher prevalence of cotrimoxazole resistance among *S. aureus* isolates of nasal and UTI origin among the HIV-infected persons, as this antibiotic is used in prophylaxis in PLWHA. The significantly higher prevalence of erythromycin and tetracycline resistance among some of the studies on PLWHA suggests a livestock-associated *S. aureus* strain (Fan et al., 2016).

In relation to the PVL-carrying *S. aureus* in PLWHA, Olalekan et al (2012), Olalekan et al (2014), and O'Malley et al (2015) reported prevalences of 10.7%, 11.2%, 21.5%, respectively of PVL-positive-*S. aureus* strains (in both MSSA and MRSA), while Babatunde et al (2019) reported MRSA-PVL carrying strains. However, the pooled prevalence of PVL-positive *S. aureus* was 13.0% (Figure 2). Previous studies from Sub-Saharan Africa suggest that the region is MSSA-PVL strains (Eibach, et al., 2019; Egyir et al., 2014). The PVL is a pore-forming toxin that is often associated with abscesses and represents an interface of *S. aureus* and host complexity (Seilie et al., 2017). Worthy to mention is that one of the three studies reported the genetic lineage of MRSA-PVL positive isolates as ST152 (*spa* type t355). This is a lineage that has been widely distributed in Nigeria and other African countries, and it has frequently been associated with

Table 3
Antimicrobial resistance phenotypes and percentages of *S. aureus* nasal and UTI isolates from PLWHA in Nigeria

Reference	Sample	AMR Phenotypes (% of isolates)	MDR (AMR to ≥3 classes) to 50% isolates	No. of studies with MDR in Urine samples	No. of studies with MDR in Nasal samples	*Chi* squared
Olowe et al (2015)	Urine	AMX (100.0), COT (69.2), ERY (46.2), CXM (92.3)	Yes	Yes		
Olalekan et al (2012)	Nasal	CHL (47), SXT (90.0)	No			
Olalekan et al (2016)	Nasal	COT (92.0), CHL (53.0), CIP (25.0), ERY (65.0), TET (71.0), PEN (100.0).	Yes		Yes	
O'Malley et al (2015)	Nasal	TET (82.0), LEV (14.3), SXT (76.0)	No			
Frank-Peterside et al (2013)	Urine	PEN (100.0), ERY (100.0), SXT (100.0), TET (100.0), AMP (100.0)	Yes	Yes		
Ifeanyichukw et al (2013)	Urine	AMP (38.9), GEN (47.2), CIP (55.6)	No			
Zakka et al (2018)	Urine	AMX (100.0), STR (96.7), CHL (96.7), ERY (93.3), GEN (93.3)	Yes	Yes		
Okechukwu and Thairu (2019)	Urine	TET (100.0), GEN (62.5), ERY (12.4)	No			
Abiye et al (2018)	Nasal	OXA (24.9), FOX (16.1)	No			
Babatunde et al (2019)	Nasal	SXT (91.0), CIP (77.0), GEN (64.0), ERY (44.0)	Yes		Yes	
Total	10	NA	5 (MDR)	3	2	0.4 (p= 0.5271)

Table 4
Molecular typing reports of *S. aureus* isolated from the nasal cavities of people living with HIV/AIDS in Nigeria

Citation	No. of Subjects/ *S. aureus* (%)/ MRSA (%)	*spa* of MSSA	ST of MSSA (%)	*spa* of MRSA	ST of MRSA	*spa* of PVL-positive
Olalekan et al (2012)	374/ 125 (33.0)/ 60 (16.0)	t774, t7806, t084, t355, t127	ST15	t064, t951, t008, t7816, t197, t7802	ST8, ST25	t064
Olalekan et al (2016)	187/ 51 (27.3)/ 20 (10.7)	t304, t967, t1476, t2658, t6863, t7808, t2304, t2554, t4976	NT	t064, t3772, t311, t084	ST5, ST8, ST15	NT
O'Malley et al (2015)	23/14 (60.9)/ 5 (21.7)	t064, t355, t091, t5066	NT	t064, t657	NT	t355

Key:
spa = staphylococcal protein A
ST= Sequence Type
NT = Not tested

skin and soft tissue infection (Shittu et al., 2011; Ruimy et al., 2008; Monecke et al., 2007).

Although there were highly diverse genetic lineages of MSSA in nasal and UTI *S. aureus* strains, the predominant Sequence Types (STs) and *spa* types detected among the MRSA-positive isolates were ST5, ST8, ST15, ST25 and *spa* type t064 and t084. Moreover, the diverse genetic lineages reported among the MSSA isolates included t774, t7806, t084, t355, t127, t304, t967, t1476, t2658, t6863, t7808, t2304, t2554, t4976, t355, t091, t5066. Most of them are associated with CA-*S. aureus* colonization and infection.

For instance, Olalekan et al (2014) indicated the detection of pig-associated LA-MRSA-ST5 of the *spa* type t311 among PLWHA. This suggests that humans in contact with livestock have the potential to become colonized with LA-MRSA ST5 isolates. LA-MRSA ST5 isolates are particularly concerning to the public health community because, unlike the isolates in the ST398 and ST9 lineages, isolates in the ST5 lineage are a significant cause of human disease in both the hospital and community settings globally (Hua et al., 2018). Conversely, the CA-MRSA- ST8 also known as the US300 pandemic clone and often hypervirulent was the most frequently detected lineage in PLWHA (Olalekan et al., 2014; O'Malley et al., 2015). It has been documented that the MRSA-ST8-t064 strain is the most common and causes severe infections in PLWHA in Nigeria (Olalekan et al., 2012; Olalekan et al., 2014; O'Malley et al., 2015).

In relation to the MSSA strains, ST15-t084 was the predominantly reported genetic lineage. This clone has previously been detected in the nasal cavity of a cow, pigs and pig farmers in Senegal (Fall et al., 2012; Mama et al., 2019). This strain was previously considered human-specific (ST15) in a previous study in the past 10 years (Cuny et al., 2010). However, the absence of immune evasion cluster biomarker, the *scn* gene as recently reported by Mama et al (2019) suggests its zoonotic potential, especially among livestock farmers.

Conclusion

Moderate and high pooled prevalences of MRSA and *luk-F/S-PV*-positive *S. aureus* were obtained from PLWHA, respectively. The reported t084 and t064 are quintessential spa types in Africa and are often associated with community-acquired (CA)-MRSA. The report of *luk-F/S-PV-Positive* MRSA is of great concern in clinical chemotherapy. These findings emphasize the importance of routine screening for MRSA among PLWHA in Nigeria and other HIV endemic countries. It is very important to implement long-term surveillance of the genetic lineages of *S. aureus* isolates as this will provide comprehensive data on the ecology and molecular epidemiology of *Staphylococcus aureus*/MRSA to understand their relevance in the care and management of HIV/AIDS.

Declaration of Competing Interest

None declared by all authors

Author Contributions

Conceptualisation: I.N.A. methodology: I.N.A. and R.I.; software analysis: I.N.A. validation: I.N.A., R.I. and Y.U.; formal analysis: I.N.A. data curation: I.N.A., R.I. and Y.U.; writing—original draft preparation I.N.A., R.I. and Y.U.; writing—review and editing: I.N.A., R.I.. and Y.U. All authors have read and agreed to the published version of the manuscript.

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Supplementary materials

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