JOHN OLADAYO AWOSANYA
EPIDEMIOLOGY OF
MRSA CARRIERS
AMONG AFRICAN
POPULATION IN
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NEAR EAST UNIVERSITY
INSTITUTE OF GRADUATE STUDIES
DEPARTMENT OF MEDICAL MICROBIOLOGY
AND CLINICAL MICROBIOLOGY

EPIDEMIOLOGY OF METHICILLIN RESISTANCE *STAPHYLOCOCCUS AUREUS* CARRIERS AMONG AFRICANS POPULATION IN NORTHERN CYPRUS

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We certify that we have read the thesis submitted by **John Oladayo AWOSANYA** titled **Epidemiology of Methicillin Resistance *Staphylococcus Aureus* Carriers Among African Population In North Cyprus** and that in our combined opinion it is fully adequate, in scope and in quality, as a thesis for the degree of Master of Educational Sciences.

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I hereby certify that all information, documents, examinations, and results in this thesis were collected and presented in accordance with the Near East University Institute of Graduate Studies' ethical guidelines and academic rules. I further declare that I have properly referenced and cited any data and information that are not original to this work, as required by these rules and conduct.

John Oladayo Awosanya

20/1/2024

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John Oladayo Awosanya

Abstract

Epidemiology of Methicillin Resistant *Staphylococcus Aureus* Carriers Among African Population In Northern Cyprus

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In order to prevent treatment failure, clinical microbiology laboratories play a crucial role in the quick and accurate diagnosis of methicillin-resistant *Staphylococcus aureus* (MRSA). The purpose of this study was to identify the optimal phenotypic approach and investigate the epidemiology of MRSA carriers in African communities by contrasting traditional methods with the cefoxitin disc diffusion method.

Study was carried out in the Northern Cyprus between October 2023 – December 2023. The methods included were Cefoxitin disk diffusion and CHROM agar-MRSA methods

Seven (4.6%) of the 150 S. aureus isolates were obtained from clinical specimens. The cefoxitin test was chosen as the gold standard technique. The cefoxitin disk diffusion demonstrated 100% and 100% sensitivity and specificity, while CHROM agar demonstrated 100% and 50% sensitivity and specificity, respectively. Using the cefoxitin disk diffusion technique and Chrom agar, 7 S. aureus were found to be MRSA. For the detection of MRSA,all phenotypic approaches shown great sensitivity and specificity. However, the sensitivity and specificity of the cefoxitin disk diffusion approach were higher than those of the other methods.

***Key Words**:* cefoxitin disk,S.aureus,crome agar,MRSA

ÖZET

Afrika Nüfusunda Metisiline Dirençli Staphylococcus aureus Taşıyıcılarının EpidemiyolojisiKuzey Kıbrıs'ta

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Tedavi başarısızlığını önlemek için klinik mikrobiyoloji laboratuvarları, metisiline dirençli Staphylococcus aureus'un (MRSA) hızlı ve doğru teşhisinde önemli bir rol oynamaktadır. Bu çalışmanın amacı, geleneksel yöntemleri sefoksitin disk difüzyon yöntemiyle karşılaştırarak, optimal fenotipik yaklaşımı belirlemek ve Afrika topluluklarındaki MRSA taşıyıcılarının epidemiyolojisini araştırmaktı.

Çalışma Ekim 2023 – Aralık 2023 tarihleri arasında Kuzey Kıbrıs'ta gerçekleştirildi. Dahil edilen yöntemler Sefoksitin disk difüzyon ve CHROM agar-MRSA yöntemleriydi.

150 S. aureus izolatının 7'si (%4,6) klinik örneklerden elde edildi. Altın standart teknik olarak sefoksitin testi seçildi. Sefoksitin disk difüzyonu %100 ve %100 duyarlılık ve özgüllük gösterirken, CHROM agar sırasıyla %100 ve %50 duyarlılık ve özgüllük gösterdi. Sefoksitin disk difüzyon tekniği ve Chrom agar kullanılarak 7 S. aureus'un MRSA olduğu belirlendi. MRSA'nın tespiti için tüm fenotipik yaklaşımlar büyük hassasiyet ve özgüllük göstermiştir. Ancak sefoksitin disk difüzyon yaklaşımının duyarlılığı ve özgüllüğü diğer yöntemlere göre daha yüksekti.

Anahtar Kelimeler: sefoksitin diski,s.aureus,krome agar,mrsa

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List of Abbreviations

TRNC: Turkish Republic of Northern Cyprus

MNE: Ministry of National Education

MRSA: Methicillin Resistance *Staphylococcus aureus*

MRSE: Methicillin Resistance *Staphylococcus epidermis*

MSSA: Methicillin Sensitive *Staphylococcus aureus*

EUCAS: European Committee on Antimicrobial Susceptibility Testing

CA-MRSA: Community-Acquired Methicillin Resistance *Staphyloccus aureus*

HA-MRSA: Hospital -Acquired Methicillin Resistance *Staphyloccus aureus*

CLSI: The Clinical and Laboratory Standards Institute

CHAPTER I

Introduction

Overview

Multidrug-resistant bacteria (MDRBs) are microorganisms that exhibit resistance to one or more antimicrobial drugs. Typically, this means that they are only vulnerable to one or two antimicrobials that are commercially accessible. This classification comprises microorganisms with developed resistance to one or more of agents included in three or more antimicrobial categories. Several multidrug-resistant bacteria (MDRBs) of Methicillin-resistant *Staphylococcus aureus* is one clinical difficulty. (MRSA), vancomycin-resistant *Staphylococcus aureus* (VRSA, VISA, and VRSA), vancomycin-resistant *Enterococci* (VRE), prolonged spectrum beta-lactamases (ESBLs) that produce gram-negative bacilli, multidrug-resistant *Streptococcus pneumoniae* (MDRSP), carbapenem-resistant *Enterobacteriaceae* (CRE), and multidrug-resistant *Acinetobacter baumannii*. Globally, contagious illnesses brought on by MDRB represent a significant burden. They've been one of the primary causes of death for a long time., and increasing threats as well as human advancement and health security, disability particularly in emerging nations (Nii-Trebi, 2017). Antimicrobial resistance management poses difficulties in community and clinical settings, necessitating a comprehensive approach incorporating cooperation amongst several stakeholders across the care continuum. For example, a significant proportion (18–33%) of those who have MRSA infections follow MRSA colonization. Furthermore, Methicillin-resistant *Staphylococcus aureus* (CA-MRSA) strains acquired in the community are responsible for an increasing percentage of MRSA infections that begin in hospitals. According to estimates from the Centers for Disease Control and Prevention (CDC), antibiotic resistance results in around 2 million illnesses and 23,000 deaths annually in the United States (HRET, 2017).

Staphylococcus aureus, especially the strain resistant to methicillin (MRSA), is a pathogen that affects humans. with significant issue since it may cause infections in hospital and community settings globally (Stefani et al., 2010). pneumonia, Skin, bacteremia, and sepsis, soft tissue infections (SSTIs), are frequently associated with MRSA (Chambers et al., 2009). The persistent recognition of MRSA as a serious

public health problem is due to the tremendous obstacles associated with both treatment and infection control of this important disease. In the past, MRSA infections were typically associated with healthcare settings; they would typically strike people who had just had surgery, dialysis, hospitalization, long-term care facility residence, or other underlying medical issues. Healthcare-associated MRSA (HA-MRSA) frequently showed resistance to many non-beta-lactam antibiotic classes and was predominantly responsible for pneumonia, bacteremia, or other invasive infections (Patel, 2009). Over the previous few decades, there has been a notable increase in MRSA infections in individuals without identified risk factors, impacting otherwise healthy members of the population who have never had contact with the medical system (CA-MRSA) (David & Drum, 2010).

Through gene transfer, MRSA gains the SCCmec element from MSSA. Specifically, it incorporates the mecA gene, which codes for PBP-2a. In MRSA, this protein confers resistance to most beta-lactam antibiotics. A serious hazard to public health is the continuous rise in MRSA incidence and transmission in veterinary clinics, hospitals, and community settings. Furthermore, the combination of antibiotic resistance and the increased pathogenicity of MRSA, which is fueled by a number of *S. aureus* produced virulence factors, weaken host immunity and causes serious infections in both people and animals.

Numerous clinical signs can be caused by MRSA., from infections of the skin and soft tissues to more serious illnesses such toxic shock, septicemia and bacteremia, scalded skin syndrome. Furthermore, growing resistance of MRSA to various medicines emphasizes the necessity of investigating substitute approaches to lessen financial and human damages. The identification of the mecA gene or its homologs, mecB and mecC, is the main technique for detecting MRSA. The staphylococcal chromosomal cassette mec (SCCmec types I–XIV) contains the genes encoding the penicillin-binding protein 2a (PBP2-a). Remarkably, PBP2-a is less receptive to beta-lactam medications. (Urushibara et al. 2020; Uehara 2022).

Research Purpose

The purpose of this study is to determine how common methicillin-resistant Staphylococcus aureus is among African residents of Northern Cyprus.

This primary purpose may lead to the subsequent secondary objectives, such as:

1. To investigate and present a numerical representation of the frequency of Methicillin-Resistant Staphylococcus aureus in African residents of Northern Cyprus.
2. Examining how MRSA proliferates in diverse populations and settings
3. Researching MRSA carriers' frequency, distribution, and patterns of transmission in Northern Cyprus

Research Significance

In order to reduce the negative effects of this antibiotic-resistant illness on public health, it is essential to know the distribution of MRSA in a particular neighborhood. In the event that MRSA infections are common, community and medical research contribute to improving our knowledge of MRSA's global circulation, which is a fear for global health. Planning to stop MRSA from spreading and from emerging in new places that would be severely damaged requires this information.

Research Questions

The following research questions are intended to be addressed by this study:

1. What is the existing prevalence rate of MRSA in Northern Cyprus?
2. What are the predominant risk factors associated with MRSA colonization among Africans in Northern Cyprus?
3. Are there variations in MRSA prevalence based on demographic factors such as age, gender, or socioeconomic status in Cyprus?
4. How does antibiotic usage history correlate with MRSA prevalence in Cyprus?
5. To what extent do existing infection control practices effectively minimize the emergence of MRSA in hospital settings and the community in Cyprus?

Limitation of Study

Potential bias in sampling might arise from the study's sample not being entirely representative of the total population. For example, the results could not apply to a larger population if the study only looks at a certain age range or health care environment.

The precision of prevalence estimations may be impacted by the sensitivity and specificity of the diagnostic techniques utilized for MRSA identification. Variability in lab methods might result in inconsistent results.

Definition of Key Terms

Methicillin-Resistant *Staphylococcus aureus*: Methicillin-Inhibited the bacteria *Staphylococcus aureus*, sometimes referred to as MRSA, is resistant to several medicines, including methicillin and other beta-lactam drugs. Healthy people frequently have *Staphylococcus aureus* on their skin and in their noses, but MRSA is a type of the bacteria that has developed resistance to several medications.

Healthcare-Associated and Community-Associated: Healthcare-associated MRSA (HA-MRSA) infections usually affect those who have just undergone surgery, as admitted to the hospital, or been in contact with medical facilities. However, apparently healthy community members may get infected with community-associated MRSA (CA-MRSA) infections.

Antibiotics: A family of drugs known as antibiotics is used to treat bacterial illnesses by either eradicating the germs or stopping their development. They have been crucial in lessening the effects of infectious illnesses and are an essential tool in contemporary medicine.

CHAPTER II

Literature Review

Staphylococcus aureus

The genus *Staphylococcus* now contains 81 species and several subspecies. Opportunistic pathogens or mammal commensals make up the bulk Species within the Genus. Many species are important for both medicine and veterinary care. *Staphylococcus aureus,* or S. aureus, is among the most significant and widespread Staphylococcus species for the pathogenicity to humans (Haag et al., 2019).

Gram-positive, cocci-shaped bacteria that are stained purple by Gram stain are known as *Staphylococcus aureus.* These bacteria are typically seen in clusters that are referred to as "grape-like." These organisms may thrive on medium in up to 10% salinity; colonies are commonly yellow or golden in color (the word "aureus" refers to these colors). These organisms can thrive at temperatures ranging from 18 to 40 degrees Celsius, both aerobically and anaerobically facultative (Lowy, 1998). According to Radigue and Vandenesch (2014), the most popular biochemical tests for identification are Mannitol fermentation positive, which is used to distinguish *Staphylococcus epidermidis* from other Staphylococcus species; coagulase-positive, which is used to distinguish *Staphylococcus aureus* from other Staphylococcus species; and catalase positive, which is used to identify all pathogenic Staphylococcus species. Most healthy individuals have *S. aureus* on their skin and mucous membranes, which are often seen in the nasal area. According to Butcher and Corey (2008), it is also found in the environment and typical human flora.

Humans are the primary reservoir for *Staphylococcus aureus,* which is found on the skin and mucous membranes. These bacteria can also be found in drug-resistant forms like MRSA. Up to 50% of individuals are thought to be colonized, and 15% of people have S. aureus in their anterior nares permanently (Chambers, 2005). Higher rates of S. aureus colonization (up to 80%) are typically seen in certain populations, including healthcare professionals, those who frequently use needles (diabetics and IV drug users), hospitalized patients, and people with impaired immune systems. *S.*

aureus can spread from person to person by intimate touch or by fomites (Tong et al., 2015).

Many human infections, including bacteremia, infective endocarditis, infections of the skin and soft tissues, osteomyelitis, septic arthritis, infections from prosthetic devices, infections of the lungs (including pneumonia and empyema), gastroenteritis, meningitis, toxic shock syndrome, and urinary tract infections, are caused by *S.aureus*, one of the most common bacteria in the world (Deleo et al., 2007). Depending on the strains and the site of the infection, these bacteria can cause invasive infections and/or toxin-mediated diseases. The pathogenesis of *S. aureus* infections varies greatly depending on the type (Tong et al., 2015) Among the strategies for avoiding the host immune response include the formation of an anti-phagocytic capsule, the sequestration of host antibodies or antigen masking by Protein A, the formation of biofilms, intracellular survival, and the inhibition of leukocyte chemotaxis (Foster, 2005). Later, TSS instances unrelated to menstruation were shown to be associated with invasive infections such as pneumonia and infective endocarditis (Garcia, 2011). TSS was first diagnosed in 1978. The syndrome's characteristics include flu-like symptoms, rash, fever, hypotension, aching muscles, vomiting, diarrhea, disorientation, abdominal pain, and eventually multiple organ failure. While childhood infections are widespread, adult cases of Staphylococcal Scalded-Skin (SSS) condition also referred to as newborn Ritter von Ritterschein illness are rare (Udo et al., 2016).

The first beta-lactam antibiotic created to treat *S. aureus* infections was penicillin. Before the discovery of penicillin, *S. aureus* infections were typically deadly (Roca et al., 2015). Nonetheless, the prognosis of patients with severe *staphylococcal* infections was significantly improved when penicillin was introduced to treat infections brought on by S. aureus. However, as penicillin was used in medicine, *S. aureus* strains resistant to it quickly emerged (Roca et al ., 2015).

Penicillin resistance results from the bacteria producing penicillinase, which renders the antibacterial antibiotic inactive. The beta-lactam ring, which is essential to these medications' antibacterial action, is hydrolyzed by penicillinase. Methicillin, commonly referred to as meticillin or Staphcillin, was developed as a result of

ongoing research into antibiotics that are effective against Staphcillin-resistant *Staphylococcus aureus* (Shallcross er al., 2013).

Methicillin is a semisynthetic derivative of penicillin that was created by changing the structure of penicillin to give it resistance to penicillinase in the late 1950s. Methicillin functions similarly to other penicillins in that it destroys bacteria by preventing the manufacture of their cell walls (Shallcross et al., 2013).

Origin of Methicillin resistant *Staphlococcus aureus*

Methicillin-Inhibited MRSA is derived from *Staphylococcus aureus,* a common bacteria that is present on both human and animal skin and mucous membranes. Its increase was primarily caused by the introduction of beta-lactam medicines, including methicillin, in the middle of the 20th century to treat penicillin-resistant strains of *Staphylococcus aureus* (Chamber, 2001).

An essential step in the evolution of MRSA is the acquisition of the staphylococcal chromosomal cassette mec (SCCmec) element. This genetic element carries the mecA gene, which codes for a modified penicillin-binding protein (PBP2a) with a decreased attachment for beta-lactam antibiotics (David & Drum, 2010).

The distinction between HA-MRSA and CA-MRSA infections as epidemiological terminology is somewhat hazy, notwithstanding their usefulness (Seybold et al., 2007). Even though there are known healthcare-associated risk factors for HA-MRSA infection, dialysis, living in a long-term care facility and indwelling percutaneous medical devices and catheters and surgery community-onset HA-MRSA infections have been observed among patients in community settings more frequently (Choo, 2017). Comparably, extraordinarily effective community-based clones have entered the healthcare environment and developed into nosocomial infections. (Maree et al., 2007).

There are notable variations in the phenotypic and genetic composition of MRSA strains associated with infection in both scenarios, despite the fact that it might be challenging to differentiate between MRSA isolates categorized as HA-MRSA or

CA-MRSA. HA-MRSA strains often contain SCCmec types I or III whereas CA-MRSA isolates typically contain SCCmec types V, IV and VI (Kong et al., 2016).

Hospital acquired *Staphylococcus aureus* (HA-MRSA)

Older adults and immunocompromised individuals who have used broad-spectrum antibiotics extensively over an extended period are important risk factors for HA-MRSA infections (Kurkowski, 2007). Hospital-acquired infections are caused by HA-MRSA since it is resistant to nearly all b-lactam antibiotics (Lindsay, 2013). Contrary to HA-MRSA, CA-MRSA may be more common in thriving individuals and may be more prevalent in those who work in prisons, day care centers, the entertainment industry, and the armed forces due to their close quarters (Daum, 2007). As a multidrug-resistant bacterium, HA-MRSA is responsible for several illnesses in both adults and children that are related to healthcare. Patients with skin wounds that might be a source of infection and those with weakened immune systems have higher infection rates.

Individuals with weakened immune systems and those with wounds on their skin that might be the source of illness transmission (Köck et al., 2010). These strains are the most common bacterial strains that cause these types of diseases in both people and animals. The important HA-MRSA stains are the sequence strain (ST), spa strain and CC strain. Among the CC are sequence type 239 (ST239), CC30, CC5, CC45, CC8, and CC8 (Klevens et al., 2007).

Community acquired *Staphlococcus aureus* (CA-MRSA)

Infections caused by community-acquired MRSA (CA-MRSA) can affect the circulation, bones, joints, lungs, surgical sites, skin, and soft tissues (Dantes et al., 2013).

A comparable strain was found in athletes with skin abscesses as well (Takizawa et al., 2005). There were records of up to 29.8% of CA-MRSA infections; At Saudi Children Hospital, unexplained risk variables were responsible for the remaining 70.2%. A study conducted on children who were outpatient in Riyadh, Saudi Arabia

between 2005 and 2008 found that 70.2% of cases had unknown risk factors, while 29.8% of cases tested positive for CA-MRSA.

In the beginning, CA-MRSA was thought to be a nosocomial strain with transmission of infected people outside of hospitals. The clinical signs of CA-MRSA clones are comparable to those of MSSA strains, and they are remarkably sensitive to non-b-lactam antibiotics, unlike the HA-MRSA strains that are commonly seen in hospital contexts. The presence of PVL, the genetic composition of the resistant genes and genetic lineage are the three important traits that separate CA-MRSA strains from HA-MRSA strains.

There are more distinctions between CA-MRSA and HA-MRSA. Because it can open holes in leukocytes thanks to the exotoxin Panton-Valentine leukocidin (PVL), it is thought to be more pathogenic. This exotoxin is assumed to be the cause of the increased frequency of sepsis, necrotizing pneumonia, soft tissue, and skin infections associated with CA-MRSA, although others disputing its link to PVL. Indeed, it is believed that 80–95% of CA-MRSA infections affect the skin and soft tissues, whereas HA-MRSA infections are also associated with bloodstream, urinary tract, and respiratory tract infections (Deurenberg &Stobberingh, 2009).Based on existing information, SCCmec, specifically SCCmec IV, introduces via a gene transfer mechanism many unique MSSA relatives stains that are already in use into CA MRSA strains (Enright et al., 2002).

LA MRSA Infections in Food and Animals

Food animals as well as the food industry are starting to face a severe threat from MRSA infections, despite the fact that it was previously believed that these illnesses spread more slowly in companion and food animals. According to Javed et al. (2021) LA-MRSA is a significant cause of buffaloes and mastitis in cows, which can lead to a reduction in or absence of milk supply. Furthermore, chondronecrosis, septic conditions and comb necrosis and septic conditions are caused by LA-MRSA in chicken (Fluit, 2012). It is possible for humans to get LA-MRSA from almost any companion animal, including cats, dogs, and horses. Interacting with these creatures, either directly or indirectly. Apart from mammals, other animals that have been

shown to be colonized by LA-MRSA include foxes, rabbits and wild birds such as pheasants, pigeons , gulls, and ducks, (Smith et al., 2009).

The primary bacteria found in goat mastitis milk that has been identified as MRSA), which can infect people who drink tainted milk.Staphylococcal enterotoxins (SE), a common why food poisoning occurs, may be present in contaminated milk in specific forms. Every SE gene has the potential to induce diseases specific to its host, such as human infection caused by staphylococcal enterotoxin B (Altaf et al., 2020). One of the main causes of clinical and subclinical mastitis in sheep and goats is MRSA, which raises the somatic cell count in milk and renders it unfit for human consumption (Muzammil et al., 2021).

Reports have also been made of livestock-associated methicillin resisntant (LA-MRSA) in nares and cloaca of healthy poultry birds. It can result in arthritis, otitis, pyoderma, omphalitis, and urinary tract infections in poultry birds (Pickering et al., 2022). Following the use of several antimicrobial drugs. MRSA of spa types T011 and T157 was discovered. While ST398 is a novel MRSA strain linked to animals that are also present in poultry.

Epidemiology of MRSA

One of the most crucial aspects of MRSA epidemiology is the organism's worldwide appearance and spread. There are two known ways that MRSA spreads: either by the dissemination of clones that already exist between people and animals, or from humans to humans or with the acquisition of SSCmec elements through horizontal gene transfer (Lee et al,. 2018). As the main nosocomial infections, MRSA is now recognized to be more prevalent in hospital settings. The CDC states that MRSA is recognized as a significant concern to public health due to its rising incidence in healthcare facilities, the general population, and animals, as well as its ability to spread between people and animals, the infection rates and problems with treatment (Ferri et al., 2017). The yearly health costs associated with MRSA infections are estimated to be $3 billion on average. Recently, CA-MRSA has also become more prominent as a pathogen. MRSA predominantly causes infections of the skin and soft tissues that result in bacteremia, which raises death rates to between 15% and 60% (Lee et al .,2013).

The incidence of HA-MRSA has been seen to differ recently throughout the nations; for instance, it was found to be 46% in India in 2009, (Arora et al. 2010), Siddiqui et al. (2017) reported a higher prevalence from Pakistan, 58.4% higher In Portugal (Tavares et al.2013) 45% in China from 2015 to 2017 (Chen et al., 2022), and (Engel et al. 2022) and reported a higher prevalence from Norway from 2008 to 2016. But as HA-MRSA incidence rises globally, MRSA prevalence falls in many other nations as well, with 4.6% reported in Germany (Sassmannshausen et al., 2016).

According to Hamdan-Partida et al. (2022), 19.1% of the population is from Mexico, 15.1% is from Australia, and 26% is from Italy. Comparable rising and falling trends in MRSA prevalence have also been observed for CA-MRSA in various countries, comprising 61% from Norway (Enger et al., 2022), 64.7% from India (Alvarez and Reddy, 2012), , 84.9% from Australia (Coombs et al., 2022), 79% from Japan (Ogura et al., 2022) and China has a higher prevalence of 1.7% (Bi et al., 2018) and 24% (Chen et al., 2022) than Egypt (16%). Improved national preventive program implementation may be connected to this drop in the prevalence of HA- and CA-MRSA. The rise and fall in HA- and CA-MRSA prevalence might be related to humans acquiring more LA-MRSA from animal reservoirs, particularly through food and companion animals.

A number of EU-EEA countries continue to report notable MRSA prevalence. As at year 2003 and 2005, Cyprus was found to have the highest percentage of MRSA (64%), when compared to many other Mediterranean countries. As an illustration of the substantial strain on the healthcare system, reports of the prevalence of invasive MRSA infections between the year 2015 and 2018 varied from 25 to less than 50% (ECDC, 2022). There is a dearth of information about the genetic traits of clinical *S. aureus* isolates from Cyprus. Results show that 27.7% of the MRSA species collected from patients at an university hospital in Northern Cyprus were PVL positive strains. Sustained monitoring and detailed analysis of MRSA strains in nation's hospitals are essential for stopping the spread of highly pathogenic nosocomial infections and putting improved infection control plans into action. The identification of MRSA SCCmec types that are prevalent in both the community and

hospital environment should be accomplished by further comprehensive molecular typing of clinical MRSA isolates.

MRSA Pathophysiology

Methicillin-Resistant *Staphylococcus aureus* (MRSA) pathophysiology entails intricate interactions between the human immune system and the bacterium. Along with other *Staphylococcus aureus* strains, MRSA can cause a different cases of infections such as skin and soft tissue infections to serious, sometimes fatal diseases or illnesses. *Staphylococcus aureus* is a commensal and infectious bacteria that commonly stays in the anterior nares of animals and humans. It can also invade the gastrointestinal tract, axillae, and groin. The key phases in the development of an infectious illness include systemic infection colonization, virulence, abscess formation,infection onset,regulation, and adaptation with the help of several virulence factors.

Colonization increases the chances of having a bacterial infection when the host's defenses are compromised by physical stress or some ailments (Wertheim et al., 2005). Many proteins at the surface known as "microbial surface components recognizing adhesive matrix molecules" (MSCRAMMs) are present in the methicillin-resistant isolates of *Staphylococcus aureus*, or MRSA. These proteins bind to host cell collagen fibers, fibronectin, and fibrinogen to attack host tissues. According to Foster et al. (2014), these variables may result in infections of the endovascular system, bones, joints, and prosthesis.

In addition to these, *S. aureus* also generates other kinds of toxins, including hemolysin toxins, enterotoxins, exotoxins, TSST-1, and PVL toxins. Furthermore, some *S.aureus* strains emit superantigens, which can lead to diseases including toxic shock syndrome (TSS) and food poisoning (Vandenesch et al., 2012). The pathophysiology of *S.aureus* is significantly influenced by the typical expression of virulence factors. Virulence factors only manifest in response to the bacterium's need to reduce needless metabolic demands. Secreted proteins like toxins, are produced in the stationary phase, the logarithmic growth phase is when MSCRAMMs usually express. While late toxin synthesis aids in the spread of infection into the circulation,

early expression of the MSCRAMM protein aids in the first colonization of tissue locations.

Hospital-acquired methicillin-sensitive *S.aureus* (MSSA) is a less virulent and less deadly bacterium than healthcare-associated MRSA (HA-MRSA). However, the precise pathogenicity mechanism remains unclear. Nonetheless, it is believed that the mecA gene-expressed PBP2-a protein, which is linked to b-lactam antibiotic resistance, directly affects immunopathology during MRSA infection. MRSA strains are more likely to survive than MSSA strains due to poor peptidoglycan cross-linking with b-lactam antibiotics induced by PBP2-a (Yao et al., 2010).

The introduction of LA-MRSA, its dissemination to humans, the discovery of human strains in animals all increase MRSA's lethality by extending its host range, changing its genome, and increasing resistance to drugs .Recent findings indicate that MRSA pathogenicity is influenced by the staphylococcal protein A gene in CC398 (Peeters et al., 2015). While CA-MRSA is mostly responsible for a range of SSTIs, from small infections like impetigo and funcles to severe infections like necrotizing fascilitis and pneumonia, athletes, children, and hospitalized patients are prone to HA-MRSA infections. CA-MRSA causes fewer serious infections in humans and animals than HA-MRSA does.

Risk Factors of MRSA

Extended hospital stays, admissions to intensive care units, recent hospital stays, use of antibiotics recently, HIV infection, MRSA colonization, nursing home admissions, invasive procedures, haemodialysis, and discharges with a long-term indwelling urinary catheter or central venous access are among the risk factors that are frequently associated with MRSA infection. MRSA infections are more common in healthcare personnel who interact directly with patients who are afflicted with the virus.

Hospitalization is significantly more likely in people over 65. even if it is not thought of as a risk factor for MRSA infection in and of itself. Therefore, there is an indirect correlation between getting older and acquiring MRSA. Being admitted to a hospital

where HA-MRSA is more common than CA-MRSA or living in an area where both are prevalent despite the fact that it is not considered an indication of risk for MRSA infection (Celbak and Malone, 2018).

Through direct or indirect contact with contaminated body fluids, MRSA may spread both in the community and in hospitals (CDC, 2014). On surfaces, MRSA can live for several days or even months. MRSA is present in around 2% of the general population, and infections can happen to anybody (CDC.2014). Nonetheless, those with compromised immune systems can be more prone to infection

Environmental Reservoirs and Fomite; MRSA has been found in a broad range of habitats, mostly the constructed environment, but also naturally occurring freshwater and marine areas including parks and beaches.

These areas consist of: wastewater treatment plants; public spaces, athletic centres; city streets; college campuses and laboratories; shared housing; day-care centres; jails; health clinics; and veterinary hospitals. ATDs, DVD rental machines, and copper alloy coins are examples of fomites, which are inanimate things that may spread infectious pathogens.

The majority of environmental reservoirs of concern were found in non-hospital individuals and animal health-care settings (clinics, ambulances,veterinary hospitals), beaches, and other similar locations, according to the number of papers found during the literature search.

Populations at risk; Based on their behaviour or interactions with certain of these surroundings, studies were able to determine specific populations that were at danger. These included disadvantaged populations, athletes, families, especially those with children, beachgoers, and emergency response personnel, in addition to occupational groups who operate in public and private community facilities. A major risk factor for athletes and visitors to the beach was having an open wound or skin condition. Sharing personal belongings was found to be a danger factor for drug users, athletes, and household members. Veterinarians worked with animals on a daily basis, and many homes had pets.

It was discovered that a significant section of the homeless, one of the underprivileged communities, had been exposed to MRSA. For instance, a 2009 Ohio research discovered that MRSA was colonized in 25.6% of homeless people tested positive at three shelters and an outreach event (Landers et al,. 2009). People who have been imprisoned are also at risk for CA-MRSA; at a Texas jail, MRSA was found on 6.1% of examined surfaces, which included chairs, toilet buttons and seats, restroom faucet buttons (Miko et al., 2013).

History and Physical Manifestations

The skin and subcutaneous tissues are most frequently impacted by MRSA infections, which can lead to a range of organ-specific diseases, including pneumonia, meningitis, abscesses, empyema and osteomyelitis,. MRSA-caused infected endocarditis has the greatest morbidity and mortality rate of any bacteria and is linked to intravenous drug abuse.

Skin and soft tissue infections (SSTIs): Cellulitis, diabetic foot ulcers and Necrotizing fasciitis and are among the SSTIs that are most commonly linked to the CA-MRSA bacterium. Additionally, it is becoming more frequently linked to chronic illnesses than non-MRSA infections. Most of the time, these infections are resistant to many drugs, which increases admission to the hospital, death, and recurring frequentities (Khan et al,. 2018)

Bones and Joints Infections; Infections of the bones and joints are most frequently caused by staphylococci. A growing number of these patients have developed oxacillin resistance. By extending a local infection from a lesion or as a component of a hemorrhaging infection, MRSA can cause osteomyelitis of the spine and long bones of the upper and lower limbs. In a similar vein, MRSA can result in septic arthritis in both natural and artificial joints.

Pneumonia: Prior to the development of antibiotics, staphylococcal pneumonia was a unique clinical entity with a death rate that ranged from 80% to 90% and a rapid start of respiratory symptoms. It showed distinct clinical symptoms such as the formation of a micro abscess and pulmonary bleeding, as well as specific radiological signs such as pyopneumothorax and cavitary lesions. The course has a

mortality rate of between 30% and 40%, has been less explosive in the post-antibiotic age, and is not always associated with viral influenza.. It is also connected with other risk factors for *S. aureus* infections (Celbak and Malone, 2018). However, there have lately been cases in the US of CA-MRSA causing necrotizing pneumonia, which can be deadly, in otherwise healthy patients. Its characteristic symptoms include haemoptysis, hypotension, high fevers, and severe respiratory problems. Quickly afterward, leukopenia, septic shock, and elevated C-reactive protein (more than 350 mg/dL) occur.

Furthermore, MRSA plays a significant role in hospital-acquired pneumonia that is caused by ventilators. Hospital-acquired pneumonia (HAP), sometimes referred to as nosocomial pneumonia, is characterized by the onset of symptoms 48 hours following being admitted to hospital or longer; this indicates that the pneumonia had not started to incubate at the time of admission. The phrase "ventilator-associated pneumonia" (VAP) describes pneumonia that appeared 48 hours or longer after the use of mechanical ventilation and intubation, but did not exist before endotracheal intubation. These two disorders share comparable microbiological sources and are linked to subpar overall outcomes and dire prognoses.

Bacteremia: S. aureus caused bacteremia has been linked to fatality rates ranging from 15% to 60%, according to reports. Patients in the critical care unit who have had central line insertions frequently develop MRSA bacteremia. Any patient with MRSA in the bloodstream should have infectious endocarditis checked out as it is linked to MRSA bacteremia. Because these individuals have a reduced response to vancomycin, when compared to other MRSA infections, the outcomes linked to MRSA bacterial infections are more severe.

Endocarditis: A significant proportion of infected people (30–37%) may die from bacterial endocarditis, which is primarily caused by MRSA. IV medication usage and IV catheter use are frequently linked to right-sided MRSA endocarditis. Cavitating lesions in the lungs can result from septic pulmonary emboli in patients with tricuspid valve vegetations. Likewise, those with abnormalities of the aortic and mitral valves may get secondary infections in other parts of the body such as the kidneys, bones, joints, brain, and kidneys. Obtaining a patient's history, doing a

thorough examination, ordering any necessary lab work, and doing radiological diagnostics on them are all crucial (Baddour et al., 2019).

Diagnosis of MRSA

In order to properly diagnose and treat individuals who have MRSA infection risk factors, clinical suspicion is essential. Treatment with empirical antibiotics against MRSA should not be postponed until confirmation of an MRSA infection. Samples of blood, sputum, urine, or wound scrapings from suspected sources of infection should be sent for analysis by clinicians (Lee et al,. 2019). Clusters of cocci and a positive Gram stain are indicative of S. aureus. If cultures are not definitive, the most sensitive test the DNA polymerase chain reaction, or PCR for MRSA is the gold standard.

DNA PCR of MRSA from nares is a commonly used diagnostic method to rule out MRSA colonization. Although a negative test is very sensitive in excluding MRSA infection, it is not an absolute indicator of MRSA infection. Therefore, bronchoalveolar lavage or a prolonged tracheal aspirate may be used to identify the organism in individuals with HAP or VAP. The identification of MRSA pneumonia is neither highly sensitive or specific when using sputum cultures.

Future and Present Methods of Treating MRSA

Nearly 50% of the population may be affected by bacteremia among those with established MRSA infections, which may be fatal (Nickerson et al., 2009). MRSA infections may decline as a result of MRSA prevention efforts and the application of a current antibiotic medication, both separately and in combination (DeKraker et al., 2013). The high fatality rate might be caused by inadequate illness treatment at the onset of infection (Simor et al., 2016). Furthermore, a number of virulence genes have been associated with higher death rates. For example, horizontal gene transfer pathways that result in the acquisition of antibiotic resistance genes are a key source of antibiotic inefficacy against MRSA infection (Albur et al., 2012).

Although they are discussed in subsequent parts, modern techniques and antibiotics can still be used to treat MRSA infections. The availability of many new drugs that may be bought alone or in combination has given patients with MRSA infections hope. Furthermore, combination therapy, immunotherapy, and some of the newest

non-antibiotic methods of treating MRSA infections such as nanoparticles,probiotics, phytochemicals and bacteriophages are replacing single-agent therapy in the research (Lee et al., 2016).

Antibiotics Used for the Treatment of MRSA Infection

An Australian investigation found that 17% of MRSA samples had resistance to ceftaroline and cephalosporin. Despite the release of several new medications, vancomycin remains the most effective treatment (Abbott et al., 2015). Moreover, the Spanish Society of Clinical Microbiology and Infectious Diseases recommends using a glycopeptide, such Daptomycin, with a b-lactam antibiotic to treat MRSA infections (Gudiol et al., 2015). However, a genetic change might make Daptomycin ineffective against MRSA.

It used to be believed that Vancomycin was the most effective antibiotic for treating serious infections caused by MRSA. Van Hal and Fowler (2013) and Holmes et al. (2012) both state that obtaining evidence of diminished effects, unreachable PK/PD objectives, and overall resistance determines the adequacy of Vancomycin's principal action. Consequently, Vancomycin starts to grow resistant to them and become less responsive to glycopeptides,leading to the emergence of Vancomycin-resistant S. aureus (VRSA).

Many recently licensed and innovative medications work well to treat MRSA infections, although further studies are needed to confirm this broad scope. A handful of the most current antibiotics that work well to treat MRSA infections are listed and explained below.

Oxazolidinones: A new family of antibiotics called oxazolidinones works well against methicillin- and vancomycin-resistant staphylococci, among other gram-positive bacteria. By attaching to the 50S ribosome subunit's P-site, oxazolidinone prevents the production of new proteins. Tedizolid, a novel oxazolidinone medication, has been approved for use in the conventional 6-day course of therapy for infections of the skin and soft tissues. Tedizolid is a medication that is more effective and provides more advantages than linezolid (Flanagan et al., 2015).

Fluoroquinolones: To treat a variety of bacterial illnesses in both humans and animals, quinolones are among the most widely used antibacterial medications in the world. Due to the presence of a quinoline ring in their structure, these medications are referred to as quinolones structurally. Bacteria are inhibited from proliferating by quinolones and fluoroquinolones through their DNA replication mechanism. The fluoroquinolone antibiotic delafloxacin has unique electrochemical characteristics that allow it to function against both gram-positive and gram-negative bacteria. At physiological pH, it is an anion, and at acidic pH, it is uncharged. The three drugs with the highest percentages of cure were vancomycin, linezolid, and levofloxacin (Kingsley et al., 2015).

Lipoglycopeptides: The antibiotic class known as lipoglycopeptides, which are made of fatty acid chains and glycopeptides, shown dose-dependent bactericidal activity. They hinder the bacterial cell membrane's ability to permeabilize and stop the formation of cell walls. Therefore, the glycopeptide core binds at the terminal acyl-d-alanyl-d. The cell wall's alanine chain interacts with hydrogen bonds and hydrophobic filling with a high affinity.

The FDA and European Medicine Agency (EMA) authorized dalbavancin, a lipoglycopeptide, in 2014 and 2015, respectively, for the treatment of ABSSSI (Van Bambeke, 2015). According to Jul et al. (2016), dalabavancin is only used to treat complicated infections in outpatients**.** 2011–2012 saw the completion of a multi-center research comparing the effectiveness of vancomycin and dalbavancin in the treatment of ABSSSI.

Futuristic approaches in treating MRSA Infections

One of the worst risks to public health, according to the World Health Organization (WHO), is the rise of germs that are resistant to antibiotics. Tagliabue and Rappuoli (2018) estimate that by 2050, antibiotic-resistant bacteria may be responsible for 10 million fatalities globally year, up from the current 700,000. A WHO study suggests that there is a very real chance that common diseases and mild infections might become lethal in the twenty-first century; if we get beyond the age of antibiotics (Streicher, 2021). Therefore, the handling and therapy of antibiotic-resistant bacterial illnesses urgently require the development of innovative antibiotic-free techniques.

The combined effects of NSAIDs and antibiotics: The exact mechanism of action of NSAIDs is uncertain, despite the fact that their antimicrobial properties have been shown in several research. Aspirin and ibuprofen had bactericidal and bacteriostatic qualities against MRSA strains, suggesting that they might be used as additional antibiotics to treat infections in place of diclofenac (Chan et al., 2017). NSAIDs and antibiotics are used to treat CA-MRSA infections.

Results showed that treating MRSA with cefuroxime and chloramphenicol individually was ineffective. Research has indicated that cefuroxime, chloramphenicol, and ibuprofen/aspirin have additive or synergistic effects on enhanced antibacterial activity (Aqib et al., 2021).

Bacteriophages as a potential antibiotic substitute: Bacteriophage therapy, sometimes referred to as phage therapy, is a kind of treatment in which viruses are used to eradicate bacterial diseases. Phage treatment is being studied since antibiotic resistance is rising.

As having a low cost, a very targeted impact, and an efficacious mode of action against certain MDR bacteria. According to Tkhilaishvili et al. (2020), bacteriophages exclusively harm the cells of bacteria; they do not harm the cells of humans or other animals.

Probiotics as therapeutic compounds: Probiotics are live bacteria that are proven to be beneficial during illnesses or after using antibiotics, which can upset the normal microbiome of the stomach. They might also assist in the treatment of a few other disorders including diarrhoea brought on by antibiotics and the symptoms of irritable bowel syndrome (IBS) (McFarland et al., 2021).Therefore, the term "probiotic" refers to more than just the gut microbiota; it also refers to a variety of other health benefits, such as immune cell up-regulation, tumor suppression, treatment of anxiety and depression, and a potential therapeutic role for COVID-19 patients as well as overweight and obese individuals (Ceccarelli et al., 2020; Daniali et al., 2020).

Management and Control of MRSA

To prevent and control MRSA, various strategies are currently being employed, such as the appropriate use of antibiotics, proper washing, controlling interactions with natural S. aureus reservoirs, preventing dissemination from infected patients, hospital environment sterilization, constant monitoring, and many more (Lee et al., 2018).

Right now, developing vaccines is the most effective strategy to control MRSA in both animal and human populations.

CHAPTER III

Materials and Methods

Introduction

Study objectives, selection of the participants, demography, data collection and analysis procedures are all outlined in this section. Concerns about ethics and practicality are also discussed.

Study area

The study was carried out in Turkish Republic of Northern Cyprus (TRCN) during the month of October to December 2023. Nasal swabs samples were collected from volunteers of African origin living across the TRCN. In this study, 150 nasal swab samples from African residents of Northern Cyprus were collected, laboratory identification and MRSA is isolated

Questionnaire

I pre-designed a questionnaire like a bio-data form for the collections of the volunteer's data such as age, country origin, gender location of their addresses in TRCN and their antibiotic usage in the past six months.

Ethical Approval

The privacy of the human participants in the current investigation was essential. The study was carried out strictly according to the applicable regulations and laws and with the greatest regard for ethical considerations. Transparency, confidentiality, privacy, informed permission, and voluntary participation thus became the guiding principles for the design and performance of this study. The project demonstrates that the methodologies and equipment employed were appropriate for this study and the

approval by the Near East University Ethics Committee with the decision number (NEU…..),

Sample collection and transportation

Sterile nasal swabs were used to collect samples from African population living Northern Cyprus. On each tube, the population name and date were marked. Nasal swabs were collected at the sample collection point in a hospital laboratory.

Statistical analysis

The Pearson chi-square was the testing method for the result in this study, with an SPSS version 27 for all statistical analysis. A P-value of 0.005 was considered significant.

Materials and Equipment used

Materials used during the course of this study include; petri dishes, nasal swab sticks, conical flasks, measuring cylinder, beakers, small test tubes, aluminium foil, spatula, cotton wool, paper tape, marker, test tubes rack, inoculating loop, inoculating needle, distilled water, syringe needle and antibiotic disc.

The equipment used includes; autoclave, incubator, refrigerator, weighing balance, Bunsen burner, spectrometer.

Media and Reagents

The media and reagents used includes HiCrome MRSA agar base, blood agar, Mueller-Hinton agar, Cefoxitin disc and distilled water

Preparation of Media.

Media	Composition	Origin
HiCrome	Peptone,sodium chloride,sodium pyruvate,chromogenic substance,inhibitor mixture.	Netherlands

Blood agar	Heart Muscle,infusion,pancreatic digest of casein,yeast extract,sodium chloride,agar	USA
Mueller-hinton	Beef extract powder,starch,agar,acid digest of casein	USA

All media used were prepared according to manufacturer's specification. First weighed the media used by using a weighing balance and the appropriate quantities were dispensed in conical flasks, distilled water was added to make up the required volume. The media in the conical were homogenized on hot plate before they were sterilized in an autoclave at 121℃ for 15 minutes. The media were then allowed to cool, poured into sterile petri dishes to solidify and set for inoculation.

Inoculation

A platinum wire loop of diameter 4mm was used for the inoculation of nasal swabs. The platinum wire loop was sterilized by flame and cooled in air. Inoculation was performed near the flame so that sterile conditions were maintained. Nasal swabs was streaked on solidified HiCrome agar plates using streaking quadrant method and incubated in the incubator at 37°C for 16-24 hours.

Macroscopic Examination of culture

After the incubation, the cultures were examined macroscopically. The phenotypic characteristics including colony morphology, pigmentation, and colony colour and size were reported etc. The microbial colonies with green and blue colours were collected and used for a further test while the rest of the colony were not used.

Mcfarland Preparation

Using a micropipette, three ml of normal saline was added to each test tube. A pure colony from the blood agar and placed it in the normal saline tubes. To achieve a uniform turbidity and bacterial colony concentration in the test tube, the liquid was stirred in the tubes using a vortex machine. After these procedures, a spectrophotometer was used to measure the turbidity of the tube which was within the range of 0.5-1.2 (McFarland standard).

Cefoxitin Disc Diffusion Test

Using 30µg of Cefoxitin, a disk diffusion test was performed in accordance with EUCAST recommendations to identify MRSA isolates. Few colonies were taken from blood agar and mixed with 0.9% NaCl solution to prepare a bacterial suspension. Then a volume of bacterial suspension was distributed evenly over the surface of Mueller-Hinton agar by a cotton swap. The density of that suspension was equivalent to 0.5 McFarland standards. Furthermore, Cefoxitin disks (ROSCO, Co., Denmark) were placed aseptically onto Mueller-Hinton agar plates. As controls, NCTC 12493 (mecA-positive *S. aureus*), ATCC 25923 (mecA-negative *S. aureus*),and water (negative control) were used.

Plates were incubated at 35ºC for 24-48 hours. The millimetre measurements of the inhibition zone widths were interpreted in accordance with EUCAST guidelines. Methicillin-susceptible(MRSE) strains were defined as having an inhibition zone of >20 mm, whereas strains with an inhibition zone of 14–20 mm were considered as methicillin-resistant and that strains were stocked at -30°C for further analysis.

mec A and mec C Detection

For DNA extraction, suspensions of MRSA-suspected strains prepared with 4 McFarland units, were boiled for 10 minutes, and then clarified by centrifugation at 10 000 g for 5 minutes. Isolated DNAs were stored at -30°C for further analysis.

Chapter IV

Results

Subject profile

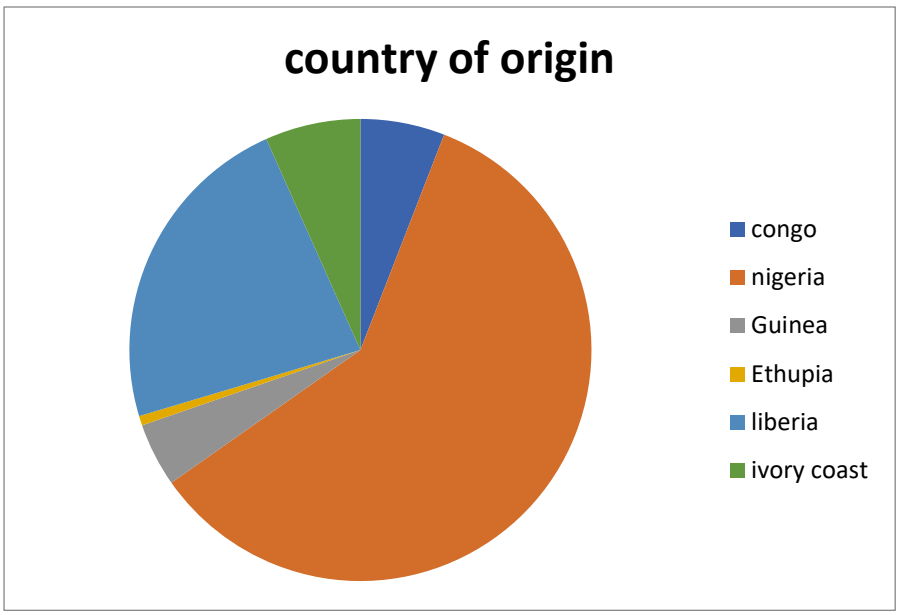
A total of 150 samples were collected through nasal swab from volunteers that are not African across TRCN .Population with MRSA infection. A detailed information on their age, gender, country of origin, addresses and a question on their antibiotics usage was also obtained. The distributions of these characteristics are detailed in Table 4.1 and Figure 4.1 was also illustrated to represent spatial distributions of the volunteer's country of origin.

Table 4. 1

Demographic Characteristics of the Study Group

variable	Characteristics	n(%)
Age	18-22/median age (20)	34
	23-27/ median age (25)	40
	28-32 /median age (30)	16.6
	33-37 /median age (35)	4
	38-42 /median age (40)	5.3
Location	Nicosia	61.3
	Magusa	17.3
	Lefke	8.6
	Kyrenia	11.3
Gender	Female	40.6
	Male	59.3

Figure 4.1 *The distribution of study group by origins*



Macroscopic examination of the Petri-plates on the Chromogenic agar

After incubation of inoculation HiCrome agar petri plates for 16-24 hours, the cultures were examined. Twenty two out of 150 samples were reported as no growth which indicates that no colony was seen on the HiCrome agar. Smooth colonies with six different colours were observed with the remaining 128 samples that showed the presence of MRSA and MRSE according to the manufacturer instructions. The presence of greenish-yellow, green were considered to be MRSA, while the blue, denim blue were considered to be MRSE.

Table 4.2 *Colony Morphology of the Isolated Bacteria on HiCrome Agar*

Name of organism	Colony characteristics	Percentage (n,%)
MRSA	Green,greenish yellow,smooth	38,25.3
MRSE	Blue,light blue,denim blue	90,60
No growth	No colony	22,14.6

MRSA: Methicillin resistant *Staphylococcus aureus.*

*MRSE:*Methicillin Resistant *Staphlococcus epidermidis.*

Figure 4.2 *Blue colonies on HiCrome agar that were considered as Methicillin resistant Staphlococcus epidermidis*

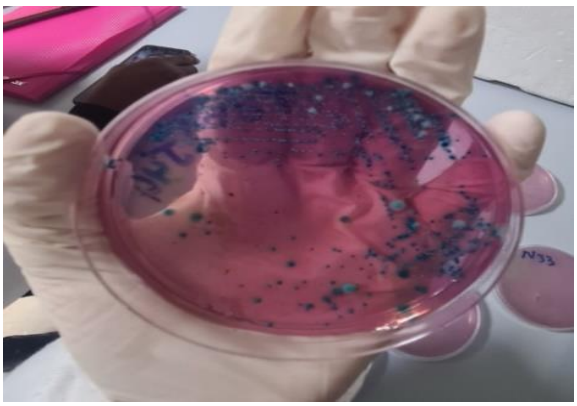


Figure 4.3 *Greenish-yellow colonies on HiCrome Agar That Were Consider As Methicillin Resistant Staphylococcus Aureus*

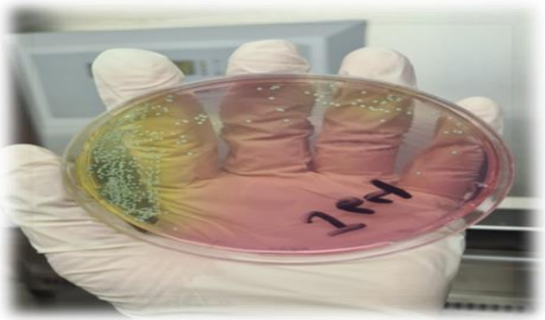
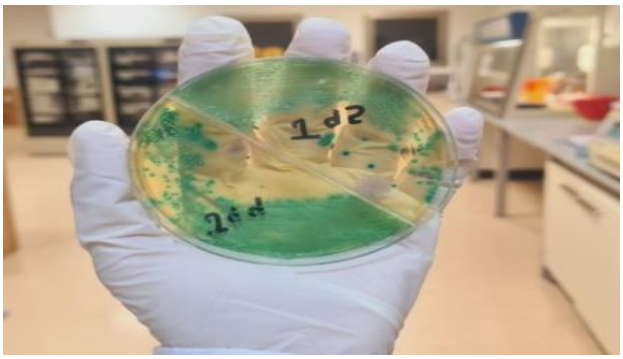


Figure 4.4 *Green Colony on HiCrome Agar That Were Considered As Methicillin Resistant Staphylococcus aureus*



Macroscopic examination petri-plates on the Blood agar

The suspected MRSA colonies were sub cultured on blood agar in order to obtain pure colonies. Different colony morphology was observed having different shapes and colors. Small white opaque with non-hemolytic were observed in 71 samples which were considered to be MRSE while gray, yellowish color with beta-hemolysis was also seen in 25 samples from the blood agar were also considered to be MRSA. Table 4.3 and Figure 4.3 represent the colony morphologies of the isolates

Table 4. 3

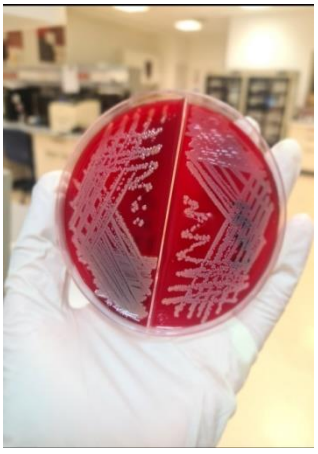
Characteristics of the Colony Morphology of the Isolated Bacteria On the Blood Agar

Organism	**Colony characteristic**	**Hemolysis**
MRSA	Smooth large yellow to grey colony	Yes

MRSA:Methicillin Resistant *Staphylococcus aureus*

MRSE : Methicillin Resistant *Staphlococcus epidermidis*

Figure 4.5 *Macroscopic Examination of isolated bacteria on blood agar*



Cefoxitin Disc diffusion test Examination

All of the *S. aureus* isolates from nasal samples were separated into MSSA and MRSA using the Cefoxitin Disc Diffusion method. After the Cefoxitin diffusion test 7 samples out of the 38(7/38,18.4%) were found to be resistance to Cefoxitin and were confirmed to be MRSA. However 31 out of 39(31/38,81.5%) were found to be sensitive to Cefoxitin and were confirmed to be MSSA.(Table 4.4,Figure 4.4a and b)

Table 4.4 *Comparison of Two Methods for MRSA Detection*

	Resistance of cefoxitin(n,%)	**Sensitive of cefoxitin (n,%)**
Hicrome positive	7	31
Hicrome negative	0	107
Total	7	138

Figure 4.6 *Isolate Sensitivite to Cefoxitin Disk*

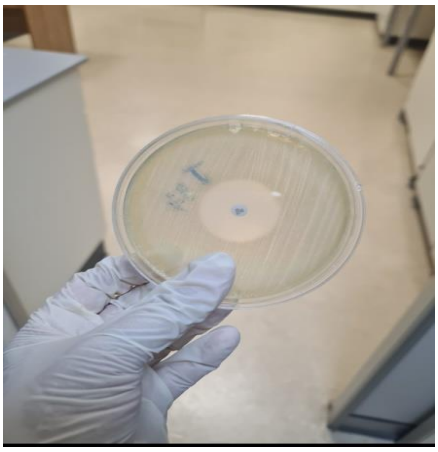


Figure 4.7 *Isolate Resistant to Cefoxitin disk*

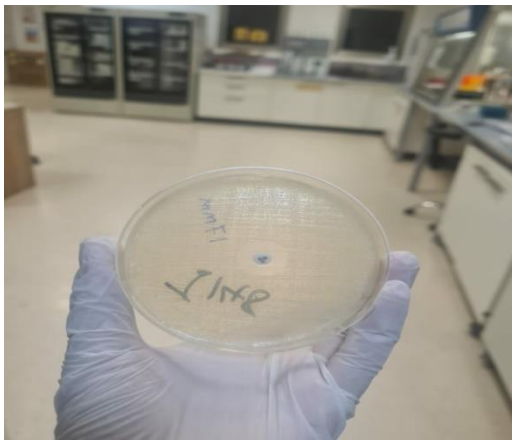


Table 4. 5 *Comparison of MRSA's sensitivity and specificity using HiCrome Agar and Cefoxitin disk*

Methods	Total number of MRSA	False Negative	False positive	Sensitivity(%)	Specificity(%)
Hi-crome Agar	38	0	31	100%	50%
Cefoxitin disk	7	0	0	100%	100%

CHAPTER V

Discussions

The management of infections acquired in hospitals and various community settings is greatly challenged by the emergence of methicillin resistance in Staphylococci. Therefore, in order to manage time by utilizing the appropriate medications and implementing isolation measures, it becomes imperative to screen clinical specimens for MRSA as soon as possible. Thus, evaluating an economical, straightforward, sensitive, and accurate method is necessary for early MRSA detection in microbiology labs.

Clinical laboratories have faced challenges in testing for methicillin resistance in *S. aureus* for a long time. Numerous investigations have shown that the gold standard for identifying MRSA in clinical microbiology labs is MecA gene detection. However, because molecular methods are expensive and cannot be used routinely in most developing countries, it is crucial to assess a simple, affordable, sensitive, accurate, and accurate method for MRSA detection that can be used in routine lab settings and that can yield results that are not entirely consistent with molecular methods.

In this work, we assessed two distinct phenotypic approaches to MRSA identification. From nasal samples, 150 *S. aureus* isolates were obtained. The Cefoxitin disc diffusion test was used to process each of the 150 *S. aureus* isolates in order to identify methicillin, as previously mentioned in the material procedure section. The Cefoxitin disc test yielded 7 (4.6%) observations of Methicillin Resistant *S. Aureus* (MRSA) with 100% sensitivity and 100% specificity. The investigation included a number of methods to find MRSA in this study. Out of 150 nasal swab samples, 38 samples of *S. aureus* (MRSA, MSSA) were isolated, with MRSA accounting for 7/150 (4.6%) of the samples.

In the current work, we looked at two different phenotypic techniques for MRSA detection. For the purpose of detecting methicillin resistance, 38 *S. aureus* isolates from nasal swab samples were processed. Methicillin-resistant *S. aureus* (MRSA)

was identified in 7 (4.6%) of these using the disk diffusion test with Cefoxitin. The Crome Agar method identified 38 as MRSA.The Cefoxitin disk test was therefore having 100% sensitivity and 100% specificity specificity with 100% positive and negative predictive value. According to other researchers, the Cefoxitin disc diffusion approach produced 100% sensitivity and 100% specificity.(Ahmadi et al., 2019)

On the other hand, 7 of the 38 MRSA strains found in the current study utilizing the chrome agar method were true MRSA, zero number false negative and 31 false positive with 50% specificity and 100% sensitivity. The sensitivity of various conventional approaches used by multiple authors for MRSA detection has been reported with varying results. Nonetheless, the majority of research using the Cefoxitin disc diffusion approach revealed 100% sensitivity and 100% specificity, which is consistent with our findings. MRSA Chrome agar has a 90% to 100% sensitivity and specificity, according to several studies.(Turner et al., 2019).

The present study indicates Chrom-agar directly detected 23.6% of the MRSA strains in this experiment within 24 hours. This Within was far more significant for early detection than the Cefoxitin disc diffusion technique, with a P-value of less than 0.005, sensitivity, specificity, 100%, 100%, and 50%, respectively. Early discovery is one of the most crucial stages in the bug's dissemination.

Cefoxitin has recently taken the place of Oxacillin in CLSI's MRSA detection protocol. Numerous research on Cefoxitin disk diffusion have shown that the presence of mecA improves the correlation between Cefoxitin disk diffusion test results. The MRSA detection diffusion method and the mecA gene PCR agreed upon each other. Anwar et al,2020 others investigation revealed a strong relationship between staphylococcus species' mecA presence and Cefoxitin MICs. Recent research has demonstrated that the Cefoxitin disk diffusion method is a more dependable approach for detecting MRSA than the Oxacillin disk diffusion and the chromogenic agar method

When a sample has a tendency to include associated commensal flora that can affect isolation, a nasal swab was used as a sample to test the effectiveness of the Chrom

agar method. Nevertheless, the Chrom agar method was effective for early MRSA identification even in circumstances when a high concentration of contaminated bacteria were present. The results were in line with the studies conducted by earlier academics. The nasal carrier may be the source of illnesses acquired in the community, according to this study's strong findings. Specifically in the hospital's high-risk area, routine screening, good health practices, MRSA surveillance, and local treatment of nasal carriers are essential to halting the spread of this dangerous illness. If the time-consuming, multistep conventional method substituted with an early detection approach, as Chrom agar, the patient will benefit from early treatment and subsequent prevention of MRSA strain transmission.

Chapter VI

Conclusion and Recommendations

Conclusion

MRSA remains a major issue in healthcare even with the advancement of diagnosis and preventive techniques. Taking care of MRSA bacteremia can be challenging, especially in patients who are at high risk of complications or who have toxic or multidrug-resistant strains. The timely delivery of the appropriate medicine depends on the early diagnosis of MRSA.

Concern is growing over the prevalence of MRSA infections among African citizens living in Northern Cyprus who have no known risk factors and have never used the healthcare system, as well as MRSA isolates with a unique genetic component. This study demonstrates a low rate of MRSA carrier African citizens (4.6% of 150 samples collected nationwide). This is attributable to increased cleanliness in public spaces and healthcare facilities, a decrease in the use of broad-spectrum antibiotics, and the application of contemporary medical techniques to successfully stop the spread of germs resistant to antibiotics.

In the current study, Cefoxitin disc diffusion is the most dependable method for identifying methicillin-resistant *Staphylococcus aureus* detection. The Cefoxitin disc is an effective technique for detecting MRSA, according to our research, however it should be augmented with an additional technique to ensure that no MRSA is overlooked. However, the biggest drawback is the amount of time it requires. Therefore, a highly specific and sensitive single step Crome agar technique would be a superior choice for the routine and quick detection and quick screening of MRSA from clinical samples, especially in high-risk wards and ICUs. This will aid in the early diagnostic process and help stop the MRSA strain from spreading further

Recommendations

In the light of the foregoing, the researcher suggests the following;

1. Regions with low levels of knowledge and negative attitudes might greatly benefit from awareness-raising campaigns, such as distributing vital information about the infection and its cure.

2. Governmental and non-governmental organizations prioritize developing long-term infection control and preventive strategies as well as expanding current preventative facilities.
3. Tailored advice and training depending on the particular needs of a certain group.
4. If patients and communities afflicted by MRSA have access to the appropriate educational initiatives, they may be able to gain an advantage over the disease.
5. Boost services for MRSA awareness, prevention, and treatment.
6. Elevate the standard of public instruction.

Limitation of the study

The study's sample isn't totally typical of the general population, which could lead to a sampling error. The results of the study might not apply to a larger population, for instance, if it only looks at a particular age group or healthcare setting.

I neglected to add the MeReSa selective supplement (FD229) and the Cefoxitin supplement (FD259) when preparing the Hicrome agar for the study, which had an impact on some of the crome agar results.

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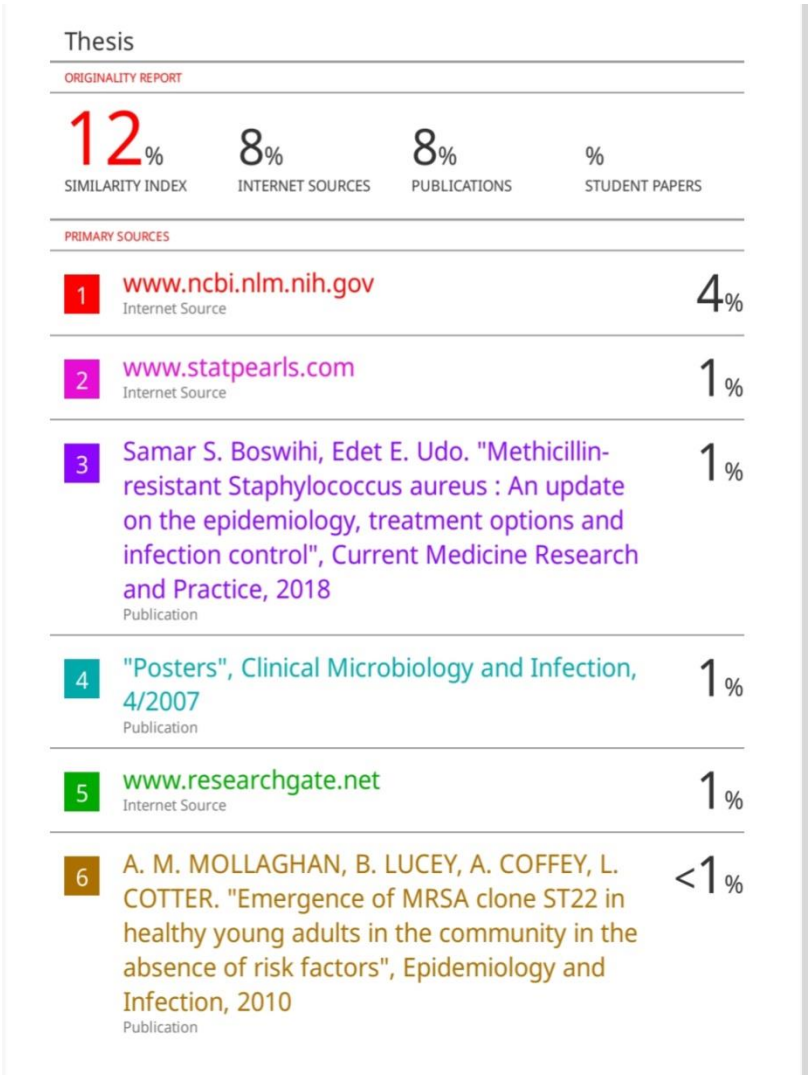
APPENDICES

Turnitin Similarity Report



Thesis

ORIGINALITY REPORT

12%	8%	8%	%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

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3	Samar S. Boswihi, Edet E. Udo. "Methicillin-resistant Staphylococcus aureus : An update on the epidemiology, treatment options and infection control", Current Medicine Research and Practice, 2018 Publication	1%
4	"Posters", Clinical Microbiology and Infection, 4/2007 Publication	1%
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6	A. M. MOLLAGHAN, B. LUCEY, A. COFFEY, L. COTTER. "Emergence of MRSA clone ST22 in healthy young adults in the community in the absence of risk factors", Epidemiology and Infection, 2010 Publication	<1%

NEAR EAST UNIVERSITY
SCIENTIFIC RESEARCH ETHICS COMMITTEE

RESEARCH PROJECT EVALUATION REPORT

Meeting date :29.02.2024
Meeting Number :2024/121
Project number :1823

The project entitled **"Investigation of Community-Acquired Antimicrobial Resistance Between People of African Origin Living in TRNC and TRNC Indigenous People"** (Project no: NEU/2024/121-1823), which will be conducted by Assoc. Prof. Dr. Ayşe Arıkan has been reviewed and approved by the Near East University Scientific Research Ethical Committee.

Prof. Dr. Şanda Çalı
Near East University
Head of Scientific Research Ethics Committee

Committee Member	Role	Meeting Attendance *Attended(✓)/Not attended(X)*	Decision *Approved(✓)/Rejected(X)*
1. Prof. Dr. Şanda Çalı	Head	✓	✓
2. Assoc. Prof. Dr. Gulifeiya Abuduxike	Rapporteur	✓	✓
3. Prof. Dr. Tamer Yılmaz	Member	✓	✓
4. Prof. Dr. Şahan Saygı	Member	✓	✓
5. Prof. Dr. İlker Etikan	Member	✓	✓
6. Assoc. Prof. Dr. Mehtap Tınazlı	Member	✓	✓
7. Assoc. Prof. Dr. Dilek Sarpkaya Güder	Member	✓	✓
8. Prof. Dr. Burçin Şanlıdağ	Member	✓	✓

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Skill and Proficiencies

- Good communication skills
- Excellent Computer literate
- Excellent Analytical and Research skills
- Digital marketing
- AWS Data Ingestion and Migration
- AWS architecting and cloud computing.
- Ability to work in a multicultural environment

Educational Background

October 2021-January 2024

M.sc Medical and Clinical Microbiology

Near East University

Yakin Dogu Bulvari Lefkosa

February 2018

B.sc Microbiology

Obafemi Awolowo University

Ile-ife Osun state. Nigeria

Job Experiences

October 2023-January 2024

Research Thesis Intern

Medical Laboratory,

Near East University Hospital

Key Duties and Responsibilities

- Carried out laboratory experiments and testing.
- Isolating and identifying Micro-organisms and testing the susceptibility to antibiotics.

February 2022-Till date

Digital Marketer (Remotely)

Mayorgraphix media house limited

Nigeria.

Key Duties and Responsibilities

- Generating and overseeing material (such as articles, videos, and blog entries).
- Creating a content strategy that is in line with marketing objectives.
- Developing and overseeing email marketing initiatives.
- Constructing and classifying email lists

September 2013- November 2018

Customer Service Manager

Glory Multipurpose ventures

Nigeria

Key Duties and Responsibilities

- Handled incoming calls, responded to emails and monitored all customers service experience
- Received and attended to all Clients Inquiries at the office.
- Performed Clerical duties of the Organization and other tasks assigned.
- Coordination and monitoring the day to day activities of the organization