An-Najah National University

Faculty of Graduate Studies

EPIDEMIOLOGY AND ANTIMICROBIAL SUSCEPTIBILITY OF METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS ISOLATES: A RETROSPECTIVE STUDY AT A TERTIARY CARE HOSPITAL IN PALESTINE BETWEEN 2020-2021

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Dedication

I dedicated this work especially

To my lovely family (My parents, my brothers Eng.Nadeem, Eng.Sabeeh, Eng.Mohammad, my sister Ph.Dina and my nephew Zidan)

And to relatives and friends.

Acknowledgment

First, I must thank God for my success.

Thanks to my supervisor, Dr. Adham Abu Taha, for helping and guiding me during the study period every time I needed.

Many thanks for An-Najah National university and to my instructors for helping.

My thanks to An-Najah National University Hospital for

facilitating the completion of our study, and to the health workers there who supported and helped.

Declaration

I, the undersigned, declare that I submitted the thesis entitled:

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I declare that the work provided in this thesis, unless otherwise referenced, is the researcher's own work, and has not been submitted elsewhere for any other degree or qualification.

Student's Name هلا زيدان نزيه سعيد

Signature هلا سعيد

Date 14/6/2023

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Abstract

Increased rates of resistance of *Staphylococcus aureus* (*S. aureus)* to different classes of antibiotics, makes the researchers think about studying the antimicrobial profile of it, and other risk factors that may be associated with infection.

The goals of our study are to determine the prevalence of methicillin-resistant *S. aureus* (MRSA) among Palestinian patients, and to identify risk factors, susceptibility patterns, and to determine the most suitable antibiotics to be used empirically.

Data of positive *S. aureus* cultures from patients' specimens during the time period between January 2020 and December 2021 was collected from An-Najah National University Hospital, Nablus-Palestine, classified to methicillin-sensitive *S. aureus* (MSSA) or MRSA by using Vitek 2 system which is available in the hospital. Each isolate was tested for susceptibility to each oxacillin, cefuroxime, amoxicillin, piperacillin-tazobactam clindamycin, erythromycin, gentamycin, levofloxacin, linezolid, moxifloxacin, ciprofloxacin, quinopristin/dalfopristin, rifampicin, tetracycline, tigecycline, trimethoprim-sulfamethoxazole (TMP-SMX), and vancomycin by Vitek2 system. Other information related to patients and other comorbidities were collected from the hospital information system.

126 (49.6%) of 254 patients with *S. aureus* were infected with MRSA, with no significant association with various age groups and gender. Prevalence of MRSA was highest in pediatric unit followed by emergency room, 61.1% and 59.6% respectively, followed by surgical unit with MRSA prevalence of 52.7%. There is a significant difference in MRSA and MSSA distribution in the kidney unit (p-value = 0.009). Lung diseases are the co-morbidities which are associated with MRSA. Skin and soft tissues,

and pus/wound specimen are associated with MRSA infection. All isolated were still susceptible to vancomycin.

The prevalence of MRSA seemed to be similar to other Asian countries. Vancomycin is the most suitable option to be used empirically for serious MRSA infections.

Keywords: Methicillin-resistant *Staphylococcus aureus*, resistance, risk factors, susceptibility pattern.

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Chapter one

Introduction

1.1 Background

1.1.1 Overview

Infectious diseases is caused mainly by microbes including bacteria, viruses, fungi and parasite, enters the body by different routes, multiply, and cause an infection (1).

Microbes can be found everywhere. Human body is a reservoir for a big number of these microbes. Some can cause illness, while others are important to our health (2). Although there are big efforts for controlling infectious diseases, there are still a millions of cases and a number of deaths causes by infectious diseases all around the world (3).

Bacteria which can be found nearly everywhere; some can live in even hard conditions. Human body estimated to have bacterial cells more than human cells (4). It is single-celled, are classified into groups according to their shapes, the groups include: cocci, bacilli, spirilla, vibrios or spirochaetes. Present as single cell, pairs, chains and also clusters (5).

1.1.2 *Staphylococcus* aureus

S. aureus which is a gram+ bacterium, present as cocci shaped and in clusters, that is why described as grape-like shape, stain purple by gram stain. These organisms can grow in up to 10% salt in media, the colonies are in golden color, that's why its name is aureus which means golden, can grow aerobically and anaerobically at different temperatures from 18^{o}C to 40^{o}C (6).

It is novobiocin sensitive which distinguish it from *Staphylococcus saprophyticus* which is no sensitive, and mannitol fermentation positive which distinguish it from *Staphylococcus epidermidis*. It is coagulase and catalase positive, which can distinguish it from other *staphylococcus* species (7).

S. aureus is one of the most important types of bacteria around the world that has emerged clearly in recent times and affects human health especially critically ill people, its impact on human health was significantly increasing due to its increased resistance to antimicrobial agents (8).

There are 52 species and 28 subspecies of *staphylococcus* genus, *S. aureus* is the most clinically relevant (9), causing skin, blood stream, bone infections, and other more disseminated infections. *S. aureus* is more commonly a commensal species, present naturally on the skin, nasal cavity, other mucous membranes, and in the gut in 25% to 50% of the population (10), one of the most important reasons that it can colonize and grow in the nasal cavity, skin and even in hard conditions, that it can live in an environment with high osmotic pressure and low moisture (11).

It can move from superficial sites via blood to infect internal organs(12). Also it can cause life threatening conditions as necrotizing fasciitis and necrotizing pneumonia (13).

1.1.3 *Staphylococcus aureus* toxins and virulence factors

Unlike other types of bacteria which contains small number of toxins, *S. aureus* have a number of virulence factors, which include large number of toxins and immune evasion factors, also protein and non-protein factors that make it easier colonies during infection (14). *S. aureus* toxins families are divided into three groups, pore-forming toxins, exfoliative toxins and superantigens. Pore-forming toxins can be further divided into four sub-types, hemolysin α, hemolysin β, leukotoxins and phenol-soluble modulins (15).

1.1.4 Antimicrobial resistance (AMR)

Antimicrobial resistance (AMR) happens when microbes develop the ability to defeat the antibiotics. That means they are not killed and continue growing, which make infections more difficult to treat, and in some cases impossible (16).

AMR infections require using the 2nd and 3rd line treatments, can be harmful by causing serious side effects, that may include organ failure, and prolong time and care to cure, sometimes for even months (16).

Multi drug resistant organisms (MDROs) are micro−organisms which is most commonly bacteria, which are resistant to one or more than one classes of antibiotics, these pathogens are resistant to the most common antimicrobial agents, these highly resistant organisms needs more attention in healthcare facilities (17). This group of resistant bacteria mainly include MRSA, extended spectrum B-lacatamses (ESBL), carbapenemase-producing enterobacterales (CPE),and vancomycin resistant enterococci (VRE) (18).

1.1.5 Methicillin resistant *staphylococcus aureus* (MRSA)

MRSA is a type of *S. aureus* bacteria causing different types of infection which are resistant to several types of antibiotics, including methicillin, oxacillin, nafcillin, cephalosporins and other beta-lactams antibiotics, which are used to treat ordinary *staphylococcus* infections (19), was initially described in England in 1960s after methicillin was used in the clinical practice, before they switch to other more stable penicillins including oxacillin, flucloxacillin and dicloxacillin, due to methicillin high toxicity(9).

Studies showed that about 1/3 of population have *S. aureus* bacteria in their nasal cavity, usually with no disease, and about 2% of them carry MRSA, most of them never develop serious MRSA infections (20).

Staphylococcal Cassette Chromosome mec (SCCmec) which carries the mecA or mecC gene, encoding for a specific penicillin-binding protein (PBP2a), in MRSA, the acquiring of SCCmec gene, causes the resistance to the β-lactam antibiotics including methicillin, naficillin, oxacillin and cephalosporins (21) because PBP-2A has less affinity to beta-lactams when compared to other PBPs types, so PBP-2A

continues the synthesis of bacterial cell wall even in the presence antibiotics. So, *S. aureus* strains that have SCCmec gene can even continue growing in the presence of many types of antibiotics even from different classes (22).

When MRSA strains first appeared, they were usually found in old age patients admitted to healthcare facilities which are called Hospital-associated MRSA (HA-MRSA) and those who had a past history antibiotic consuming. Over time, it has become noticeable that MRSA is isolated from the community without a history of disease or previous use of antibiotics; these new MRSA strains were called Community-Associated MRSA (CA-MRSA), which can spread among children, prisoners, athletes and others (23).

Further studies mentioned that CA-MRSA strains can be distinguished from the other types of MRSA based on their microbiological, genotypic and epidemiological features. This was followed by a new strain of MRSA that isolated from animals, which is called Livestock-associated MRSA (LA-MRSA) (24).

1.1.6 Vancomycin resistant *staphylococcus aureus* (VRSA)

Vancomycin, a glycopeptide antibiotic, is an important antimicrobial agent to treat MRSA infection. In 1996, in Japan, *S. aureus* which has intermediate resistance to vancomycin (VISA) was firstly isolated (25), then were isolated in USA, Europe and other Asian countries (26)(27), VISA strains have firstly occurred in patients with MRSA infections undergoing long history of vancomycin therapy, which is usually ended in failure of the treatment (28).

In 2002, the first case of MRSA which is totally resistance to vancomycin was isolated in the USA (29). The prevalence of VRSA was only 2% before 2006, between 2006 and 2014 was 5%, and 7% in the time period between 2015 and 2020 which means 3.5-folds increase in the VRSA count between before 2006 and 2020 all over the world. The prevalence of VRSA was 5% in Asia, only 1% in Europe,

4% in America, 3% in South America, and the highest percentage in Africa which is 16% (30).

The resistance to vancomycin in *S. aureus* happens when (MIC ≥ 16 μg/ml), which is caused by the vanA operon encoded on transposon (Tn1546), which is a part of a VRE conjugative plasmid, *S. aureus* acquire enterococcal plasmids during conjugation. Vancomycin resistance in *S. aureus* is maintained by an original enterococcal plasmid or by a transposition of Tn1546 from the VRE plasmid (31)(32).

1.1.7 MRSA prevention

Despite the severity of being infected with MRSA, it is also not hard to protect us and people from transmission. Successful prevention is possible by adhering to a number of basic core prevention elements described by centers for disease control and prevention (CDC) (33):

1. Hand hygiene

It is one of the most essential steps taken to prevent infection transmission, as part of hand hygiene, we should consider:

- Easily access to soap and water and the disinfectant hand gels.
- Education for both medical staff and patients about hand hygiene.
- Observation of action and Feedback.

According to world health organization (WHO), every health-care worker has to implement “The five moments” for hand hygiene to prevent or reduce the transmission of infection: before touching a patient and the procedure,and after the procedure or body fluid exposure, touching a patient and touching a patient's surround (34).

2. Contact precautions: which include using of the gown and gloves before room entry and remove before the patient's room exit, isolation is preferred for MRSA infected patient.
3. Recognizing patients who are previously colonized: colonization with MRSA could be for long period of time, there is no typical strategy for stop continuing isolation precautions for MRSA patients. Recognition of previously colonized or infected patients allows them to be subject to interventions in the suitable time.
4. Laboratory Reporting: there should be a good communication system in the hospital between the laboratory and the clinical area, and immediate informing of MRSA positive culture, in order to make the best intervention.
5. Education: in order to improve adherence to hand hygiene and other standard precautions, and also motivation to change their habits in order to understand and avoid problems.
6. Device and Procedure-Associated Prevention Measures: In addition to the rules that have been developed regarding MRSA, there must be special strategies for prevention of device related and procedure-associated infections, which include:

    - Central line-associated bloodstream infections (CLABSI).
    - Surgical site infections.
    - Catheter-associated urinary tract infections.
    - Ventilator-associated pneumonia.

1.2 Problem statement

It is very important to make studies focusing on MRSA infection prevalence, anti-microbial profile, and risk factors based on new data, because of the importance of this type of infection and the continuous changing in its morbidity, mortality, prevalence rate and antimicrobial profile. These types of studies will help us make interventions based on new collected data.

Patients with MRSA face more serious outcomes than MSSA, and for sure costs more money (35), for example, a study mentioned that nosocomial blood stream infections caused by MRSA cause 3-folds increase of health care costs relative to MSSA (36).

MRSA is a major problem since it is a cause of infections all around the world either community or hospital acquired. Among hospital acquired infection, MRSA infections affects 150,000 patients annually in Europe which costs about 380 million EUR (37).

It still considered as serious healthcare problem and prevention of MRSA infections is one of the priorities for CDC. Also mentioned in CDC that MRSA is a cause for around 70,000 severe infections and 9,000 deaths annually (38).

HA-MRSA becomes a challenge for discovering new antibiotics, MRSA infection leads to significant morbidity and mortality, and significant socio- economic effect specially to people in hospital. Vancomycin is the most suitable antibiotic for multi-drug resistant MRSA, despite resistance is reported in different region in the world in different continents. (39).

Development of resistance even for glycopeptides had also occurred that result in difficulty in treatment of *staphylococcal* infections. Asia is considered as a region with high incidence of MRSA. VISA and VRSA strains are also being increasingly identified in many countries in Asia (40).

Humans use about 34.8 billion antibiotic doses yearly. The global use of antibiotics increased by 65% between 2000 to 2015. In the UK, 1/5 antibiotics are prescribed with no essential need. In the USA, this number rises to 1/3. 17% of the substandard or false medications reported to the WHO are antibiotics (41).

AMR is increasing rapidly, many multi-resistant micro-organisms have emerged in the past century (42). A study mentioned that 700,000 deaths occur annually due to

AMR around the world, and predict that by 2050, the rate of deaths will be around 10 million globally if effective steps are not taken (43).

The mortality of invasive MRSA infections can reach about 20%. It is estimated that MRSA infections are leading cause of death in the USA which cause more deaths than which is caused by Human Immunodeficiency Virus (13).

The number of MRSA infections varies from one region to another, and their antimicrobial profile for sure varies (44).

1.3 Significance of the study

MRSA is a frequently silent infection which cause serious diseases or complications, which is resistant to various types of antibiotics, which is for sure increase morbidity and mortality, in addition financial health-care costs.

By knowing, the risk factors related to MRSA infection, and susceptibility patterns, these would help us to make interventions and instructions in order to reduce the infection, for either patients or health-care providers. MRSA is very important to control, which will be very good for workers themselves, patients, and for health care financial costs.

1.4 Aim and objectives

Up to our knowledge, our study would be the 1st study to tackle the antimicrobial resistance profile of *S. aureus* in Palestine at An-Najah National University Hospital in the period between Jan 2020 and Dec 2021.

The purpose of our study is to find out facts related to MSSA and MRSA infection, using data from isolates from patients who admitted to An-Najah National University Hospital.

Specific objectives

- To investigate the prevalence of MRSA and VRSA among all *S. aureus* cases.
- To study the relationships between age and gender and having MRSA infection
- To check the relationships between patient setting (inpatient {medical, surgical, pediatric}, K.U, emergency room and outpatient) and being MRSA infection.
- To check the relationships between comorbidities (cardiovascular diseases, cancer, chronic kidney diseases, diabetes mellitus, hepato-biliary disorders, central nervous system disorders and lung disorder) and being infected with MRSA.
- To check the associations between the site of isolation (Skin and soft tissues, blood stream, body fluids, urinary tract system, respiratory system, and bone marrow) and being infected with MRSA.
- To examine the association between the specimen (wound/pus, swab, tissue, blood, fluid, sputum, trap, urine, and bone marrow) and being infected with MRSA.
- To determine the resistance and sensitivity patterns of MSSA and MRSA to antibiotics.
- To investigate the most appropriate empirical antibiotics for patients with MRSA depending on the site of the infection.

1.5 Research questions

- What is the prevalence of MRSA and VRSA isolates among all *S. aureus* cases?
- Are there significant relationships at (*P*-value =0.05) between age and gender and having MRSA infection?
- Are there relationships at (*P*-value =0.05) between patient setting (inpatient {medical, surgical, pediatric}, K.U, emergency room and outpatient) and being infected with MRSA?
- Are there significant relationships at (*P*-value =0.05) between comorbidities (cardiovascular diseases, cancer, chronic kidney diseases, diabetes mellitus,

hepato-biliary disorders, central nervous system disorders and lung disorder) and being infected with MRSA?

- Are there a statistically significant differences at (*P*-value =0.05) between the site of isolation (Skin and soft tissues, blood stream, body fluids, urinary tract system, respiratory system, and bone marrow) and being infected with MRSA?
- Are there a statistically significant differences at (*P*-value =0.05) between the clinical specimen (wound/pus, swab, tissue, blood, fluid, sputum, trap, urine, and bone marrow) and being infected with MRSA?
- What are antibiotic susceptibility profiles of MSSA and MRSA to each tested antibiotic?
- What are the most appropriate empirical antibiotics for treating patients with MRSA based on the site of the infection?

1.6 Hypotheses

- H_o: there are no significant relationships at (*P*-value =0.05) between age and gender and having MRSA infection.
- H_1: there are significant relationships at (*P*-value =0.05) between age and gender and having MRSA infection.
- $H_{o:}$ there are no relationships at (*P*-value =0.05) between patient setting (inpatient {medical, surgical, pediatric}, K.U, emergency room and outpatient) and being infected with MRSA.
- H_1: there are relationships at (*P*-value =0.05) between patient setting (inpatient {medical, surgical, pediatric}, K.U, emergency room and outpatient) and being infected with MRSA.
- H_o: there are no relationships at (*P*-value =0.05) between comorbidities (cardiovascular diseases, cancer, chronic kidney diseases, diabetes mellitus, hepato-biliary disorders, central nervous system disorders and lung disorder) and being infected with MRSA.

- H1: there are relationships at (*P*-value =0.05) between comorbidities (cardiovascular diseases, cancer, chronic kidney diseases, diabetes mellitus, hepato-biliary disorders, central nervous system disorders and lung disorder) and being infected with MRSA.
- Ho: there are no statically significant differences at (*P*-value =0.05) between the site of isolation (Skin and soft tissues, blood stream, body fluids, urinary tract system, respiratory system, and bone marrow) and being infected with MRSA.
- H1: there are statically significant differences at (*P*-value =0.05) between the site of isolation (Skin and soft tissues, blood stream, body fluids, urinary tract system, respiratory system, and bone marrow) and being infected with MRSA.
- Ho: there are no statically significant differences at (*P*-value =0.05) between the specimen (wound/pus, swab, tissue, blood, fluid, sputum, trap, urine, and bone marrow) and being infected with MRSA.
- H1: there are statically significant differences at (*P*-value =0.05) between the specimen (wound/pus, swab, tissue, blood, fluid, sputum, trap, urine, and bone marrow) and being infected with MRSA.

Chapter Two

Literature review

2.1 Overview

Several international studies have been done in order to know the prevalence, risk factors, and anti-microbial profile of MRSA and MSSA.

The WHO 2014 published a picture of MRSA spreading around the world in global report on AMR surveillance. Although antibiotic resistance information was available just for Europe, America, and Australia, MRSA was reported in all continents around the world. Large number of countries reported prevalence of MRSA with more than 20% and some countries reach around 80%. This means antibiotic choices are limited (45).

HA-MRSA risk factors include, prolonged hospitalization, present in intensive care unit, long antibiotics therapy, surgeries, and being very close to a patient who has MRSA (46).

CA-MRSA risk factors for included one or more of the these factors: recent hospitalization,outpatient visit,recent nursing home admission, recent use of antibiotic, chronic illnesses, malignancy, injection drug use, and close contact with a person who has one or more of the risk factors (46).

MRSA is highly prevalent in hospitals around the world. For sure the collected data from different studies of different regions are usually not always comparable due to differences in study design and sample population.

A meta-analysis mentioned that the highest rates which is more than 50% are reported in North and South America and Asia. MRSA was around 52.5% of *S.aureus* infection with HA-MRSA of 64% in Asia (47).

A study was conducted in orders to calculate prevalence of MRSA in invasive isolates from south and east Mediterranean countries, the median of MRSA prevalence was 39%. The highest prevalence of MRSA were in Jordan, Egypt and Cyprus, methicillin resistant isolates were more than 50% of all invasive isolates (48).

2.2 Previous studies in Europe

In Europe, in 2011, 31 observational studies were included in a review; screening for MRSA was done in short and long- and short-term care units. Prevalence rates highly varied, the prevalence of MRSA was range between 1% and 24% among all patients, and range between 5% and 54% among *S.aureus* (49).

In 2013, in Sweden, a study of epidemiology of *S. aureus* bloodstream infections, the study mentioned that 4.4% of blood stream infections were MRSA, and the incidence was higher in old people and very young age patients, with higher incidence in female than male with significant association (50).

A review was conducted in Germany; there were around 132000 cases of MRSA in German hospitals annually. MRSA occupied about 20% of all inpatient *S. aureus.* CA-MRSA is not an endemic, risk factors include traveling to areas with high MRSA prevalence, and being close to people have MRSA infection. Animals are also reservoir for MRSA, which can transmitted to human (51).

Other study was conducted in German university hospital, over 7-years period, 789 sample was isolate, male to female ratio showed a significant association ($p<0.001$) of being male, patients with MRSA were between 50 to 74 years (52).

In Denmark, a study mentioned that the prevalence of MRSA was less than 1% for more than 30 years. Increasing started in 2002. No significant difference in MRSA distribution between male or female and also no significant difference between

different age groups, the prevalence of MRSA was higher among patients who took antibiotics in the last 2 years (53).

In 2011 a retrospective study was done for acquisition of MRSA and risk factors in Scottish hospitals, of the 5,155 patients screened for MRSA on discharge, risk factors for acquisition of MRSA were, age above 64 years, renal failure, and having an open wounds (54).

2.3 Previous studies in America

A study in USA was done to know the risks for development of active MRSA infection among patients who were colonized with MRSA at the time they admitted hospital, risk factors included diabetes mellitus, renal diseases, post colonization inpatient admission within 90 days, surgeries, and patients who undergo hemodialysis (55).

Isolates of *S. aureus* were collected from 72 centers in the USA between the start of 2004 and September 2005, 52.0% of 1692 *S.aureus* isolates were MRSA. All isolates including MSSA and MRSA were sensitive to tigecycline, linezolid and vancomycin. Minocycline was active: 99.2 % of isolates. Amoxicillin, piperacillin/tazobactam, levofloxacin and ceftriaxone, demonstrated susceptibilities between 40% to 90% against *S. aureus* samples(56).

A systematic review in Canada mentioned that MRSA numbers increased steadily in the 1990s and 2000s, especially among high-risk populations. High susceptibility to TMP-SMX with more than 85% was reported, 0% resistance for each vancomycin, linezolid, or rifampin was reported. Risk factors for MRSA infection related to infection control strategies, low socioeconomic status, and some demographic characteristics (57).

2.4 Previous studies in Africa

Meta-analysis was done to know MRSA prevalence in Africa. Tunisia prevalence raised from 16% in 2002 to 41% in 2007, and in Libya it was about 31% in 2007. In South Africa, the prevalence was 36% in 2006 and 24% during 2007 to 2011. In Algeria it was 45% and in Egypt it was 52% during 2003 to 2005. In Nigeria, the prevalence was more in north than the south areas. In Ethiopia, the prevalence was 55%. Overall, most of African countries have prevalence less than 50% (58).

In Egypt, 631 *S. aureus* samples were isolated from 2005 to 2013. Resistance of HA-MRSA isolates to 11 used antibiotics was from 55.6% to 100%. Low percentages of resistance to rifampicin and TMP-SMX were reported, 20.4% and 17.2% respectively. CA-MRSA showed higher susceptibility to most antibiotics when compared to HA-MRSA, with resistance rates ranging from 9% to 20%, except for tetracycline 85%, and a total resistance for penicillin (59).

In Libya, from 2013 to 2014, 218 isolates of *Staphylococci* were obtained, 39.7% were MRSA. HA-MRSA was 61.3% and CA-MRSA was 38.7% among all S.aureus isolates. For all MRSA, they were entirely susceptible to vancomycin, tigecycline, linezolid, quinupristin/dalfopristin, daptomycin and moxifloxacin (60).

In Tunisia, a multicenter study was done to study antimicrobial susceptibility and epidemiology of MRSA. 36.3% were CA-MRSA. HA-MRSA strains showed higher resistance to antibiotics than the CA-MRSA. Vancomycin, teicoplanin, linezolid and tigecycline have demonstrated high activity against MRSA. Only one HA-MRSA was classified glycopeptide intermediate *S. aureus* (GISA) (61).

2.5 Previous studies in Asia

Asia is considered as one of the continents with high MRSA prevalence when compared to other regions in the world. Most hospitals in Asia have MRSA as an endemic, with a proportion varies from 28% in Hong Kong and Indonesia, and reached more than 70% in Korea among all *S. aureus* isolates in the early 2010s. resistance to glycopeptides has been reported. Prevalence of CA-MRSA in Asian countries varies from less than 5% to more than 35% (40).

A study was conducted in tertiary care center in Malaysia, in order to study the prevalence of MRSA and other characteristics that may associated with MRSA, reveals that being male and being over 50 years, are significantly associated with being infected with MRSA, *p*-value less than 0.0001 (62).

A study was performed in a tertiary hospital in Thailand showed that 17% of *S. aureus* infections were MRSA. Only one sample was resistant to vancomycin. Chronic lung diseases, cardiac fibrillation, dementia, and prostatic hyperplasia were all have significant association with MRSA infection. Taking antibiotics in the previous 3 months before the infection is considered as a risk for MRSA infection (63).

in India, in 2006, a study mentioned that from 906 isolates of *S. aureus* isolated from clinical and carrier patients, 31.1% and 37.9% were MRSA respectively, nearly all MRSA isolates from clinical patients were resistant to penicillin, 93.6% to ampicillin, and 63.2% for each gentamicin, TMP-SMX, cephalexin, erythromycin. MRSA strains from carriers were all resistant to penicillin, and nearly 71.8% were resistant to ampicillin and 35.9% to TMP-SMX. 0% resistance to vancomycin was detected (64).

Other study was conducted in India for 2008 and 2009 years, mentioned that out of 26310 isolates of *S. aureus*, MRSA was 41% of them. Most of *S. aureus* were from patients with skin and soft tissue infections, followed by bloodstream and respiratory

system infections. MSSA isolates were more sensitive to gentamicin, TMP-SMX, erythromycin and clindamycin than MRSA isolates, with 0% resistance to vancomycin or linezolid (65).

In Saudi Arabia, a prospective study for HA-MRSA was conducted from 2000 to 2004 at a tertiary care hospital, 442 HA-MRSA isolates were collected, 51.2% were infections, and 48.8% were colonization. Most cases were found in surgical and medical units, 33.3% and 32.1% respectively (66).

Retrospective pilot study was conducted at private hospital in Amman, Jordan in 2008 - 2010, 95 total MRSA isolates, MRSA was 29.6% in 2008, increased in 2009 to 64.3% and dropped to 46.2% in 2010.No statistically significant age or gender differences were reported (67).

In Jordan, in the period between the start of 2008 and November 2010, a study mentioned that 31.6% of infections were MRSA among *S. aureus*, large number of them were isolated from wounds, no resistance to vancomycin was reported. Susceptibility to chloramphenicol, linezolid, nitrofurantoin, rifampicin and teicoplanin was more than 80%, but resistant to erythromycin and penicillin was in high rates (68).

Between the start of 2011 and the end of 2013, a total of 20684 Gram-positive and 55594 Gram-negative bacteria were collected in Lebanon from a total of 16 hospitals. 4890 *S. aureus* were found in total, and MRSA percentage was 27.6% (69).

2.6 Previous studies in Palestine

During the period of 2015 to 2017, a study conducted in Palestine which included 112 MRSA specimens from various hospitals in the West Bank and Jerusalem revealed that all of the samples were resistant to beta-lactam antibiotics, 18.8% to TMP-SMX, 23.2% to gentamicin, 34.8% to clindamycin, 39.3% to ciprofloxacin, and 63.4% to erythromycin. No VRSA was found (70).

200 healthcare professionals participated in a study in Gaza to determine the prevalence of MRSA nasal carriage among hospital staff at Al Shifa hospital. Of the 31% of S. aureus carriers, 82.3% were MRSA, and 25.5% of all healthcare workers were found to be MRSA carriers. Internal medicine and surgery department employees made up 41.3% and 35%, respectively, of MRSA carriers (71).

S. aureus nasal carriage among patients was statistically linked with prior chronic diseases, diabetes mellitus, and prior skin lesions, according to a study conducted in North West Bank to estimate the prevalence of MRSA nasal carriage among patients and healthcare workers in K.U (11).

The percentage of MRSA among all S. aureus isolates was 29% and 8.2% at Rafidia Hospital and Thabet Hospital, respectively, according to a study in 2013 on the molecular characterization of MRSA isolates from environment of hospitals and patients (72).

Chapter Three

Methodology

3.1 Study design and setting

Retrospective study was done over all patients who diagnosed with *S. aureus* regardless community or hospital acquired at An-Najah National University Hospital, an educational hospital, which is located in Nablus -West bank- Palestine.

Information about patients with *S. aureus* who visited outpatient, inpatient, emergency rooms, and K.U departments, from the beginning of January 2020 to the end of December 2021, was collected from the hospital's microbiology laboratory database and hospital archive.

3.2 Study population

The sample will be all specimens of patients who are positive for *S. aureus* either if it is community-acquired or hospital-acquired in the period between January 2020 to December 2021 at An-Najah National University Hospital.

3.3 Surveillance, inclusion criteria and exclusion criteria

Demographic and clinically significant comorbidities information was retrieved from hospital information system including: patient gender, age, patient setting and co-morbidities which include: cardiovascular diseases, cancer, chronic kidney diseases, diabetes mellitus, hepato-biliary disorders, central nervous system (CNS) disorders, and lung diseases. Sources of specimens included: skin and soft tissue, respiratory tract, bloodstream, urinary tract system, bone and joint and body fluids.

Inclusion criteria

All samples which were isolated at An-Najah National University microbiology laboratory during the study time period that had positive culture of *S. aureus* were included.

Exclusion criteria

- Patients' samples with insufficient health records will be excluded.
- Only the first isolate from patients who had more than one episode of *S. aureus* evidence from the same clinical specimen during the research period would be used in the analysis, and other will be excluded.

3.4 Study variables

- Dependent variable:

MRSA or MSSA infection.

- Independent variables:

1. Age

- Childhood age from 2 to 10.
- Adolescence age from 11 to 17.
- Young adults age from 18 to 40.
- Adults age from 41 to 65.
- Elderly age above 65.

2. Gender

- Male.
- Female.

3. Patient setting

- Inpatient (medical ward):
  - Intensive care unit (ICU).
  -Cardiac critical unit (CCU).
  -Vascular department.

- Inpatient (surgical ward):
  - Cardiac surgical ward (CSW).
  - Surgical intensive care unit (SICU).
- Inpatient (pediatric ward):
  -Pediatric ward (PW).
  - Pediatric intensive care unit (PICU).
- Outpatient
- Kidney unit (K.U).
- Emergency room (E.R).

4. Co-morbidities

- Cardiovascular diseases:
  - Deep venous thrombosis.
  - Peripheral artery diseases.
  - ischemic heart diseases.
  - Angina.
  - Hypertension.
  - Cardiac myopathy.
  - Atrial fibrillations.
- Cancer
  - T-cell lymphoma.
  - Colon cancer.
  - Esophageal cancer.
  - B-cell ALL.
  - Brain masses.
  - Leukemia.
  - Prostate cancer.
  - Adenocarcinoma.

- Lymphomas.
- Breast cancer.
- Ductal carcinoma.
- Leukocytosis.
- Myeloma.
- Rectal tumor.
-Salivary gland carcinoma.

- Kidney diseases:
  - kidney failure in its different stages.
  - Acute kidney diseases.

- Diabetes mellitus:
  - Diabetes mellitus type 1.
  - Diabetes mellitus type 2.

- Hepato-biliary disorders:
  - Hepatitis
  - Liver cirrhosis
  - Liver injuries.

- Central nervous system (CNS) disorders:
  - Epilepsy and different types of seizures.
  - Neuropathy.
  -Autism.
  -Neurogenic bladder.

- Lung disorders
  - Asthma
  - Chronic obstructive pulmonary disease (COPD)

5. Site of the isolation

- Skin and soft tissues (SST):
  - Wound.
  - Pus.
  - Swab.
  - Tissues.
- Blood stream:
  - Central-line blood sample.
  - Peripheral blood sample.
- Body fluids:
  - Ascetic fluid.
  - Cerebrospinal fluid (CSF).
- Urinary tract system:
  - Urine.
- Respiratory system:
  - Sputum.
  - Trap.
- Bone marrow:
  - Bone marrow biopsy.

6. Specimen type

- Wound/Pus
- Swab
- Tissue
- Blood
- Fluid
- Sputum

- Trap
- Urine
- Bone marrow biopsy

3.5 Bacterial identification and antibiotic susceptibility

The Vitek 2 compact system (bioMérieux, Marcy-l'Étoile, France) was used to identify the bacteria and test their susceptibility to several antibiotics. *S. aureus* isolates are classified to MSSA or MRSA depending on oxacillin minimum inhibitory concentration (MIC). *S. aureus* considered to be MRSA if the MIC > 4 μg/ml. If the MIC of Vancomycin is greater than16 μg/ml, *S. aureus* isolate will be considered VRSA according to the Clinical and Laboratory Standards Institute 2020 (73).

VITEK-2 AST GP67 cards are used to detect the susceptibility of the isolates to antibiotics including oxacillin, cefuroxime, amoxicillin, piperacillin-tazobactam, clindamycin, erythromycin, gentamicin, levofloxacin, linezolid, moxifloxacin, ciprofloxacin, quinopristin/dalfopristin, rifampicin, tetracycline, tigecycline, TMP-SMX and vancomycin. The results are reported as sensitive or resistant.

3.6 Outcomes and statistical analysis

The data which was gathered from the hospital laboratory system will be used to calculate the prevalence of MRSA or VRSA. In the hospital microbiology lab, patterns of MRSA susceptibility and resistance to various antibiotics were identified.

With the use of the Chi square test and the SPSS version 20 program, the relationship between various variables and the various strains of S. aureus will be examined. Statistics will be considered significant for P-values less 0.05.

3.7 Ethical issues

- An-Najah National University's research committee examined and approved the proposal.
- An-Najah National University's Institutional Review Boards (IRB) gave their approval.
- An-Najah National University Hospital gave permission for access to patient records.

Chapter Four

Results

4.1 Prevalence of MRSA and associations between demographic characteristics and co-morbidities with MRSA infection

During the period of 2 years of the study, 329 samples with *S. aureus* were collected. From the 329, total of 280 isolates from patients with first episode of *S. aureus* positive were reported. Other 26 specimens from outpatients with incomplete medical records, comorbidities, and details about *S. aureus* infection, were excluded from the study. So, our sample study was 254 specimen, 84 samples from year 2020 and 170 samples from year 2021.

Of 254 patients with different age categories, with mean age of 45.1 ± 21.3 years, ranging from 2 and 85 years, 52% were male and 48% were female. MSSA isolates were identified in 128 patients (50.4%) and MRSA were detected in 126 patients (49.6%). No significant association in MSSA and MRSA distribution between male (51.5% vs. 48.5%) or in female (49.2% vs. 50.8%) (*p*-value =0.710). Our study reveals that there was no significant relationship in MSSA and MRSA distribution between different age groups in our study sample.

Table 4.1

Association between gender, age and MRSA infection

Variable (Count, percentage)	MSSA count (Percentage)	MRSA count (Percentage)	*p*-Values
Gender			
Male (132,52)	68(51.5)	64(48.5)	0.710
Female (122,48)	60(49.2)	62(50.8)	
Age			
Childhood (14,5.5)	4(28.6)	10(71.4)	0.093
Adolescence (21,8.3)	9(42.9)	12(57.1)	0.471
Young adults (63,24.8)	32(50.8)	31(49.2)	0.942
Adults (109,42.9)	58(53.2)	51(46.8)	0.436
Elderly (47,18.5)	25(53.2)	22(46.8)	0.671

Medical and surgical units show highest percentages of *S. aureus* isolates among all hospital units, 24.4% and 21.7% respectively, followed by emergency room with prevalence of 18.5%. Regarding MRSA there is no significant association between MRSA infection and patient's location in either inpatient units (medical, surgical, pediatric), emergency room or outpatient.

There is a significance difference in MSSA and MRSA distribution in kidney unit (p-value = 0.009).

Table 4.2

Association between patient's setting and MRSA infection

Variable (Count, percentage)	MSSA count (Percentage)	MRSA count (Percentage)	p-Values
Patient's setting (254,100)			
Inpatient (Medical) (62,24.4)	34(54.8)	28(45.2)	0.421
Inpatient (Surgical) (55,21.7)	26(47.3)	29(52.7)	0.601
Inpatient (Pediatric) (18,7.1)	7(38.9)	11(61.1)	0.311
Kidney unit (32,12.6)	23(71.9)	9(28.1)	0.009
Emergency room (47,18.5)	19(40.4)	28(59.6)	0.130
Outpatient (40,15.7)	19(47.5)	21(52.5)	0.690

Comorbidity which is associated with MRSA isolation was only chronic lung diseases which includes asthma and COPD (p-value = 0.001), other comorbidities including cardiovascular diseases, cancers, chronic kidney diseases, hepato-biliary diseases, and CNS disorders, showed no significant difference in MSSA and MRSA distribution between patients since p-value is more than 5%.

Table 4.3

Association between co-morbidities and MRSA infection

Variable (Count, percentage)	MSSA count (Percentage)	MRSA count (Percentage)	p-Values
Co-morbidities			
Cardiovascular diseases (106,41.7)	51(48.1)	55 (51.9)	0.538
Cancer (70,27.6)	39(55.7)	31(44.3)	0.296
kidney diseases (64,25.2)	37(57.8)	27(42.2)	0.170
Diabetes mellitus (73,28.7)	32(43.8)	41(56.2)	0.184
Hepato-biliary disorders (5,2)	2(40)	3(60)	0.639
Central nervous system disorders (17,6.7)	10(58.8)	7(41.2)	0.472
Lung disorders (10,3.9)	0(0)	10(100)	0.001

Skin and soft tissues (127,50%) was the biggest source of *S. aureus* isolate, which is the source significantly associated with being infected with MRSA (*p*-value =0.024), followed by blood stream (52,20.5%) with no significant association (*p*-value =0.136). The remaining samples collected from other sources including respiratory system, urinary tract, body fluids, and one sample from bone marrow, all without significant association with MRSA.

Table 4.4

Association between site of isolation and MRSA infection

Variable (Count, percentage)	MSSA count (Percentage)	MRSA count (Percentage)	p-Values
Site of isolation (254,100)			
Skin and soft tissues (127,50)	55(43.3)	72(56.7)	0.024
Blood stream (52,20.5)	31(59.6)	21(41.2)	0.136
Body fluids (23,9)	13(56.5)	10(43.5)	0.538
Urinary tract system (21,8.3)	13(61.9)	8(38.1)	0.271
Respiratory system (30,11.8)	16(53.3)	14(46.7)	0.732
Bone marrow (1,0.4)	0(0)	1(100)	0.313

By anatomical specimen, wound/pus specimens showed the highest percentage of isolates (92, 36.2%) (*p*-value =0.015), isolates from other anatomical sites, there counts and percentages are shown in the attached Table (4.5).

Table 4.5

Association between Source of specimen and MRSA infection

Variable (Count, percentage)	MSSA count (Percentage)	MRSA count (Percentage)	P-Values
Anatomical specimen			
Wound/Pus (92,36.2)	37(40.2)	55(59.8)	0.015
Swab (23,9.1)	11(47.8)	12(52.2)	0.796
Tissue (12,4.7)	7(58.3)	5(41.7)	0.573
Blood (52,20.5)	31(59.6)	21(40.4)	0.136
Fluid (23,9.1)	13(56.5)	10(43.5)	0.538
Sputum (16,6.3)	9(56.2)	7(43.8)	0.628
Trap (14,5.5)	7(50)	7(50)	0.976
Urine (21,8.3)	13(61.9)	8(38.1)	0.271
Bone marrow (1,0.4)	0(0)	1(100)	0.313

4.2 Antimicrobial profile of MSSA and MRSA isolates

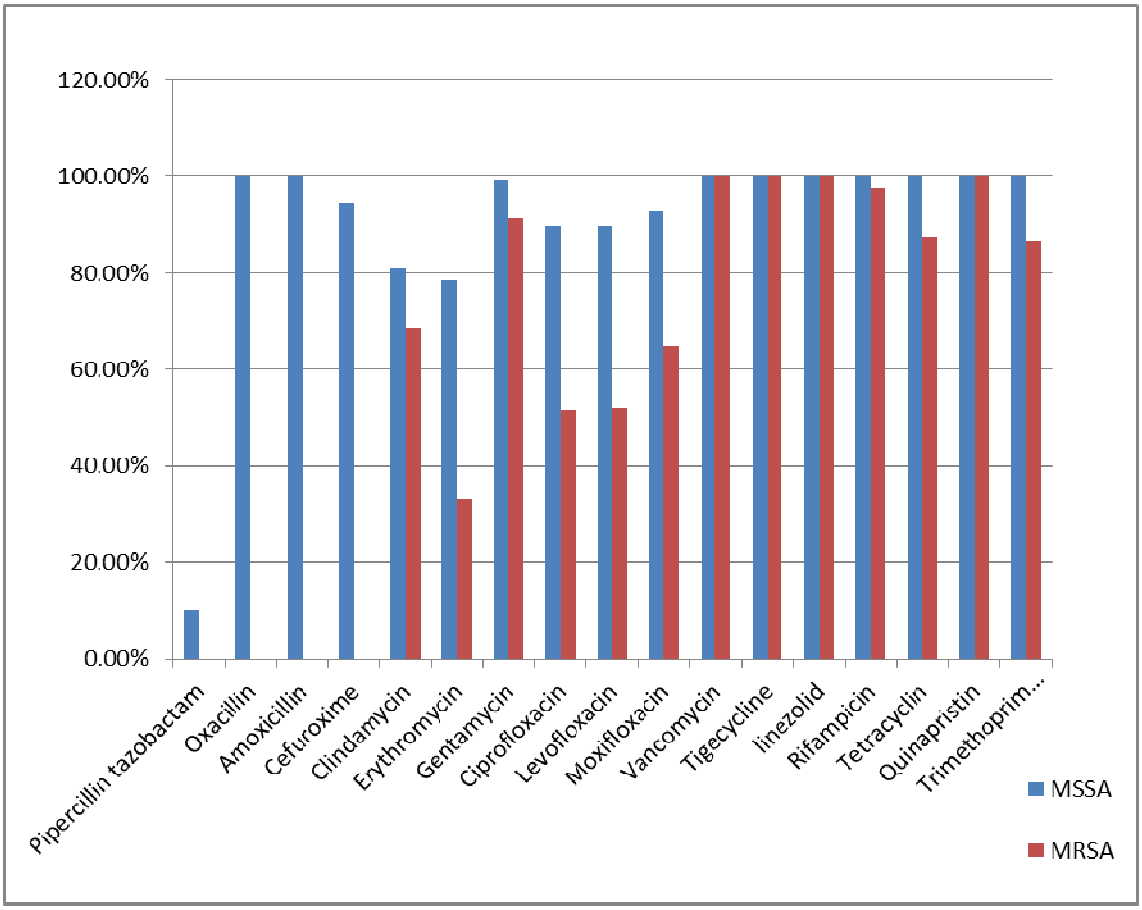
For all isolated samples, MSSA isolates were susceptible to each amoxicillin, vancomycin, tigecycline, rifampicin, tetracycline, quinapristine/dalfopristin and TMP-SMX with 100%. Percentage of Isolates which are sensitive to gentamycin was 99.2%. All other antibiotics in the chart below show a sensitivity with more than 80% except erythromycin 78.6% and Pipercillin /tazobactam has a low rate of sensitivity with just 10.2%.

For MRSA, tigecycline, linezolid, vancomycin, and quinapristin/dalfopristin were having high sensitivity rate of 100%, followed by rifampicin and gentamycin with susceptibility rate of 97.6% and 91.3% respectively, then tetracycline and TMP-SMX demonstrate nearly the same susceptibility of 87.3% and 86.5 respectively, and 68.5% for clindamycin.

Nearly 52% of the MRSA samples were sensitive to each ciprofloxacin, levofloxacin. However, MRSA isolates demonstrated better susceptibility for moxifloxacin than other flouroquinolones, with present of 64.8. Only 33.1% of MRSA isolates are susceptible to erythromycin, and 0% are susceptible for each pipercillin tazobactam, amoxicillin and cefuroxime.

Figure 4.1

Antibiotic Susceptibility of MSSA and MRSA



4.3 Antimicrobial profile of MRSA and MSSA isolates based on site of infection

For all MSSA samples, regardless to the site of infection, they were entirely susceptible to each vancomycin, tigecycline, quinapristin/dalfopristin, linezolid, rifampicin, oxacillin and amoxicillin.

More than 90% of skin and soft tissues isolates were susceptible for each gentamycin and TMP-SMX, moxifloxacin, tetracycline and cefuroxime.

For MSSA isolates from the blood stream, they are sensitive with percent more than 90% for each ciprofloxacin, levofloxacin, moxifloxacin, tetracycline, TMP-SMX, cefuroxime; also, they are all sensitive for gentamicin.

Regarding body fluids infection, more than 90% of the samples are sensitive for each ciprofloxacin, levofloxacin, moxifloxacin, and 100% for TMP-SMX and gentamicin.

For MSSA isolates from upper and lower respiratory tract, they show lower percentage of sensitivity for antibiotics, the highest percentage was for gentamicin with 100% sensitivity, followed by erythromycin and moxifloxacin with sensitivity of 87.2%.

For urinary tract infection (UTI) that is caused by MSSA, it shows high sensitivity rates for antibiotics, 100% of the isolates are sensitive to each ciprofloxacin, levofloxacin, moxifloxacin, gentamicin, TMP-SMX, and more than 90% were sensitive to each clindamycin, erythromycin, tetracycline.

Table 4.6

Antibiotic susceptibility of MSSA isolates in relation to the site of infection

Body site Antibiotic	SST	Blood stream	Fluids	Respiratory system	Urinary tract system
Vancomycin	100	100	100	100	100
Tigecycline	100	100	100	100	100
Quinapristin/ dalfopristin	100	100	100	100	100
Linezolid	100	100	100	100	100
Rifampicin	100	100	100	100	100
Clindamycin	80	77.4	83.3	81.2	91.7
Erythromycin	76.4	77.4	66.7	87.5	91.7
Gentamicin	98.2	100	100	100	100
Ciprofloxacin	87.3	93.5	91.7	81.2	100
Levofloxacin	87.3	93.5	91.7	81.2	100
Moxifloxacin	92.7	93.5	91.7	87.5	100
Tetracycline	92.7	93.5	83.3	100	92.3
TMP-SMX	96.4	96.8	100	100	100
Pipercillin tazobactam	9.3	12.9	15.4	0	15.4
Oxacillin	100	100	100	100	100
Amoxicillin	100	100	100	100	100
Cefuroxime	96.4	93.5	92.3	100	84.6

For all MRSA samples, regardless to the site of infection, they were entirely susceptible to each vancomycin, tigecycline, quinapristin/dalfopristin, linezolid.

There were only three skin and soft tissues samples are resistant to rifampicin, and all others are sensitive.

More than 90% of skin and soft tissues isolates are susceptible for each gentamicin and TMP-SMX.

For MRSA isolates from the blood stream, they are sensitive with more than 90% for each clindamycin and gentamycin; also, they are all sensitive for tetracycline. Regarding MRSA isolates from body fluids, 90% of the samples are sensitive for each gentamicin, tetracycline and TMP-SMX.

For MRSA isolates from upper and lower respiratory tract, they show lower percentage of sensitivity for antibiotics, the highest percentage was for gentamycin 85.7 followed by TMP-SMX with sensitivity of 78.6%.

For UTI that is caused by MRSA, it shows low sensitivity rates for antibiotics, the highest sensitivity was for gentamicin (87.3%), then tetracyline (71.6%). There was one sample isolated from bone marrow and it sensitive to all tested antibiotics except beta-lactams.

Overall, vancomycin, tigecycline, quinapristin, and linezolid could be used for all serious cases or HA-MRSA regardless to the site of infection, rifampicin and gentamicin are a good choice to be used as synergism antibiotic. TMP-SMX, tetracycline, clindamycin are good choices for less severe infections or CA-MRSA, flouroquinolones and erythromycin are not good choices since MRSA susceptibility show lower percentages than other mentioned antibiotics before.

Table 4.7

Antibiotic susceptibility of MRSA isolates to each antibiotic in relation to the site of infection

Body site Antibiotic	SST	Blood stream	Fluids	Respiratory system	Urinary tract system
Vancomycin	100	100	100	100	100
Tigecycline	100	100	100	100	100
Quinapristin/dalfopristin	100	100	100	100	100
Linezolid	100	100	100	100	100
Rifampicin	95.8	100	100	100	100
Clindamycin	66.7	90.5	70	57.1	33.3
Erythromycin	26.4	57.1	30	35.7	16.7
Gentamicin	91.7	95.2	90	85.7	87.3
Ciprofloxacin	50	61.9	40	57.1	37.5
Levofloxacin	48.6	61.9	40	57.1	57.1
Moxifloxacin	61.1	76.2	50	71.4	71.4
Tetracycline	88.9	100	90	64.3	75
TMP-SMX	95.8	71.4	90	78.6	50
Pipercillin –tazobactam	0	0	0	0	0
Oxacillin	0	0	0	0	0
Amoxicillin	0	0	0	0	0
Cefuroxime	0	0	0	0	0

Regarding the location of the patient when MRSA was acquired, from either hospital or community, it was difficult for us to divide them in groups based on the time of onset of infection, because there are 28 samples that was sent from emergency room and 21 sample from out-patients.

Infections are classified as community acquired or hospital acquired depending on the time of the onset of infection, if the infections start after 48 hours or more after hospital admission, it classified as hospital acquired (74).

Regarding isolates from inpatients, in medical ward, there is 28 MRSA isolates, 12 of them are isolated after 2 days of admission. In surgical ward, there is 29 sample, and 11 are after 2 days of admission, in pediatric ward, there is 11 isolated and 8 of the isolates after 2 days of admission.

Chapter Five

Discussion

5.1 Discussion of the results

Antimicrobial profiles of MSSA and MRSA isolates, as well as knowledge of risk factors linked to MRSA infection, aid in the development of prevention and treatment methods.

Knowing MRSA's epidemiology, risk factors, and antimicrobial profile is one of the most efficient ways to stop the spread of this infection. It is one of the leading causes of nosocomial infections worldwide, has few effective treatments, and can result in serious infections as we have already mentioned.

In our study, MRSA percentage was 49.6 % of *S. aureus* samples. Previous study which was conducted in 2013 in Rafidia Hospital and Thabet Hospital mentioned that MRSA prevalence among all *S. aureus* isolates was 29% and 8.2%, respectively, samples are from patients and hospital environment surrounding patients (72). There is a difference between the two studies, because our study is only for patients and the other study is for patients and the environment, but the percentage of isolated MRSA from all *S. aureus* in our study, is relatively high when we compared them.

When we compare the prevalence of MRSA in our study to other studies in Asia and around the world, we classified our hospital in the middle, since it is nearly 50%, as a review in Asia reveals that most hospitals in Asia have MRSA prevalence with an proportion from 28% to more than 70% among all clinical *S. aureus* isolates (40). A worldwide picture of MRSA expansion is displayed in the global report on antimicrobial resistance, released by the WHO 2014 observed that most countries reported a proportion of MRSA more than 20% and, some countries approach 80% (45).

In general, when we talk about 50% of *S. aureus* sample are MRSA, it is not a small percentage, increasing antibiotic resistance is happening for many reasons including antibiotics overuse, inappropriate prescribing, extensive agriculture use, and regulatory barriers that limit the approval of new antibiotics (75). One of the limitations of our study that there is no enough data related to patients' antibiotics use history which is a big risk factor for having multidrug resistant organisms as we mentioned.

Antibiotic resistance in microbes is exacerbated by overuse and abuse of antibiotics. According to a meta-analysis research, people who had taken antibiotics had a 1.8-fold higher chance of acquiring MRSA. The flouroquinolones, glycopeptides, cephalosporins, and other beta lactam antibiotic groups had relative risks of 3, 2.9, 2.2, and 1.9 respectively (76).

Regarding distribution of MRSA in male or female, MSSA and MRSA distribution did not significantly differ between males and females, male(51.5% vs. 48.5%) and female (49.2% vs. 50.8%) (*p*-value =0.710), this is supported by a study was conducted in Denmark mentioned the same result that there is no significant relationship in MRSA distribution between male and female (53). Retrospective pilot study was conducted at a private hospital in Amman, Jordan between 2008 and 2010 mentioned that there is no statistically significant gender difference was reported (67).

Another study in Sweden mentioned that incidence of blood stream MRSA was higher incidence in female than male with significant association (50). While a study in medical facility in Germany mentioned that male to female ratio have a significant association ($p<0.001$) of the male gender (52), also a study in hospital in Malaysia, reveals that being male are significantly associated with being infected with MRSA with *p*-value less than 0.0001 (62). As we have seen, some studies supported our study and some opposed it, this may because different studies were done in different places, time, population and different conditions.

According to our research, there were no discernible variations in the spread of MSSA and MRSA between different age groups in our study sample. Also a study in Amman, Jordan mentioned that there is no statistically significant age differences were reported in MRSA distribution (67)

This is supported by a study in Denmark, mentioned that no significant differences in different age ranges in MRSA distribution (53). Also supported by study in Thailand revealed the distribution of MSSA and MRSA did not differ significantly between adults and children (63). While other study in 2011 in Scottish hospitals mentioned that being above 64 years, is one of the risk factors of having MRSA infection (54). In 2013, a study was conducted in Sweden to study epidemiology of *S.aureus* bloodstream infections, mentioned that incidence was higher in older age and very young age (50).

There is no significant relationship between different age groups and MRSA distribution among patients. There are many factors that can influence this relationship including other demographic characteristics and other factors that may affect the patient immunity and make him/her more vulnerable to infections, we think this is the reason that there are differences between the study's results, that some support us, while others not.

Regarding the location of the patient, medical and surgical units show highest prevalence of S. *aureus* isolates among all hospital units, 24.4% and 21.7% respectively. Prevalence of MRSA was highest in pediatric unit followed by emergency room, with percentage of 61.1% and 59.6% respectively, followed by surgical unit with MRSA prevalence of 52.7%, there is no significant association between MRSA and MSSA infection and patient's setting in either inpatient units (medical, surgical, pediatric), emergency room and outpatient. The percentages of MSSA and MRSA in these units are nearly the same with no significance difference. According to a study conducted in Saudi Arabia, samples of HA-MRSA

colonization and infection were taken from 2000 to 2004 from a tertiary hospital, and the majority of cases were found in the medical and surgical wards (66).

K.U setting was found to be the only setting which has significant association with MRSA and MSSA isolation (*p*-value = 0.009), the percentage of MSSA is higher than MRSA. Hemodialysis patients have weakened immune system which make them at high risk for acquiring infections, patients must frequently stay in hospitals and the procedure necessitates the repeated use of catheters and needles to reach the bloodstream (77).

Infection is the is a main cause of morbidity and the 2nd leading cause of death after cardiovascular diseases in patients undergo hemodialysis, gram-positive bacteria are most type of bacteria isolated from bloodstream from hemodialysis patients (78). Studies mentioned that ESRD patients have a 100-fold higher risk of MRSA infection acquiring compared with the other healthy population (79). Among hemodialysis patients with all *S. aureus* infections, those with MRSA infections have significantly leads to longer hospitalizations, higher costs, with higher mortality rate (80).

Our results showed no associations between MRSA and general comorbidities except for chronic lung diseases which include asthma and COPD, which show a significant association in MRSA distribution among patients (*p*-value =0.001), supported by study was conducted in a tertiary hospital in Thailand mentioned that chronic lung disorders, cardiac fibrillation, dementia, and prostatic hyperplasia were all significantly associated with being infected with MRSA (63).

One of the causes that patients with chronic lung diseases as COPD are at high risk for acquiring respiratory infections compared with healthy people (81).

Beta lactams and macrolides which are used for treating lung infections, the standard duration of antibiotic course in COPD took 10 days, but shorter course

therapy is preferred, since it can reduce the adverse effects and the development of resistance to antibiotics (82).

A meta-analysis of 7 studies, reveals that shorter duration treatment include 5-day fluoroquinolones provide higher effectiveness and more safe, also increase compliance and reduce cost of therapy, and better efficacy compared to that of standard therapy of infections in COPD patients, this therapy also demonstrates more rapid symptom resolution and faster recovery (82).

Due to their potent anti-inflammatory and immunosuppressive effects, inhaled corticosteroids are crucial in the treatment of asthma and are also an option for COPD patients who suffer from recurrent exacerbations. (83), as it has an immunosuppressive effects, so it considered as a risk factor for acquiring infections (84).

Some others co-morbidities which considered as risk factors in other studies including, cancer, diabetes and cardiovascular diseases, showed no association between MSSA and MRSA distribution between patients in our study sample. It is possible that if we conducted the study on these co-morbidities in a different time period, and hospital, the sample would be surely different, so the results may change.

Skin and soft tissues (127,50%) was the biggest source of *S. aureus* isolate, which is the source significantly associated with being infected with MRSA (*p*-value =0.024), and by anatomical specimen, wound/pus specimens showed the highest percentage of isolates (92, 36.2%) (*p*-value =0.015). Followed by blood stream (52, 20.5%) with no significant association (*p*-value =0.136). This was supported by a research done in India, which revealed that 26310 isolates in total were included, 41% of them were MRSA-positive, and most S. aureus isolates were taken from people who had skin and soft tissue infections, blood stream infections, and respiratory infections (65). Also in 2011 a study about acquisition of MRSA and risk factors

after implementation of universal screening in Scottish hospitals mentioned that open wounds is associated with being infected with MRSA (54). In Jordan, in the period between the start of 2008 and November 2010, a study showed that 31.6% of *S. aureus* infections were MRSA, Most of these strains were isolated from wounds (68).

One of the key reasons that S. aureus is more frequently a commensal species, present on the skin, mucous membranes, and in the gut of 25–50% of the population, is one that was previously described (10). Therefore, skin and soft tissue are at high risk for developing MRSA infection due to several things including surgeries, open wounds or using intravenous catheter.

The typical method of choosing an antibiotic for S. aureus infections depends on a number of variables, including the exact site of the infection, the patient's potential risk factors for MRSA, the degree of severity and invasion of the infection, the patient's immune system status, comorbid conditions, medication regimen, and local susceptibility to antimicrobial profiles.

For MSSA infections, infection is certainly not very serious and invasive as in MRSA, and there is many options for treating since sensitivity to different classes of antibiotics is higher than MRSA. A study mentioned that for simple skin infections, cephalexin and dicloxacillin are used and clindamycin is an alternative, for more complex skin infection, bacteremia, pneumonia, osteomyelitis and catheter related infections, naficillin is recommended, cephazoline and clindamycin are alternatives, and in serious infections including bacteremia, pneumonia, and catheter related infections, vancomycin could be used. In osteomyelitis, clindamycin, flouroquinolones plus rifampin are used as alternative (85).

In our sample, for all isolated MSSA, they were susceptible to each oxacillin amoxicillin, vancomycin, tigecycline, rifampicin, tetracycline, quinapristine/ dalfopristin and TMP-SMX with 100%. Percentage of Isolates which are sensitive to

gentamycin is 99.2%. Many of other tested antibiotics showed sensitivities with more than 80%, including cefuroxime and flouroquinolones.

Regarding MRSA antimicrobial profile in general, tigecycline, linezolid, vancomycin, and quinapristin/dalfopristin were displaying high susceptibility rate of 100%, followed by rifampicin and gentamycin with susceptibility rate of 97.6% and 91.3% respectively, then tetracycline and TMP-SMX demonstrate nearly the same susceptibility of 87.3% and 86.5 respectively, and 68.5% for clindamycin. Nearly 52% of the MRSA samples were sensitive to each ciprofloxacin, levofloxacin. Only 33.1% of MRSA isolates are sensitive to erythromycin and 0% sensitive to beta lactam antibiotics.

Our results was supported with other study was conducted in Palestine between 2015 to 2017, included 112 MRSA samples from hospitals in west bank and Jerusalem, showed that 100% of the samples are resistant to beta-lactams antibiotics, 18.8% were resistant to TMP-SMX, 34.8% to clindamycin, 39.3% to ciprofloxacin, and 63.4% to erythromycin, 23.2% were resistant to gentamicin (70) while our study results in only 2.4% resistance rate for gentamycin.

We will discuss the appropriate antibiotics to be used for MRSA infection based on the site of infection, compared to 2011 Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA) for the treatment of MRSA Infections (86), For each skin and soft tissue, blood stream, respiratory system and bone infection.

According to IDSA, skin and soft tissue infection empirical coverage if it is mild or CA-MRSA, oral antibiotic including: clindamycin, TMP-SMX, tetracycline and linezolid are recommended. In our study, skin and soft tissue infections with MRSA demonstrated lower sensitivity for clindamycin (66.7%) compared to tetracycline and TMP-SXZ, 88.9% and 95.8 respectively, and 100% for linezolid.

For hospitalized patients with more severe skin and serious soft tissue infections, broad-spectrum antibiotics are recommended to be used empirically for MRSA

before culture result. Options include the vancomycin, linezolid, daptomycin, telavancin, and IV clindamycin. Vancomycin and linezolid are good options in our study since MRSA demonstrated 100% sensitivity for them, clindamycin is not a good choice since the sensitivity of MRSA isolates is 66.7% as we mentioned.

One of the most frequent *S. aureus* infections is blood stream infection. The first thing to do if you have an infection is remove the catheter from its source. The first line of defense against bloodstream MRSA should be antibiotics. Vancomycin or daptomycin are suggested by IDSA. Since all of our samples are sensitive to vancomycin and daptomycin is not accessible at our facility, vancomycin is the best option.

The use of IV vancomycin for uncomplicated bacteremia caused by MRSA is strongly advised, and linezolid is an option where it is contraindicated, per the new revised UK recommendations published in 2021. As a second-line option, think about daptomycin or teicoplanin. It is not advised to treat MRSA bacteremia with TMP-SMX alone as a first line of treatment (87).

According to IDSA, to treat pneumonia caused by MRSA, IV vancomycin or linezolid which is the alternative, are recommended, due to the potentially of life-threatening pneumonia. Clindamycin only if the isolate is susceptible. In our study, all of our samples are entirely susceptible to vancomycin and linezolid. Regarding clindamycin, respiratory tract MRSA showed a susceptibility of 57.1% for it, so, it is not highly recommended in our study.

Regarding bone and joint infection, there is only one sample of bone marrow infection with MRSA in our study sample, which is sensitive for vancomycin, linezolid, tigecycline, quinapristine/dalfopristin, rifampicin, clindamycin and TMP-SMX. According to IDSA, parenterally administered antibiotics such as IV vancomycin or daptomycin are advised. The following are some antibiotic choices for parenteral and oral routes: Combination of rifampin, linezolid, and clindamycin with TMP-SMX.

Regarding body fluid which is mainly ascetic fluids, empiric treatment should be used against MRSA to patients with HA-MRSA intra-abdominal infection who are colonized or who are at risk of having the infection, vancomycin is recommended for suspected or proven MRSA infection according to guidelines by the Surgical Infection Society and the Infectious Diseases Society of America (88). In our study, all samples are sensitive to vancomycin, so it is the best choice.

According to the new updated recommendations from the UK in 2021, depending on susceptibility, you may choose to treat a lower UTI brought on by MRSA with an oral medication such doxycycline, ciprofloxacin, or TMP-SMX. Consider IV vancomycin or teicoplanin as the first-line therapy for more serious MRSA-related UTIs. Since linezolid is poorly eliminated by the kidney, it is not advised to use it. Since catheter-caused UTI by MRSA is not well studied in clinical trials, all of the treatments have weak recommendations. These include replacing the catheter, with or without a single dose of gentamicin if the MRSA isolate is known to be susceptible, and glycopeptides as alternatives (87).

In our study, all of the samples from urinary tract system are sensitive for each vancomycin, tigecycline, quinapristine/Dalfopristin and rifampicin. For gentamicin, MRSA demonstrated a susceptibility of 87.3%, followed by tetracycline with sensitivity of 75%, only 50% and 37.5% of MRSA isolates were sensitive to TMP-SMX and ciprofloxacin respectively.

Overall, vancomycin works best for the empiric treatment of all MRSA infections, including serious infections of the skin, soft tissues, lungs, and bloodstream. linezolid could be an option due to its high price and toxicity.

The incidence of VISA has significantly increased recently (p-value 0.05), according to a systematic review and meta-analysis that calculated the global prevalence of VRSA, VISA, and heterogeneously vancomycin intermediate S. aureus (Hvisa) from 1997 to 2019. Between various continents, there were 12, 24, and 14 isolates of

VRSA, VISA, and hVISA, respectively (89). In our study there were no VRSA or VISA infections reported which is very good result, so vancomycin is still the best choice for severe infections.

Finally, due to the Covid-19 pandemic, consequent modifications in preventative measures, and the increased use of antibiotics, it is possible to view the years 2020 and 2021 as extraordinary ones in the field of infection prevention and control.

5.2 Limitations and strengths

There are a number of limitations in our study that should be considered, included:

- That there is no antibiotics use history for the patients, which can help us getting better results.
- Another thing that we cannot classified all infections as community or hospital acquired which may help us to have better results.
- Due to the fact that this was one-center research, it might not be indicative of other centers.
- Changes in the preventive measures and antibiotics use in the study period due to covid-19 pandemic.
- If we want to discuss this study's positives, we should point out that:
- The study at An-Najah National University Hospital in the West Bank, Palestine, is the first study to investigate the prevalence of MRSA as well as their sensitivity profiles, on the basis of new data gathered in 2020 and 2021
- We highlighted the most suitable antibiotics to be used empirically.
- We also investigated additional potential risk factors for MRSA infection.

5.3 Conclusion

According to results obtained, we conclude that the prevalence of MRSA was 49.6% from all *S. aureus* samples with no significant differences between male or female, or different age groups. Lung diseases which include asthma and COPD are significantly associated with MRSA acquisition with (*p*- value = 0.001). K.U setting

was found to be the only patient setting show a significant difference in MSSA and MRSA distribution (*p*-value = 0.009). Skin and soft tissues (127,50%) was the biggest source of *S. aureus* isolate, which is the source significantly associated with being infected with MRSA (*p*-value =0.024), and by anatomical specimen, wound/pus specimens showed the highest percentage of isolates (92, 36.2%) (*p*-value =0.015). For MRSA, tigecycline, linezolid, vancomycin, and quinapristin/dalfopristin were displaying high susceptibility rate of 100%, followed by rifampicin and gentamycin with susceptibility rate of 97.6% and 91.3% respectively, then tetracycline and TMP-SMX demonstrate nearly the same susceptibility of 87.3% and 86.5 respectively, and 68.5% for clindamycin. Nearly 52% of the MRSA samples are sensitive to each ciprofloxacin, levofloxacin. However, MRSA isolates demonstrated better susceptibility for moxifloxacin than other flouroquinolones, with present of 64.8. Only 33.1% of MRSA isolates are susceptible to erythromycin.

No VRSA or VISA were isolated.

5.4 Recommendations

1. Many additional studies should be conducted, in order to further enhance, support and more interpretation to our results.
2. Studying other factors that could have been a risk factor of acquiring MRSA or factors affecting the results of our study, this include, previous prolonged hospitalization, prolonged antibiotics use, surgeries, and being close to a patient in the hospital who is infected or colonized with MRSA, injection drug use and other risk factors that are not included in our study.
3. To stop MRSA from spreading to the public, it is critical to reduce its prevalence among patients and HCWs.
4. All health care workers should wear personal protective equipment, including masks and gloves, whenever they have direct patient contact.

5. Taking more care about patients who are at high risk of acquiring MRSA and try to be careful when dealing with them.
2. To determine the precise frequency of HCW nasal carriage in Palestine, a widespread screening program for MRSA is required in all hospitals. A program must also be developed to identify and treat MRSA colonization in all HCWs.
3. To stop the emergence of bacterial resistance, try using fewer antibiotics and dosing them carefully in accordance with regional recommendations.
4. Global efforts must be made in order to discover new antibiotics that could be an alternative in case of increase resistance to vancomycin and linezolid.

List of abbreviations

Abbreviation	Explanation
AMR	Antimicrobial resistance
CA-MRSA	Community-associated Methicillin-resistant *Staphylococcus aureus*
CCU	Cardiac Critical Care Unit
CDC	Centers for Disease Control and Prevention
CLABSI	Central line-associated bloodstream infections
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
CPE	Carbapenemase-producing Enterobacterales
CSF	Cerebrospinal fluid
CSW	Cardiac surgical ward
E.R	Emergency room
ESBL	Extended-spectrum beta-lactamases
GISA	Glycopeptide-intermediate *Staphylococcus aureus*
HA-MRSA	Health care-associated Methicillin-resistant *Staphylococcus aureus*
Hvisa	Heterogeneous vancomycin-intermediate *Staphylococcus aureus*
ICU	Intensive Care Unit
IDSA	The Infectious Diseases Society of America
K.U	Kidney unit
MDRO's	Multidrug-resistant organisms
MRSA	Methicillin-resistant *Staphylococcus aureus*
MSSA	methicillin-sensitive *Staphylococcus aureus*
NNUH	An-Najah National University Hospital

Abbreviation	Explanation
PICU	Pediatric Intensive Care Unit
PW	Pediatric ward
S. aureus	*Staphylococcus aureus*
SICU	Surgical Intensive Care Unit
SST	Skin and soft tissues
TMP-SMX	Trimethoprim/ Sulfamethoxazole
UTI	Urinary tract infection
VISA	Vancomycin intermediate *Staphylococcus aureus*
VRE	Vancomycin Resistant Enterococci
VRSA	Vancomycin resistant *Staphylococcus aureus*
WHO	World Health Organization

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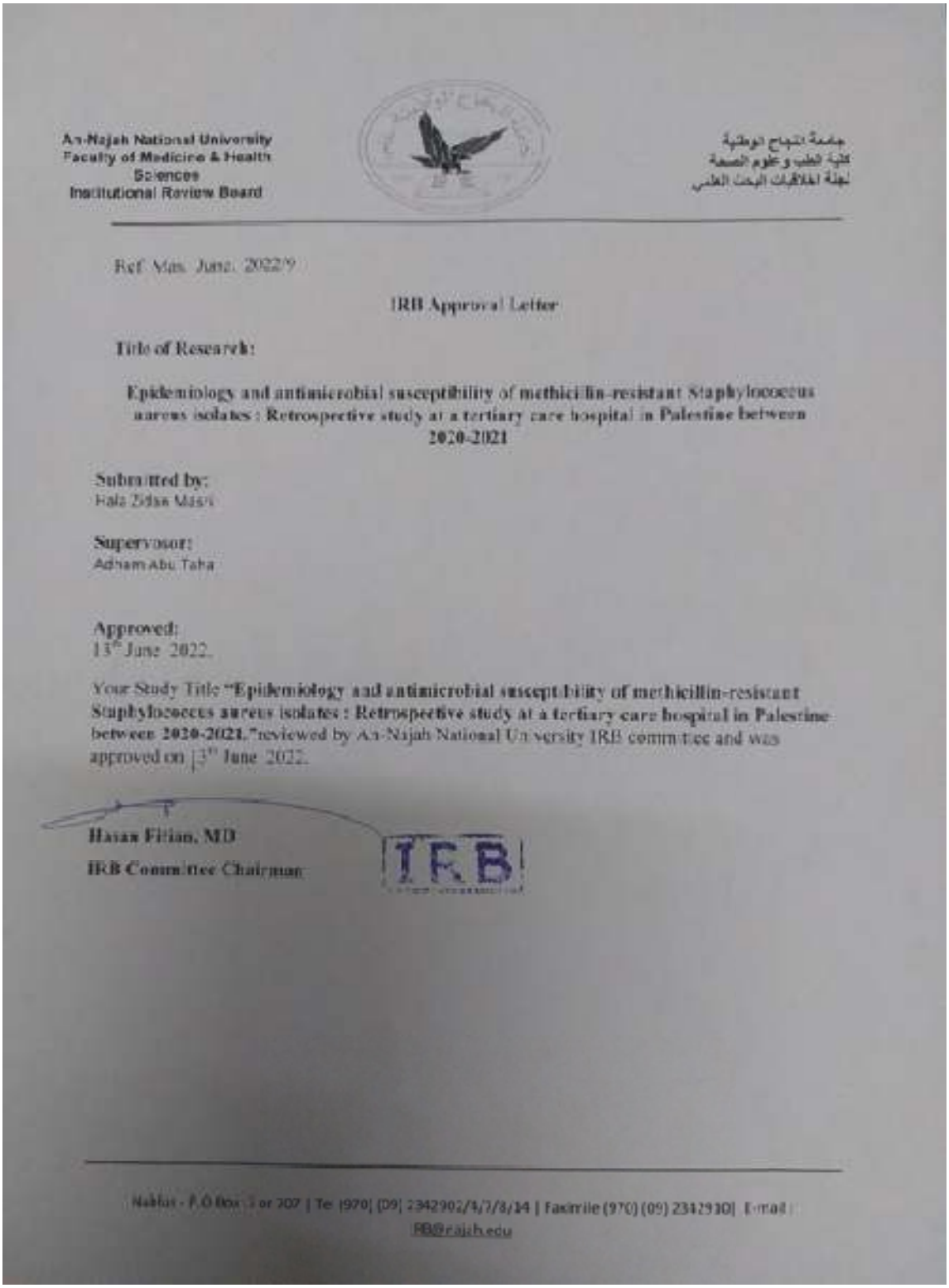
Appendices

Appendix A

Institutional review board (IRB) approval letter



An-Najah National University
Faculty of Medicine & Health Sciences
Institutional Review Board

جامعة النجاح الوطنية
كلية الطب وعلوم الصحة
لجنة الاخلاقيات البحث العلمي

Ref: Mas. June. 2022/9

IRB Approval Letter

Title of Research:

Epidemiology and antimicrobial susceptibility of methicillin-resistant Staphylococcus aureus isolates : Retrospective study at a tertiary care hospital in Palestine between 2020-2021

Submitted by:
Hala Zidan Masri

Supervisor:
Adham Abu Taha

Approved:
13th June 2022.

Your Study Title "Epidemiology and antimicrobial susceptibility of methicillin-resistant Staphylococcus aureus isolates : Retrospective study at a tertiary care hospital in Palestine between 2020-2021." reviewed by An-Najah National University IRB committee and was approved on 13th June 2022.

Hasan Fitian, MD
IRB Committee Chairman

IRB

Nablus - P.O.Box 7 or 707 | Tel: (970) (09) 2342902/4/7/8/14 | Facsimile (970) (09) 2342910 | E-mail: IRB@najah.edu

Appendix B

Requesting facilitation form from An-Najah National University Hospital

جامعة النجاح الوطنية
كلية الدراسات العليا

An-Najah National University
Faculty of Graduate Studies

التاريخ: 2022/7/17

حضرة الدكتور كمال حجازي المحترم
مدير عام مستشفى النجاح الوطني الجامعي

الموضوع: تسهيل مهمة الطالبة/ حلا زيدان نعيم مصري رقم تسجيل (12053382)
تخصص ماجستير في مكافحة وضبط العدوى

تحية طيبة وبعد ...

الطالبة/ حلا زيدان نعيم مصري ، رقم تسجيل 12053382 ، تخصص ماجستير في مكافحة وضبط العدوى في كلية الدراسات العليا/ جامعة النجاح الوطنية، وهي بصدد اعداد الأطروحة الخاصة بها والتي عنوانها:

علم الأوبئة وحساسية مضادات الميكروبات لعزلات من المكورات العنقودية الذهبية المقاومة للميثيسيلين دراسة رجعية في مستشفى رعاية ثالثية في فلسطين بين 2020-2021

يرجى من حضرتكم تسهيل مهمتها في جمع البيانات والمعلومات لمعرفة حساسية بكتيريا المكورات العنقودية الذهبية المقاومة للميثيسيلين للمضادات الحيوية المختلفة، وايضا بحاجة الى جمع المعلومات من ملفات المرضى من سنة 2020 – 2021 من خلال انظمة المستشفى الرقمية والورقية.

علما بأن البيانات والمعلومات سوف تستخدم لأغراض البحث العلمي واستكمال مشروع البحث فقط.

شاكرين لكم حسن تعاونكم،

مع وافر الاحترام ...

أ.د. وليد صويلح
عميد كلية الدراسات العليا

فلسطين، نابلس، ص.ب 7، هاتف 2345115، 2345114، 2345113 (09)(972)، فاكسميل 2342907 (09)(972)
Nablus, P. O. Box (7) *Tel. 972 9 2345113, 2345114, 2345115
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جامعة النجاح الوطنية
كليَّة الدراسات العليا

علم الأوبئة وحساسية مضادات الميكروبات لعزلات من المكورات العنقودية الذهبية المقاومة للميثيسيلين: دراسة رجعية في مستشفى رعاية ثالثية في فلسطين بين 2020-2021

إعداد
حلا زيدان مصري

إشراف
د. أدهم أبو طه

قدمت هذه الرسالة استكمالاً لمتطلبات الحصول على درجة الماجستير في مكافحة وضبط العدوى، من كلية الدراسات العليا في جامعة النجاح الوطنية، نابلس-فلسطين.

2023

علم الأوبئة وحساسية مضادات الميكروبات لعزلات من المكورات العنقودية الذهبية المقاومة للميثيسيلين: دراسة رجعية في مستشفى رعاية ثالثية في فلسطين بين 2020-2021

إعداد

حلا زيدان مصري

إشراف

د. أدهم أبو طه

الملخص

زيادة مقاومة عدوى البكتيريا العنقودية الذهبية لفئات مختلفة من المضادات الحيوية، وتأثيراتها المرضية، جعلتنا نفكر أكثر في دراسة نمط مقاومة مضادات الميكروبات الخاص بها، وعوامل الخطر الأخرى التي قد تترافق مع العدوى.

تشمل أهداف دراستنا، حساب انتشار عدوى البكتيريا العنقودية الذهبية المقاومة للميثيسيلين بين مرضى فلسطينيين، وكذلك لتحديد عوامل الخطر وأنماط الحساسية للمضادات الحيوية، وتحديد أنسب المضادات الحيوية لاستخدامها تجريبياً.

تم جمع بيانات الزراعات الإيجابية من عينات المرضى خلال الفترة الزمنية بين كانون الثاني (يناير) 2020 وكانون الأول (ديسمبر) 2021 من مستشفى جامعة النجاح الوطني، نابلس-فلسطين، المصنفة على أنها حساسة للميثيسيلين او مقاومة للميثيسلين باستخدام نظام Vitek 2 المتوفر بالمستشفى. تم اختبار حساسية كل عزلة لكل من أوكساسيلين، سيفوروكسيم، أموكسيسيلين، بيبراسيلين-تازوباكتام، كليندامايسين، إريثروميسين، جنتاميسين، ليفوفلوكساسين، لينزوليد، موكسيفلوكساسين، سيبروفلوكساسين، كينوبريستين/ دالفوبريستين، ريفامبيسين، تيتراسيكلين، تايجيسايكلين، ترايمثوبريم-سلفاميثوكسازول وفانكومايسين. تم جمع المعلومات الأخرى المتعلقة بالمرضى والأمراض المصاحبة الأخرى من نظام معلومات المستشفى.

126 (49.6٪) من 254 مريضا مصابين بعدوى بكتيريا المكورات العنقودية الذهبية كانت اصابتهم مقاومة للميثيسلين، مع عدم وجود علاقة ما بين مختلف الفئات العمرية والجنس والاصابة ببكتيريا المكورات العنقودية المقاومة للميثيسلين. أظهرت الوحدات الطبية والجراحية للمرضى أعلى نسبة من بكتيريا المكورات العنقودية الذهبية المعزولة 24.4٪ و21.7٪ على التوالي، وكان انتشار بكتيريا المكورات العنقودية المقاومة للميثيسلين أعلى في وحدة طب الأطفال تليها غرفة الطوارئ بنسبة 61.1٪ و59.6٪ على التوالي، تليها الوحدة الجراحية مع انتشار بكتيريا المكورات العنقودية الذهبية المقاومة للمثيسيلين بنسبة 52.7٪. هناك فرق في توزيع عدوى بكتيريا المكورات العنقودية الذهبية الحساسة والمقاومة للميثيسلين في وحدة الكلى (القيمة الاحتمالية = 0.009). أمراض الرئة هي الأمراض المصاحبة المرتبطة بعدوى بكتيريا المكورات العنقودية المقاومة للميثيسلين. يرتبط الجلد والأنسجة الرخوة، وعينة القيح / الجرح بعدوى بكتيريا المكورات العنقودية المقاومة للميثيسلين. جميع العينات كانوا لا يزالون حساسين للفانكومايسين.

يبدو أن انتشار بكتيريا المكورات العنقودية المقاومة للميثيسلين مشابه للبلدان الآسيوية أخرى. فانكومايسين هو الخيار الأنسب لعلاج عدوى بكتيريا المكورات العنقودية المقاومة للميثيسلين.

الكلمات المفتاحية: المكورات العنقودية الذهبية المقاومة للميثيسيلين، المقاومة، عوامل الخطر، نمط الحساسية.