An-Najah National University

Faculty of Graduate Studies

INCIDENCE AND MICROBIOLOGICAL PROFILE OF BLOODSTREAM INFECTIONS AMONG PATIENTS ADMITTED TO JENIN GOVERNMENTAL HOSPITAL: A PROSPECTIVE STUDY

By

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Dedication

I dedicated this Thesis to my love my homeland, state of Palestine, to the martyrs and prisoners, who are more generous than all of us.

To my great father, who has always dreamed of seeing me to complete my study in Faculty of graduate studies, to my mother my school in life, to my great brothers, to my only sister, to the great woman my wife who supported me in my scientific career, to my sons and my daughters, to everyone who has taught me, to my family and my friends to everyone who supported and helped me in my thesis.

Acknowledgment

First of all, thanks be to God alone for the completion of this research, all thanks to my God Allah, for his helping and facilitating me to do my work and complete my study successfully and prayers and peace be upon the Prophet Muhammad, the last one of prophets.

I am very grateful to my supervisor, Dr. Motasem Al-Masri for the support and assistance in my research, to Dr. Souad Belkebir the program supervisor who always support us and inspired me to complete the study, to all program doctors, to everyone who has taught me.

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Many thanks to everyone who helped me in this research, especially my university, An-Najah National University. Thanks are extended to Jenin Governmental Hospital and the laboratory department for completing this work. Thank you all.

Declaration

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

INCIDENCE AND MICROBIOLOGICAL PROFILE OF BLOODSTREAM INFECTIONS AMONG PATIENTS ADMITTED TO JENIN GOVERNMENTAL HOSPITAL: A PROSPECTIVE STUDY

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: Shadi Adel Yousef Museheh

Signature: ____________________

Date: 16.11.2023

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Abstract

Introduction- Bloodstream infections (BSIs) occur when pathogens enter the patient circulating blood, this leads to serious complications, increase length of stay in hospital and increase mortality rate. The reported considerable BSI incidence rates worldwide are considered a challenge for world health.

Objectives- To determine the incidence of BSIs, to characterize BSI patients at Jenin hospital, determine the distribution of antibiotic use, study microbiological profile, antibiotic susceptibility, association with antibiotic resistance, clarify the causative source.

Methodology- The present study is a four month prospective cohort study conducted from October 2022- February 2023 in different wards of Jenin governmental hospital in the north of West Bank of Palestine. A total of 1495 blood cultures for 1190 patients were included in the study.

Results- The study showed that 152 (10.2%) positive blood cultures were detected among the total 1495 blood culture tests, which were included in the study. The incidence for BSIs was 132 cases per 100000 per year. Regarding the type of pathogen in the present study, 55.9% of positive results were Gram-negative and 43.4% were Gram- positive, the most common Gram-negative bacteria were *Klebsiell*a spp (19.2% of all detected pathogens), *E.coli* (11.2%), and *Pseudomonas* spp (9.2%). In addition, *Staphylococcus aureus* (32.4%) was the predominantly isolated Gram-positive bacteria. Out of the isolated bacteria, 40% possessed different resistance phenotypes. There was a significant association between BSIs developing and diabetes mellitus (DM) (P=0.012), hypertension (HTN) (P=0.036), and dialysis (P=0.000). Ceftriaxone (32.8%) was the most common antibiotic used for infected group and it was the most common antibiotic

(31%) used for all suspected BSIs. The most effective antibiotic used for Gram-positive bacteria was vancomycin (100%). The most effective antibiotic used for Gram-negative was colistin (100%). Furthermore, the infected group was shown to have a significantly longer hospital stay (9.6 days) in comparison to non-infected group (6.5 days;P=0.000). Those who acquired BSIs had a significantly (P=0.000) higher mortality rate (22.5%) than that of non-infected group (11%).

Conclusion- Relentless effort should be given to develop infection control policies and programs within hospitals. There must be development of antibiotic stewardship program because of high rate of detection of MDROs.

Keywords: Bloodstream infection, Demographic data, Inflammatory marker, Antibiotic resistance, Etiological agent.

Chapter One

Introduction and Theoretical background

1.1 Overview

Numerous functions are carried out by the blood that constantly flows through our veins and arteries, such functions are important to our survival processes. In addition to delivering oxygen, this substantial circulatory mechanism makes transfer of nutrients easier, prevents infections and distributes heat a part of us. Since it has long been believed that human blood is totally using just blood cells, platelets, and plasma in a sterile environment. The presence of microorganisms in blood was considered as a sign of illness.

Edme Vulpian (1826–1877), a French physician, first used the term "bacteraemia" (bacteriemie) to underline the spread of the infection in the blood in 1872. Any type of microorganism such as bacteria, virus, fungi, and parasite that enter in to the blood are called bloodstream infections (BSIs). Bacteremia indicates the presence of bacteria in blood without any multiplication, while in septicemia, bacteria circulate and multiply and may produce their toxins that cause harm to the host (1).

Bacteremia may be occurring in three different types, which are transient, continuous, or intermittent. Transient, accidental bacteremia can develop spontaneously or as a result of everyday activities like tooth brushing or eating. Another scenario when germs are only momentarily present in the blood is when damaged organs are handled, infected mucosal surfaces are instrumented, or non-sterile locations are used during surgery, severe bacteremia could also result from these conditions. In continuous bacteremia as in infective endocarditis or other endovascular infections, at a very constant rate, pathogens are discharged into the circulation, additionally, pathogens are persistently present in the circulation in the initial stages of some illnesses, including typhoid fever, brucellosis, and others. In intermittent bacteremia, pathogens can be irregularly discovered in the bloodstream in the majority of other illnesses, such as in individuals with causative agent of meningitis, pneumonia, pyogenic arthritis, osteomyelitis, and patients with undrained ulcers.

Nosocomial infections (NIs) are acquired in the hospital but they are not incubating or present at the time of admission (2). NIs are a subgroup of infectious diseases contracted in a healthcare setting. They are also known as health-care associated infections (HCAIs) or hospital acquired infections (HAIs). The infection must occur at least 48 hours following admission in order for it to be deemed nosocomial; it cannot exist at the time of admission. These infections have the potential to cause fatal outcomes like sepsis. Multidrug-resistant organisms (MDROs) obtained through medical interventions, overuse or misuse of antibiotics, and disregard for standard precautions and preventive protocols are the main causes of NIs (3).

BSIs are a leading cause of mortality and morbidity across the world, those infections account for 40% of community-acquired (CA) and hospital-acquired (HA) sepsis and septic shock cases, as well as 20% of intensive care unit (ICU)-acquired cases (4). Nosocomial BSIs are major cause for mortality and morbidity (5). BSIs may be divided into two main groups: intravascular, those whose source is the cardiovascular system and extravascular, those that happen when germs from one infection site invade the lymphatic system and then enter the bloodstream (6).

Critically sick patients frequently develop BSIs, which are linked to greater fatality rates, longer hospital stays, and more expensive medical care (7). Infective endocarditis, central venous catheter-associated bloodstream infections, initial bacteremia, and secondary bacteremia owing to abscesses, osteomyelitis, urinary tract infections, or pneumonia are all examples of BSIs or their sources (8).

BSIs are found all over the world and have both direct and indirect social and economic consequences. BSIs are estimated to afflict 30 million people worldwide, resulting in 6 million fatalities each year (9).

Primary BSIs are a laboratory confirmed BSIs that are not secondary to an infection at another body site. Secondary BSIs are infections seeded from another infected body site (10). At another words primary bacteremia when no documentation of a source of infection before, but when there is a laboratory documentation of the same microorganism at another site at the same time or up to three days before (11).

Globally, infective endocarditis, which is an important source of BSIs, is characterized by infection of the endocardial surface, a natural or artificial heart valve, or an

implanted cardiac device. With the average patient age doubling over the past two decades and a rise in the number of patients with indwelling cardiac devices, the disease's etiology and epidemiology have changed (12).

A laboratory-confirmed BSI that appears within 48 hours of the installation of a central line and is unrelated to an infection at another location is known as a central line-associated bloodstream infection (CLABSI). With the right aseptic procedures, oversight, and management tactics, the majority of instances may be avoided. The examination and treatment of patients having central line installation are described in this activity, which also emphasizes the importance of the professional team in enhancing patient care (13).

Depending on the location of infection and risk factors, BSI cases were categorized as CA, HA, or health-care acquired (HCA), According to prospective nationwide surveillance conducted in Korea between October 2006 to September 2007, the study indicated that 48.8% of the samples were HA-BSI, 33.2% were CA-BSI, and 18.0% were HCA-BSI. The likelihood of having significant comorbidities was higher in HA-BSI and HCA-BSI (14).

1.2 Problem Statement

Infection is frequently a risk for patients admitted to hospitals. Infections caused by bacteria resistant to antibiotics could arise while receiving medical treatment due to overuse and unnecessary use of antibiotics. Among HAIs, the incidence of BSI was previously reported to be the third (14%), after urinary tract infections (UTI) (34%) and surgical-site infections (SSI) (17%) (15).

In this study, the researcher will try to obtain useful results and important recommendations that will help in developing and enriching infection control programs and reducing BSIs rates, as well as narrowing the scientific research gap, and contributing to the wealth of knowledge that serves the medical reality, educating the medical staff on this subject and giving evidence based on medicine, and that this study will serve as a basis for future studies that will form a national research map for the development of the health services.

Infections are a significant cause of long hospital stays and serious complications, leading to excessive and unnecessary use of antibiotics and increase the financial burden. This requires collecting more information on this subject and thus conducting research and studies to reduce the problem (16,17).

An estimated 1,200,000 cases of BSIs, 157,000 fatalities per year in Europe and multiple consequences were reported in a systematic review study published in 2013 that was done to investigate the burden of BSIs and nosocomial BSIs. According to the study, there were 79,000–94,000 fatalities and 575,000–677,000 cases of BSIs every year in North America (with 536,000–628,000 cases in the USA and 40,000–49,000 cases in Canada). So that BSI is a growing public health problem and considering among the top seven causes of death in every country in north America and Europe, BSI has a significant influence on the morbidity and mortality of the general population (18).

1.3 Importance of the Study

In our region, there is a clear lack of data related to the microorganisms causing BSIs, risk factors and the development of antibiotic-resistant microorganisms. The results of this study will be an important source of information to increase awareness among the medical staff about microorganism's resistant to antibiotics, ways of occurrence of blood infection for patients in the hospital and reduction of the financial burden to treatment. The results of this study will also assist in the development of local, regional and international policies and strategies for the diagnosis and treatment of BSIs, and reduce the patients' length of stay (LOS) in hospital and the resulting consequences for the patient and the treatment budget.

Searching for BSIs in Palestine in the literature reviews was done, there are no comprehensive studies on the northern west bank region that show the incidence of BSIs, microbiology profile or antimicrobial resistance, this is the first research in the northern west bank, and it focuses on surveillance, in our area. This data is critical for comprehending current epidemiology and enhancing infection control in various hospital wards.

The present study was conducted in Jenin governmental hospital, which is located in the city of Jenin. Jenin governorate is located in the north of the West Bank, Palestine. The

total population of the governorate, which includes the main city, the surrounding villages, and the refugee camp, was estimated at about 345,875 people in 2022, and it is estimated that the population will reach 374,041 in 2026. This hospital is the only governmental hospital in the governorate, and therefore it suffers from great work pressure (19).

1.4 Objectives of the Study

A. General Objective:

Investigate the different epidemiological aspects of BSI in Jenin governmental hospital during four months.

B. Specific Objectives:

1. Estimate the incidence of BSIs in Jenin and compare it with global results,

2. Determine if a patient's demographic data, such as age and gender, inpatient or outpatient origin, and medical history such as diabetes mellitus (DM), hypertension (HTN), dialysis, and cancer, has an impact on the occurrence of BSIs.

3. Determine the BSI causative pathogens, antibiotic used for suspected and confirmed BSIs, and study antibiotic susceptibility for different detected microorganism.

4. Assess the infected patients' outcomes in terms of length of stay in the hospital and mortality. In addition, signs and symptoms related to patients who were suspected to have BSIs will be evaluated.

5. Determine the causative sources for BSIs such as infective endocarditis, initial bacteremia, secondary bacteremia owing to abscesses, osteomyelitis, urinary tract infections (UTI), or pneumonia.

6. Determine the relationship between positive blood culture and available inflammatory marker (laboratory results) such as white blood cells count (WBCs) and C-reactive protein (CRP).

7. Clarify the relationship between blood culture result and patient's ward, and admission from other hospital.

1.5 Research Hypothesis

This study will examine several research hypotheses, some of which are shown below. P- value < 0.05 will be considered significant. There is a significant difference related to:

1. The development of BSIs and patients' demographic data (age and gender).

2. Development of BSIs and patient origin (inpatient or outpatient, ward in hospital).

3. The development of BSIs and medical history, chronic diseases, signs and symptoms.

4. The development of BSIs and increase WBCs count and CRP level.

5. Previous presence of infection source (secondary BSIs), other positive requested samples culture and development of BSIs.

6. The development of BSIs and patient admission from other hospital.

7. The outcome of the patients in terms of length of hospital stay, mortality and development of BSIs.

1.6 Definitions

In Jenin governmental hospital for patients more than 13 years old, a blood culture set includes one pair of bottles (aerobic and anaerobic), while patients less or equal to 13 years old only one pediatric bottle include BACTEC Ped medium is used for aerobic culture. Aerobic and facultative anaerobes are typically the pathogens responsible for BSI in younger people, and BSIs with obligate anaerobic bacteria are less common to occur (20). The definitions of the present study were similar to Ljungquist *et al* study (21), the results of blood culture were obtained from hospital system. The blood culture was considered positive when positive results were found in aerobic or/and anaerobic culture of one set.

Potential contaminants were bacteria that are part of the normal skin microbiota (e.g. Coagulase-negative *Staphylococci*, *Corynebacterium*, and *Cutibacterium*). These cases were evaluated and considered contaminants by the treating physician and laboratory director where the contaminants were not detected on repeated blood culture.

The period during which only one BSI episode was registered was considered the deduplication period, which was set to 14 days.

A duplicate was defined as a culture for which there was another positive blood culture with the same finding, taken within the deduplication period. The positive blood cultures remaining after removal of duplicates were considered relevant findings. To be mentioned contaminants were considered negative results.

BSIs are diagnosed when a patient had two positive blood cultures for a common skin contaminant and at least one positive blood culture for a known pathogen or at least one of this signs or symptoms: fever (higher than 38 °C), chills, or hypotension. From two separate blood samples, usually within 48 hours, Coagulase-negative *Staphylococci*, *Micrococcus* spp, *Propionibacterium acnes*, *Bacillus* spp, and *Corynebacterium* spp, are examples of skin contaminants (22).

In case definition of bacteremia and BSI are commonly interchanged, and they both refer to the development of a microbe from a blood culture acquired from a patient who exhibits clinical indications of infection but has been ruled out for contamination. Although BSI can be defined as either hospital- or community-acquired (HA or CA), it is now commonly acknowledged that a third type of healthcare-associated BSI (HCA-BSI) exists among individuals with community-onset BSI and considerable recent healthcare system exposure (23).

Laboratory confirmed bloodstream infections that are not secondary to infection at another body location are classified as primary BSI. When a potential non-pathogen (usually skin contaminants such as coagulase-negative *Staphylococci, diphtheroid, or Bacillus* spp) is isolated from more than one positive blood culture collected from two different sites or drawn on separate occasions and the patient has a fever >38°C, chills, or hypotension, the patient is diagnosed with laboratory confirmed bloodstream infection (LCBSI) (10,24,25).

LCBSI that appears within 48 hours of the installation of a central line and was unrelated to an infection at another site is known as a central line-associated bloodstream infection (CLABSI). With the right aseptic procedures, surveillance, and management protocols, the majority of events can be avoided (26).

HA-BSI was defined if blood cultures that were positive more than 48 hours after admission or in patients who had just been released from an acute care hospital in the last 10 days. CA-BSI was defined when Patients had their first positive blood culture within 48 hours of arrival and did not have any risk markers for HCA-BSI. HCA-BSI was defined if the patients had a history of receiving intravenous medicine or home wound care in the 30 days before their admission, receiving hemodialysis, or living in a nursing home or long-term care facility (14).

Bacterial culture is a technique, which enables the controlled growth of bacterial cells in or on a culture medium in a scientific setting. The precise circumstances needed for optimum reproduction will vary depending on the type of bacteria being targeted. Most bacteria can grow to some extent when there is oxygen present; this process is called aerobic culture. Anaerobic culture is often the optimum habitat for growing species that are present in low oxygen conditions naturally, such as deep wounds or abscesses. Some bacteria referred to as obligate anaerobes cannot grow at all in the presence of oxygen, while others referred to as obligate aerobes cannot grow in the absence of oxygen. Facultative anaerobes, on the other hand, can grow in both aerobic and anaerobic environments and can switch from aerobic respiration to fermentation or anaerobic respiration if oxygen is not present (27).

Antimicrobial resistance occurs when bacteria, fungi, and other microorganisms adapt to resist the medications meant to kill them. That indicates that the germs survive and develop in patients body (28).

NIs, also known as healthcare-associated infections (HAI), are an infection or infections that develop while undergoing medical treatment but were absent at the time of admission. They may manifest in a variety of healthcare delivery settings, including ambulatory settings, long-term care institutions, and hospitals, as well as after discharge. Occupational infections that may impact workers are also included in HAIs. HAIs include central line-associated bloodstream infections, catheter-associated urinary tract infections (CAUTI), ventilator-associated pneumonia (VAP), and surgical site infections (SSIs) (29).

In the US, 3.2% of all hospitalized patients had HAI, compared to 6.5% in the European union /European economic area (EU/EEA), and the frequency is probably substantially

greater globally (30). According to government facilities included, the projected number of HAIs in US hospitals in 2002 was around 1.7 million (31). In retrospective cohort study of BSIs conducted in Ontario in 2017, the study found 22,935 positive BSI cases from 531,065 blood cultures in 19,326 patients. The most common isolated pathogens were *Escherichia coli*, *Staphylococcus aureus*, coagulase-negative *Staphylococci*, *Klebsiella* species, and *Enterococcus* species. The study showed increase in mortality rate patients with positive culture compared to patients with negative culture (32).

During a five-years research period, a single-center retrospective analysis was undertaken in Japan on 2,105 patients with BSIs, 1,786 of whom survived and 319 dead. The 30-day mortality rate was 15.2%. BSIs brought on by yeasts were separately linked to thirty-day mortalities. The ratio of BSIs caused by Gram-negative bacteria after 30 days owing to extended-spectrum beta lactamase development was significantly higher than that caused by nonproducing bacteria (33).

Inappropriate use of antibiotics (broad spectrum use, misuse, unnecessary use, and overuse), low information about microbiological profile, lack of antibiotic stewardship programs, lack of evidence based medicine, and others lead to development of antibiotic resistance, which is recognized as a global health problem.

Antibiotic resistance poses a serious danger to global public health, causing killing at least 1.27 million cases globally, and connected to approximately 5 million deaths in 2019. Each year, more than 2.8 million illnesses in the united states of America are resistant to antibiotics. The healthcare department workers, veterinary department, and agricultural sectors, as well as individuals (patients, visitors) at any stage of life, could be impacted by antimicrobial resistance. This makes it one of the most important public health issues in the entire planet. Antibiotic resistance doesn't mean to all antibacterial or all antifungal to recognize it as a serious or dangerous. In some cases, when we use second and third line therapies for antibiotic resistant infections it can damage patients by resulting in severe adverse effects, such as organ failure, and delaying treatment and recovery for weeks or even months. According to CDC, antibiotic resistance affect the development of several medical procedures, such as joint replacement, organ transplantation, cancer therapy, and the management of chronic conditions including DM, asthma, and rheumatoid arthritis (28).

1.7 BSIs Signs and Symptoms

Signs and symptoms of BSIs include fever and chills, very low body temperature, peeing less than usual, fast heartbeat, diarrhea, fatigue or weakness, blotchy or discolored skin, sweating or clammy skin, severe headache pain, respiratory distress, abdominal discomfort (nausea, vomiting), joint pain, disorientation. Many studies show that at least 75% of patients who are 65 years of age or older have fever (34).

Depending on the time of day and the individual, body temperatures might fluctuate slightly. Tradition dictates that the average temperature is 98.6 F (37 ºC). In general, a temperature measured with a mouth thermometer (oral temperature) of 100 F (37.8 C) or greater is regarded as a fever.

BSIs occurs when pathogen invade blood vessels or lymphatic vessels or by using medical devise with low aseptic technique and wrong procedures and protocol. LCBSI to be reported as confirmed case, we take in account LCBSI criteria, we must find one of the following criteria:

1- The cultivated organism is a "known pathogen" and is unrelated to an infection at another place. Common skin contaminants are not considered to be recognized pathogens by this criterion.

2- Exhibits at least one of this symptoms, if the patient is older than one-year-old, a temperature (>38°C), chills, or hypotension, or If the patient is under one-year-old, apnea or bradycardia, as well as a fever (core temperature >38°C), must also be present.

Another criterion indicates that blood cultures include microorganisms that are unrelated to an illness at another place as determined by microbiology or a typical skin contaminant, such as a *Diphtheroid* (*Corynebacterium* spp.), *a Bacillus* (but not *B. anthracis*) spp, *Propionibacterium* spp, a coagulase-negative *staphylococcus* (including *S. epidermidis*), viridans streptococci, an *Aerococcus* spp, or a *Micrococcus*.

Acute renal injury, leukocytosis, severe sepsis or septic shock, fever, and/or other classic symptoms/signs of BSI would likely be present in older patients. The urinary system and the respiratory tract are the most frequent sources of BSIs in older persons (more frequently than in younger adults). Gram-negative bacteria account for between 40 and 60 percent of all isolates in older people (35).

1.8 Laboratory Markers

Leukocytosis indicates increase white blood cells (WBC) count, often exceeding 11.0 x 10^9 /L. Leukocytosis's cause may be determined by the raised cell type, the most prevalent form of leukocytosis is increase in neutrophil number or percentage, which typically accounts for 40% to 60% of the total leukocyte count, neutrophilia indicates increase of neutrophil cells over the normal and it indicates bacterial infection (36).

The C-reactive protein (CRP) is inflammatory marker that increases according to severity of the inflammatory reaction, it is elevated after 12–24 hours and reach highest result within 2–3 days. Erythrocyte sedimentation rate (ESR) calculates the vertical distance traveled in a hour by a column of anticoagulated blood, it elevated between 24 and 48 hours after inflammation starts, then gradually decreases as it goes away.

According to age, WBCs normal range for male and female was divided to three groups, neonates include newborn up to one month in age (9000-30,000/mm^3), children aged 2 years or below (6200-17,000/mm^3), and adults and children >2 years (5000-10,000/mm^3)(37).

Male and female normal value for CRP test is 0-6 mg/dl, and levels over 100 mg/L are linked to serious damage as acute bacterial infection, or active inflammation, several acute inflammatory disorders are excluded by concentrations up to 10 mg/dl, however inflammatory processes are not expressly excluded (38).

In Jenin governmental hospital, CRP test (quantitative method) was performed in hospital by Abbott Alinity system (USA). WBCs count was performed through CBC test by Nihon Kohden Cell Counte, cell tac 9100/5D (China).

1.9 Common Isolated Microorganism of BSIs

Organisms commonly isolated from BSIs culture include *Staphylococcus aureus*, *Escherichia coli*, Coagulase-negative *Staphylococci*, *Enterococcus* spp, *Candida albicans, Pseudomonas aeruginosa, Klebsiella pneumoniae, Viridans streptococci, Streptococcus pneumoniae, Enterobacter cloacae, Proteus* spp, Beta-hemolytic *Streptococci*, *Bacteroides* and *Clostridium* spp (6).

BSIs can occur due to infective endocarditis, central venous catheter (CVC), primary bacteremia, and secondary bacteremia. In Gram-positive bacteria, *S. aureus* is a major

cause of community acquired and health care associated bacteremia and endocarditis. Bacterial meningitis is caused by *S. pneumoniae*. Necrotizing fasciitis and toxic shock syndrome are caused by *S. pyogenes.* Endocarditis and diabetic bacteremia are caused by *S. agalactiae, E. faecium* and *E. faecalis*. Gram-negative bacteria, which constitutes between 25% to 50% of all BSIs and responsible of septic shock and severe sepsis, *Klebsiella pneumoniae* carbapenemase (KPC), *E. coli*, *Klebsiella* spp and extended spectrum beta lactamases (ESBL), were an examples of Gram- negative bacteria that responsible of hospital acquired pneumonia and UTI. These bacteria represent increased MDROs development (39).

Any organism's microbial invasion of the circulation can have fatal rapid effects, such as shock, multiple organ failure, and disseminated intravascular coagulation (DIC). Bacteremia and fungemia account for around 200,000 cases annually in the United State per year, with death rates varying from 20% to 50%. Two of the most crucial tasks of the microbiology lab are the prompt detection and identification of blood-borne infections. Blood may be found to include pathogens from all four major families of microbes: bacteria, fungi, viruses, and parasites during the course of many illnesses. (6). In the present study there was a focus on bacterial results, because the laboratory is designed and equipped for bacterial and fungal results. In addition, the laboratory in the hospital is not designed and equipped to follow up on the results of viruses and parasites.

A retrospective study was conducted on blood culture samples in Maldives country to detect microbiological profile and antibiotic resistance in BSIs. The study showed that 28.2% of isolated bacteria were Gram-negative organisms and 71.8% were Gram-positive species. In addition, Coagulase-negative S*taphylococci* (CoNS) were the most common pathogens, representing 53.6% and 50.9% of the detected microorganisms in 2016 and 2017, respectively. *Staphylococcus aureus* (15.9% and 10.3%), *Klebsiella* spp. (10.5% and 16.4%), and *Escherichia coli* (7.1% and 10.8%) were other pathogens that were commonly identified at this study in 2016 and 2017, respectively. CoNS shows a significant proportion of resistance to the studied antibiotics: ampicillin, cephalexin, cefotaxime, and gentamicin. In addition, high resistance rates to ampicillin, gentamicin, second- and third-generation cephalosporins were also seen in isolates of the *Enterobacteriaceae* family (40).

ESBLs are enzymes that degrade antibiotics like penicillin and cephalosporin, rendering them useless. According to center for diseases control and prevention (CDC) in the United States in 2017 there were 197,400 estimated cases of ESBLs in hospitalized patients, 9,100 Estimated deaths and $1.2B estimated attributable healthcare costs (41). The incidence of ESBLs is obviously growing in many regions of the world, 10-40 % of *Escherichia coli* and *Klebsiella pneumoniae* strains express ESBLs. ESBLs are commonly found on plasmids that are transferable from strain to strain and across bacterial species (42). In Jenin governmental hospital, ESBLs detection was determined by disc method through using amoxicillin and clavulanic acid combination applied next to the third generation cephalosporin antibiotics as cefotaxime, ceftriaxone or ceftazidime. The inhibitory zones surrounding any cephalosporin disc that were enhanced in the direction of the disc containing clavulanic acid and the appearance of synergistic effect and key hole shape indicates the presence of ESBL bacteria (43).

MRSA and inducible clindamycin resistance are becoming a public health concern, with increased morbidity and death if correct diagnosis and treatment are not performed. MRSA was reported to have greater inducible clindamycin resistance. D-tests on erythromycin-resistant and clindamycin-sensitive isolates are required to prevent treatment failure due to clindamycin inducible resistance (44).

In Jenin governmental hospital, methicillin-resistance was detected by using cefoxitin disc method. Methicillin was used to diagnose and treat infections brought on by *S. aureus* at the time of the first description of resistance in 1961. But in the beginning of the 1990s, oxacillin, which was a medication in the same family as methicillin was chosen as the preferred agent for *Staphylococci* testing. Cefoxitin was added later, due to its historical significance, many people continue to refer to these isolates by using the abbreviation MRSA (45).

Carbapenem resistance is a serious and ongoing public health issue across the world. It's mostly seen in Gram-negative bacteria including *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*, and it's either intrinsic or mediated by carbapenemase-encoding genes. Resistance genes of this sort are already common in some regions of the world, including Europe, Asia, and South America (46).

In Jenin governmental hospital, carbapenemase were detected by using ertapenem disc diffusion method, which was found to be a sensitive method for identifying CRE. According to a study published in 2020 and aimed to compare ertapenem disc with imipenem, meropenem, and doripenem discs, the results showed that compared to other individual carbapenem discs or their combinations, the ertapenem disc was separately able to detect the most resistant isolates (64/76). The ertapenem disc's results had the best agreement with the relevant E test among the four carbapenem discs (47).

Results of antibiotic susceptibility tests, which were carried out in Jenin hospital using disk diffusion method were collected. Antibiotic susceptibility tests, extended-spectrum beta-lactamases (ESBLs), MRSA, and carbapenem-resistant *Enterobacteriaceae* (CRE). These tests were carried out according to CLSI (48).

In a prospective descriptive research conducted in 2004 at the Neonatal Intensive Care Unit (NICU) of the AL-Nasser and AL-Shifa hospitals in Gaza city, 328 neonates out of 2487 cases showed positive blood cultures, resulting in a 13.2% infection rate. Coagulase negative *Staphylococci*, *Escherichia coli*, and *Klebsiella* spp. were the most often isolated pathogens. Meropenem, amikacin, vancomycin, chloramphenicol, ciprofloxacin, and third-generation cephalosporin were the most responsive antibiotics for these isolates (49).

A retrospective study was conducted in 2003 for 2844 bacterial isolates obtained from clinical sources such as urine, pus, blood, and cerebrospinal fluid (CSF) in governmental hospitals in Gaza strip. The study examined the susceptibilities of all 16 prevalent clinical bacterial isolates using microbiology laboratory records. The study showed that 924 isolates were Gram- positive and 1920 were Gram-negative. The resistance of *Staphylococcus aureus* was 73.2% to amoxicillin and 1.8% to vancomycin. On the other hand, 40.4% of *Streptococcus pneumoniae* isolates were resistance to penicillin and 7.4% to erythromycin (50).

According to a prospective nationwide surveillance conducted in Korea between October 2006 to September 2007, Gram-negative aerobes constituted 59.2% of all BSI isolates, whereas Gram-positive aerobes constituted 38.9%. The most prevalent isolate in CA-BSI (47.1%) and HCA-BSI (27.2%) was *Escherichia coli*. In contrast, the most prevalent isolates in HA-BSI were *Staphylococcus aureus* (15.2%) and coagulase-

negative *Staphylococcus* (15.1%.). The CA-BSI had the greatest incidence of adequate empiric antibiotic treatment (89.0%) followed by HCA-BSI (76.4%), and the HA-BSI (75.0%). HA-BSI had the greatest 30-day fatality rate (23.0%) followed by HCA-BSI (18.4%) and CA-BSI (10.2%) (14).

In a review of population-based studies conducted in 2013, involving determination of incidence of BSIs, few studies published since the 1970s have covered all BSI etiologies and reported rates between 80 to 189 per 100 000 per year, with greater rates recorded in more recent years, the study demonstrated that *Escherichia coli*, *Staphylococcus aureus*, and *Streptococcus pneumoniae* were the three most frequent a etiologies of BSI, with incidence rates of around 35, 25, and 10 per 100,000 people, respectively. The results showed that there were large regional variations in the incidence of BSIs, which was partly explained by variations in blood culture rates, population demographics, and risk factor distribution. (23).

A cross-sectional study was conducted on positive blood cultures collected from the hospital information system at An-Najah National University Hospital from January 2019 to December 2020. In this study, in cases of BSIs with end stage renal disease, 118 microorganisms were isolated, 99 (83.89%) isolates were Gram-positive and 19 (16.1%) were Gram-negative, in the Gram-positive isolates, coagulase negative *Staphylococci* (CoNS) (74.57%) were predominant. As for the Gram-negative isolates, the most frequent were both *Escherichia coli* and *Stenotrophomonas maltophilia* (51).

Another research looked at the short term peripheral venous catheters related bloodstream infection rates in 246 intensive units of 83 hospitals in 52 cities of 14 countries of Middle East for six years started at 2013. The microbiological profile of Gram-positive bacteria showed predominance of coagulase negative *Staphylococci* (31%) and *Staphylococcus aureus* (14%). Gram-negative bacteria included *Escherichia coli* (7%), *Klebsiella pneumoniae* (8%), *Pseudomonas aeruginosa* (5%), *Enterobacter* spp (3%), and others (29.9%) (52).

A study including central line related bloodstream infections and microbiological profile was carried by an Egyptian ministry of health hospital at 2020. In this study after insertion of central line, following the collection of 120 central line catheters from patients and sending them for culture department immediately and other collections

were done after seven days from first collection, 13 (10.83%) were positive for BSIs. *Staphylococcus epidermis* was found in 10 out of the 13 infection cases, whereas *Staphylococcus aureus* was found in the rest. Furthermore, the majority of infected individuals were overweight or obese, diabetic, had a subclavian route, and were in the hospital for more than seven days (53).

A study published online by Cambridge university on BSIs in cancer patients with central venous catheters (CVCs). In this study, comparison between two cohorts separated by more than a decade was done, the study showed that Gram-negative organisms have become the most common causative organisms of BSIs (52%); they currently contribute to 41% of catheter-related BSIs (CRBSIs) (54).

In 2019, at least one relevant pathogen was identified in 13.2% of blood cultures during a four-year prospective monitoring research in Germany. The most prevalent pathogen found was *Escherichia coli* (25.4%), followed by *Staphylococcus aureus* (15.2%), *Staphylococcus epidermidis* (8.1%), and *Klebsiella pneumoniae* (7.1%). Also this study showed methicillin resistance in *Staphylococcus aureus* has decreased from 10.4% in 2015 to 2.5% in 2019. Vancomycin resistance in *Enterococcus faecium* (VREF) has risen steadily from 16.7% in 2015 to 26.9% in 2019, with a peak in 2018 (42.5%) (55).

Another study conducted on neonatal BSIs in tertiary referral hospitals in Kurdistan and Iran. The study was carried out from September 2009 to June 2010. The study showed that among the 472 patients admitted to the neonatal intensive care unit (NICU), 6.4% (n = 30) of the cases developed BSIs, which included 17 girls (56.7%) and 13 boys (43.3%). The most common bacterium isolated from blood cultures was *Enterobacter* spp (36.7%). Tetracycline and ciprofloxacin had the highest antibiotic resistance and sensitivity, respectively. Age 7 days (P = 0.001), prior antibiotic usage (P = 0.013), and low birth weight (P = 0.001) were all risk factors for BSIs (56).

A prospective study conducted in 2010 in the medical surgical intensive care unit (MSICU) of an inner city hospital in New York city, the study showed one or more positive blood cultures in 12.6% of tested patient, from identified isolates, 59% were Gram-positive bacteria, 31.1% were Gram- negative organisms, and 9.8% were fungi. Multi-drug resistance (MDR) bacteria were found in 34.2% of Gram-negative organisms and in 19.4% of Gram-positive bacteria (57).

According to patient records from a comparative historical analysis of the Iranian nosocomial infection monitoring system done between 2018 and 2019, the rate of NIs in the hospital was 2.95% from admissions. ICU wards had the highest reported incidence of NIs, 45.61% of patients were female, 98.95% had underlying illnesses, and 30.88% of deaths were attributed to NIs. *Acinetobacter* spp was the most frequently isolated agent, regardless of the organ implicated, accounting for 22.75 % of all NIs (58).

A study conducted on BSIs caused by MDR-Gram-negative organisms for 12 months in the São Rafael Hospital in Brazil, included 143 cases of Gram-negative bacteria, the study showed that 28.7% of bacteria were MDR-Gram-negative pathogens, the most common causative agents were *K. pneumonia* (74%), *E. coli* (60%), *P. mirabilis* (50%). The study considers, age ≥ 60, liver disease, male gender, previous antibiotic therapy, and *K. pneumoniae*-related bacteremia as risk factors associated with MDR- BSIs. (59).

According to a retrospective study conducted on pediatric BSIs in Australia, the most frequent site of infections was respiratory system (16.6%), followed by osteomyelitis (15.6%) urinary tract infection (11.5%). *Staphylococcus aureus* (27.0%), *Escherichia coli* (14.0%), and *Streptococcus pneumoniae* (12.0%) were the most common isolated bacteria (60).

A study (published in 2007) was conducted on BSIs cases admitted to urban hospital in west Africa. The study indicated that *Streptococcus pneumoniae* (45.2%), *Staphylococcus aureus* (18.3%), and *Escherichia coli* (9.7%) accounted for 73% of bacteraemias samples collected from patients. In addition, Penicillin had a very high antibacterial activity for *S. pneumoniae* (97.5%), whereas co-trimoxazole had a very high antimicrobial resistance. Cloxacillin, gentamicin, and chloramphenicol were typically highly effective against *S. aureus.* All strains of *E. coli* and non-typhoidal *Salmonella* (NTS) were responsive to ciprofloxacin, but predominantly to gentamicin (61).

A retrospective study involving investigating epidemiology and outcomes of patients hospitalized into burn units in 20 hospitals was carried out in eastern China. In this research, catheter-related BSIs (CRBSIs) represent 41.5% of the total cases. The most prevalent microorganisms were *Acinetobacter baumannii* (19.5%), *Klebsiella pneumoniae* (13.9%), and *Candida* (12.7%). Furthermore, 63.5% of the samples had

antibiotic resistance, mostly in Gram-negative bacteria. Patients who experienced BSIs had worse outcomes and more severe illnesses when they were admitted to the intensive care unit and they were linked to a high death rate (62).

According to CDC in the United States in 2017, there were 13,100 estimated cases of Carbapenem-resistant *Enterobacteriaceae* (CRE) in hospitalized patients, 1,100 estimated deaths and $130M estimated attributable healthcare costs (63).

Secondary BSIs are infections that spread from another infected body location, in other words there is bacteremia and laboratory evidence of the same microbe at a different location at the same time or up to three days earlier, which may be related to UTI and pneumonia. A retrospective study conducted for 15 years among four hospitals and published in 2018, the study showed that more than half of all cases (56.7%) had infections caused by Gram-negative bacterial species, the most frequent species is coagulase-negative *Staphylococcus*, which accounts for 36.5% of infections, *Escherichia coli* (19.2%), *Candida* spp (10.2%) and *Klebsiella* spp (8.4%) (64).

People of all ages can suffer from minor to severe disease from the lung infection known as pneumonia, the BSIs with bacteria as a result of the pneumonia infection spreading from the lungs. A retrospective observational study was carried out at Zhejiang University School of Medicine's second affiliated hospital and published in 2022, this study was conducted on secondary BSIs after pneumonia among patients infected with methicillin-resistance *Staphylococcus aureus* (MRSA), the study showed increase in average length of stay (ALOS) and mortality rate compared with patients diagnosed with pneumonia alone without BSIs (65).

The type of bacteremia, sampling techniques, the volume of blood, the number and timing of blood cultures, the results interpretation and the type of patient population being served by the laboratory are just a few of the numerous, frequently complex factors that affect the laboratory's ability to successfully detect microorganisms from blood. In order to optimize the identification and recovery of microorganisms and assure top-notch patient care, all of these factors must be taken into account while developing the blood culture procedure in the laboratory (6).

Bactec automated blood culture system (USA) was the automated system that employed to perform blood culture test, which is a microbiological culture quick approach for the

identification of BSIs. It is used to find illnesses that are spreading via the bloodstream such as bacteremia, and sepsis. A blood culture is a laboratory test that looks for the presence of infection-causing microorganisms including bacteria or fungi in the patient's bloodstream by injecting the patient's blood into bottles containing culture media. These methods have boosted blood culture efficiency, and decreased organism detection time (66).

Data from BSIs culture can confirm the presence of an infection and determine the specific type or types of microorganisms that are causing it when a patient exhibits signs or symptoms of a systemic infection. Blood testing, for instance, can detect the germs that cause severe meningitis, puerperal fever, pelvic inflammatory disease, postnatal epiglottitis, sepsis, and fever of unknown origin (FUO).

The majority of bacteria can be detected in the culture in 2 to 3 days, but others can take up to seven days to be detected. It may take up to 30 days for fungus to appear in the culture. The American society for microbiology advises using 10 to 30 cc for each blood culture. Since there are often few germs per milliliter of blood, it's crucial to draw a sufficient amount of blood: 20 ml for adults, 2–5 ml for children, and 1-2 ml for newborns and infants (66). Other references indicate that the optimum time to obtain more than 10 ml of blood from the patients while they are feverish (67).

It has been shown that, 67% of the pathogens were identified in 24 hours, 90% of the pathogens were identified in 72 hours, fungi and mycobacterium may need more time (maybe in weeks) (67).

The growth media in blood culture bottles promotes the growth of microorganisms while the anticoagulant in the bottles keeps the blood from clotting. The most widely used anticoagulant is sodium polyanethol sulfonate (SPS), which does not inhibit the development of the majority of pathogens (68).

1.10 Risk Factors Associated with BSIs

In general, there are many risk factors, which increase NIs, older age, duration of hospital stay, overuse or incorrect use of broad-spectrum antibiotics, and the use of different surgical equipment’s and procedures are all variables that increase the probability for a NIs. UTI, CAUTI, SSI, gastrointestinal infections (including

Clostridioides difficile), and (VAP) are considered as causative sources for BSIs later on. The majority of patients frequently have additional illnesses such DM, persistent lung disease, kidney failure, or malnutrition (3).

The most frequent HAI in acute hospital settings, according to a point-prevalence survey done in the United States in 2015, was pneumonia, followed by gastrointestinal infections, SSI, BSIs, and UTI. Point-prevalence surveys conducted in 2011 revealed that pneumonia (21.8%) and SSI (21.8%) were the most prevalent infections, followed by gastrointestinal infections (17.1%), urinary tract infections (12.9%) and bloodstream infections (9.9%) (69).

A retrospective matched case-control study to detect risk factors associated with BSI due to susceptible strains of *Acinetobacter baumannii*, the study indicated that immunocompromised cases, hemiplegia or paralysis, the disease of liver, peptic ulcer patients, and female gender, are considered risk factors for BSIs (70).

A prospective study was conducted on BSIs in cancer patients to assess clinical features from August 2016 to July 2017 in Mexico City. The study showed that ineffective antimicrobial therapy and multidrug resistance (MDR) development correlated with greater risk of death due BSIs. According to Gram stain for isolates, Gram-negative constitute 72.8% and Gram-positive 27.2%. In Gram-negative bacteria, *Escherichia coli* was the most frequently isolated bacterium (42.3%), followed by *Klebsiella* spp (9.1%) and *Pseudomonas aeruginosa* (5.8%). Contrasting *Enterobacteriaceae* ESBL producers (38.1%). In Gram-positive bacteria, the most frequently isolated bacteria were coagulase negative *Staphylococci* (11.7%), *Staphylococcus aureus* (10.1%) and *Enterococcus* spp 4.4% (71).

In contrast to the average global prevalence of DM which was 6%, the prevalence of DM among the Palestinian population in the West Bank and Gaza, was 15.3% by 2010 (72). Nearly 8% of Americans had DM, making it a widespread disease in the country. A diagnosis of DM and a HbA1c of 6.5% or higher is associated with an increased risk of CA-BSI, according to a study published in 2014 and conducted on patients and laboratory data collected from two academic teaching hospitals in Boston, US (73). BSIs were more common in diabetic patients than in non-diabetics (2.58/100 admissions vs. 0.58/100 admissions, P-value 0.0001), this result according to a

retrospective cross-sectional study that was published in 2008 and conducted for four years in Switzerland, this result indicated that BSIs risk was more than four times higher in diabetics (74).

1.11 BSIs in Premature Birth and Neonate

A birth that occurs more than three weeks before the baby's expected due date is considered preterm. In other terms, a preterm delivery is one that happens before the 37th week of pregnancy officially begins. They frequently have challenging medical issues; prematurity-related problems often differ. However, the danger of difficulties increases with the time of birth for the baby (75). Neonatal infection can be spread through the birth canal or environmentally as a result of inadequate medical facilities (76).

Western Iranian hospitals' neonatal intensive care unit (NICU) wards were the site of a case-control study from September 2009 to June 2010, the study was conducted on 472 patients who were hospitalized in NICU, the study showed that 6.4% of 472 hospitalized patients had BSIs (17 females and 13 males), The most common isolated bacterium from blood culture was *Enterobacter* spp (36.7%), *Klebsiella* (20.0%), *Escherichia coli* (10.0%) and *Staphylococcus epidermidis* (26.7%) and others (6.6%). Tetracycline and Ciprofloxacin were shown to have the highest levels of antibiotic sensitivity and resistance, respectively (56).

The rate of BSIs in a prospective descriptive study, conducted on neonatal septicemia in Gaza city in 2005, was 13.2%, the study showed the following microbiological profile of common microorganisms: coagulase negative *Staphylococcus* (57.3%), *E. coli* (10.4%), *Klebsiella* spp (8.0%), *Pseudomonas aeruginosa* (5.8%), *Streptococcus viridance* (3.4%), *Staphylococcus. aureus* (2.7%), *Proteus* spp (1.8%), *Streptococcus pneumoniae* (1.2%), *Klebsiella pneumonia* (1.2%), *Serratia* spp (1.2%), *Acinetobacter bumannii* (1.2%) and others (5.5%). Meropenem was the best antibiotic for treatment of Gram-negative isolates, while vancomycin was the best antibiotic for Gram-positive isolates (76).

1.12 Empirical Treatment

A study published in 2017 included a multicenter retrospective cohort study of newborns (90 days old). This study was conducted in eight US children's hospitals. The

study showed that 90% of all ages had received empirical treatment from a third-generation cephalosporin, only four cases of bacteremia and meningitis had received better coverage with the addition of ampicillin to the third-generation cephalosporin. More than 95% of all patients had been treated with ampicillin and gentamicin regimen (77).

Group B Streptococcus (GBS) *Streptococcus agalactiae*, *E. coli*, *Listeria*, the majority of *S. pneumoniae*, and *N. meningitides* are all covered by ampicillin and gentamicin or ampicillin and cefotaxime for the neonate. Ampicillin, cefotaxime, and vancomycin are suggested as part of the empiric therapy for newborns between the ages of one and two months in order to adequately protect against community-acquired infections (78).

In cases of classic fever of unknown origin (FUO), empiric therapy typically plays little to no role. Once a diagnosis has been made, treatment should be focused on the underlying cause, where necessary. Gram-negative *Enterobacteria*, *P. aeruginosa*, *S. aureus*, and *Streptococci* should all be included in the first-line antibacterial treatment spectrum for high-risk patients. In severely neutropenic high-risk patients with FUO, first-line empirical antibiotic monotherapy with imipenem, meropenem, cefepime, or ceftazidime is appropriate (79).

1.13 The Average Length of Stay in Hospitals (ALOS)

LOS, is the number of days that patients typically spend in hospital as inpatient hospital care. ALOS is often calculated by dividing the total number of all patients’ days that were stayed as inpatient cases over the course of a year by the number of admissions or discharges in the same year. ALOS in a U.S. hospital is 5.4 days in 2019, 4.5, 5.5 days for Turkey, France respectively in 2020 (80).

According to the annual health report in Palestine 2021, the gender ratio in the West Bank was 103.8 males for every 100 females. The average number of hospitals per 100,000 people in this governorate was 1.5, and the average number of beds per 10,000 people was 10.4. ALOS in Palestinian hospitals (Except for mental and psychiatric hospitals) was 2.9 day in 2021, 2.6, 3.0, 2.2 for the years 2020, 2019,2018, respectively (81).

Chapter Two

Methodology

2.1 Overview

In methodology chapter we had written important information about research methods, study design, research population, inclusion and exclusion criteria, research tools, data collection techniques, ethical issues, and data analysis.

2.2 Study Design, Study Population and Sample Size

The present study is a four month cohort study. Regardless of age and gender, patients with clinical indications of sepsis and/or systemic inflammatory response syndrome (SIRS) and there was blood culture done for them were included in this study. For all the cases that were examined by blood culture, during the study period, the results of the tests of blood culture, clinical information and other information were collected.

Patients were divided to six groups according to age, the first group included neonate (from birth to one month), the second group included patients from one month to two years, the third group included patients from 2 years to 18 years, the fourth group included patients from 19 years to 39 years, the fifth group included patients from 40 years to 59 years, the sixth group included patients over 60 years.

2.3 Study Period

After approval of the research topic data collection was carried out for four months (120 days), where data collection started in 24 October 2022 and ended in 21 February 2023.

2.4 Data Collection

Data on patients' age, sex, disease, inpatient or outpatient classification, ward, medical history, the causative sources of BSIs, antibiotic used during admission, and outcome details were obtained from patient's records. The study tool was a set of questions placed in a table to collect data about patients.

2.5 Inclusion Criteria

1- Admission to Jenin governmental hospital from October 2022 to February 2023.

2- All ages for which the blood culture was requested.

3- Both male and female patients.

2.6 Exclusion Criteria

1- Patients that did not made blood cultures test.
2- Results with the same pathogen for the same patient within 14 days after the first recorded result.

2.7 Study Variables

Age and gender, patients ward, patient diagnosis, duration of hospital stays, outcome, risk factors, incidence of infection and antibiotic used for suspected BSIs.

2.8 Study Protocol

The positive or negative samples that appeared during the study period were recorded and their data were followed up through the laboratory of Jenin governmental hospital, pathogen determination, Gram's reaction (Gram-positive or Gram-negative), susceptibility test to determine antibiotic sensitivity and resistance. Other data collected from patient’s record were gender, patient admission, symptoms, medical history, diagnosis, causative pathogens, antibiotic used, LOS in the hospital, mortality, WBCs count, and CRP test results.

2.9 Ethical Consideration

Study was carried out in Jenin governmental hospital, in the north of west bank, after taking approval of the institutional review board (IRB) of An-Najah national university. In addition, approval was obtained from Palestinian ministry of health.

All data collection was in coordination with the Palestinian ministry of health and after obtaining approval from them and sending official books to the directors of the targeted hospital to facilitate the conduct of the study and in accordance with the ethical standards of the IRB of An-Najah national university.

Medical staff and laboratory technicians were approached, acquainted with the study and its purpose. Participants' privacy and confidentiality of data was guaranteed and data was collected in the hospital by professional and qualified method.

2.10 Quality Control

Data was collected and entered on a daily basis, and the data was analyzed on a daily basis, the study tool sheets were saved in a protected file so that they could be checked in the event of data interpretation.

Clinicians heavily rely on data from the microbiology laboratory for the treatment of their critically ill patients. Antimicrobial susceptibility test findings must be conducted under ideal conditions, and laboratories must be able to offer results, selection of appropriate antibiotics, interpretation, and quality control using the protocols defined. Laboratory culture results play important rule in clinical assessment of patients, these culture results were assessed according to CLSI, which considered as important reference for performance and standards for antimicrobial susceptibility testing (48,82).

2.11 Statistical Analysis

Statistical tests were used to examine the data with the help of a statistical specialist. The version of statistical package for social science (SPSS Statistics V22.0), was used to analyze the data.

The relation between the infection and risk factors based on data taken from patient's records, were tested by chi-square ($\chi 2$) statistical test. The chi-square test is a type of hypothesis test used with categorical variables that have a nominal or ordinal measurement scale. The chi-square test determines whether the sample's frequency distribution significantly deviates from expected frequency distribution. As a result, the chi-square compares the observed and expected frequencies, and the variances between the two are calculated.

Chi- square test was used to test the relations between the two categorical variables, as gender, age, and others. T test was used to test the relations between quantitative variables as LOS in hospital. Excel 2016 was used for data entry, data management, charting and graphing, data classifications, count calculations, mean and average for data and other calculations. Data tab program was used to calculate frequencies, percentages and charting and graphing.

Chapter Three

Results

This chapter describes the study's findings, which were produced from an analysis of data that were collected during study period.

The study findings are presented in this chapter together with information about the patients' characteristics and the laboratory results of patients. The results were categorized into:

- Age and gender (demographic data)

- Ward data.

-Chronic diseases

- Diagnosis, Signs and symptoms

- Antibiotics profile used during blood culture and admission

- Inflammatory marker (laboratory results), WBCs and CRP.

- Other infection and complications associated with suspected BSIs

- Admission from another hospital

- Outcome details (LOS, mortality, and discharged)

- Microbiological profile, sensitivity and resistance

- Infected group and non-infected group

- Research hypothesis

3.1 Age and Gender (Demographic Data)

The demographic data of the patients and study sample are shown in the Table 1 below. This study included 1495 samples culture for 1190 patients, 210 (17.7%) patients had cultures range from 2 to 7 for the same patient, 980 (82.3%) patients have just one sample culture, all of them were from all ages. Regarding the gender of patients of the study population, blood cultures were done for 621 (52.2%) males, and 569 (47.8%)

females patients. In more detail, 783 blood culture tests were done for 621 males and 712 tests were done for the 569 female patients.

Table 1

Demographic Data for the Patients and the Cultured Samples (Age and Gender)

Variable	Category	Number of Patients (%)	Number of specimens (%)
Gender	Male	621 (52.2)	783 (52.4)
	Female	569 (47.8)	712 (47.6)
	Total	1190 (100)	1495 (100)
Age	Less than 1 month	292 (24.5)	370 (24.7)
	1 month-2 years	242 (20.3)	270 (18)
	2 to 18 years	112 (9.4)	121 (8.1)
	19 to 39 years	57 (4.8)	76 (5.1)
	40 to 59 years	116 (9.7)	156 (10.4)
	60 years or more	371 (31.1)	502 (33.4)
	Total	1190 (100)	1495 (100)

Age distribution of the patients is also shown into Table 1 above. Blood culture test was requested most frequently (31.1%) for patients aged 60 years old or more, followed by less than one month (24.5%). On the other hand, the least frequency (4.8%) of blood culture test was for patients 19 to 39 years. Similarly, the higher number and lower number of specimens were obtained from patients aged 60 years old and patients 19 to 39 years, respectively.

3.2 Ward Data

Table 2 below, shows numbers and percentages of patients that made blood culture tests at each ward (department) and numbers of specimens are also shown. The highest number of patients that made blood culture tests were at internal ward, where from 440 (37%) patients 552(36.9%) specimens were examined. The frequency of patients at pediatric ward, was followed by those frequencies at NICU and ICU as shown in Table 2.

During the research period, most blood culture specimens for suspected BSIs came from internal and pediatric ward, where they represent 37%, 23.9%, respectively from all samples cultured. In addition, more than half of the all samples (60.8%) came from these two wards, (Table 2).

Table 2

Frequencies of Blood Culture Patients (and their Specimens' Numbers) at each Ward and Regarding Inpatient and Outpatient Classification

Variable	Number of patients (%)	Number of specimens (%)
Ward		
Internal	440 (37%)	552 (36.9)
Pediatric	317 (26.6)	358(23.9)
NICU	259 (21.8)	347 (23.2)
ICU	106 (9%)	152 (10.2)
Dialysis	16 (1.2)	24 (1.7)
surgery	52 (4.4%)	62 (4.1%)
Classification of patient		
Inpatient	1138 (95.6)	1441(96.5)
Outpatient	52 (4.4)	54 (3.5)
Total	1190 (100)	1495(100)

Hospital medical services classified patients to inpatient and outpatient according to hospital stay of patient. The patient is placed in an observation state while doctors assess if hospitalization is necessary. Normally, if this time frame doesn't exceed 24 hours the patient was considered outpatient, otherwise the patient was considered inpatient (83).

Table 2 above shows that most of the patients (95.6%) that made blood culture test were inpatients. On the other hand, only 4.4% of the patients were outpatients.

3.3 Chronic Diseases

In the present study, hypertension (24.4%) was the most predominant chronic non-contagious disease followed by diabetes mellitus (22.2%). On the other hand, there were clearly lower percentages of hemodialysis and cancer patients, which were 4.2% and 4.7%, respectively. The data details for the chronic diseases are shown in the Table 3 below.

Table 3

Chronic Disease of the Study Sample

Chronic Diseases	Number of patients (%)	Number of specimens (%)
Hypertensive patients	290 (24.4)	357 (23.9)
Diabetic patient	264 (22.2)	322 (21.5)
Hemodialysis patients	50 (4.2)	77 (5.2)
Cancer patients	56 (4.7)	82 (5.5)
Patients without any chronic disease	820 (68.9)	983(65.7)
Total	1190	1495

3.4 Diagnosis, Signs and Symptoms

In this study, data collection was conducted for different diagnosis, signs, and symptoms that were accompanied with each cultured sample separately, regardless that the patients had one sample or more but without duplications as shown into materials and methods. Different diagnosis, signs, and symptoms were followed (Table 8).

The most commonly recorded signs and symptoms for patients who made blood culture were fever (39.5%), followed by acute pain (39.3%) and cough (28.5%). On the other hand, the least signs and symptoms were grunting and bradycardia. In addition, the most common diagnosis of patients who were examined by blood culture test were prematurity and COPD.

3.5 Antibiotic Used During Blood Culture and Admission

In this section, we follow up different antibiotic used as treatment for suspected BSIs or antibiotics that were taken after blood sample collection. After removal of duplicated cases, antibiotics were recorded for each cultured samples separately, regardless of the

patient made more than one sample culture. Different types of antibiotics were recorded (Table 10 in the Appendix).

The most common antibiotic used for patients who made blood culture was (31%), followed by ampicillin (26.5%), and gentamicin (17.7%). On the other hand, the least antibiotic used for study population was rifampicin (0.1%).

3.6 Inflammatory Marker (Laboratory Results), WBCs and CRP

In the hospital, most of the blood culture tests were associated with WBCs and CRP tests. In more details, WBCs tests were performed for 1455 (97.3%) cases out of total 1495 cases for whom blood culture test was requested. The assessment of WBCs results (normal, high, and low) were performed for each sample separately according to the classification of patients to three age groups as mentioned before (37). A total of 798 (54.8%) cultured samples were associated with normal result of WBCs count. While 533 (36.7%) of cultured samples were associated with high result. On the contrary, 124 (8.5%) cultured samples were associated with low result.

At the time of blood culture collection, the assessment of CRP results (positive and negative) were performed for each sample separately. CRP tests were performed in association with 1460 (97.7%) blood cultures tests out of the total 1495 cases. A total of 443 (30.3%) cultured samples were associated with CRP negative results, while 1017 (69.7%) cultured samples were associated with positive results.

3.7 Other Infections and Complications Associated with Suspected BSIs

This section is divided into three parts:

1- UTI, chest problem (pneumonia and/ or other complication), and CSF infection.
2- Other cultures done such as urine, CSF, sputum, throat, nasal, rectal, and swabs.
3- Secondary BSIs.

3.7.1 UTI, chest problem (pneumonia and/ or other complication), and CSF infection

Clinical data were collected to follow up other infection associated with suspected BSIs such as UTI, chest infection or respiratory failure, and CSF infection. A total of 389 (26%) out of 1495 blood cultured samples were done for patients diagnosed with chest infection (pneumonia), bronchitis, bronchiolitis, respiratory distress, or respiratory

failure, 165 (11%) out of cultured samples were done for patients diagnosed with UTI, 3 (0.2%) out of cultured samples were done for patients diagnosed with meningitis.

3.7.2 Culture of other Specimens other than Blood

The results in Table 4 bellow show the types and percentages of other samples that were cultured simultaneously to blood culture test such as urine, CSF, throat swab, etc.

Table 4

Results of Culture of Samples other than Blood

Type of culture	Total	Positive		Negative	
		N	%	N	%
Urine	691	149	21.6	542	78.4
CSF	114	1	0.8	113	99.2
Sputum	186	73	39.2	113	60.8
Throat	4	1	25	3	75
Nasal	19	0	0	19	100
Rectal	17	10	58.8	7	41.2
Swabs	47	21	44.6	26	55.4

The results in the Table 4 show that 691 urine cultures were conducted in the same period of blood culture tests, where 149 (21.6%) urine cultures were positive. Among the detected pathogens, 111 (75%) cultures were Gram-negative bacteria, 11 (7%) cultures were Gram-positive bacteria, 27 (18 %) cultures were yeast, the most common organisms were *E.coli* spp (45 isolates*)*, *klebsiella* spp (36), *pseudomonas* spp (10), *proteus* spp (5) and *Enterococcus* spp (3).

A total of 114 CSF cultures were conducted in the same period for patients who had suspected BSIs, 113 CSF culture results were negative and only 1 CSF culture was positive, where the pathogen was *Enterococcus* spp.

A total of 186 sputum cultures were conducted in the same period, 73 (39.2%) sputum culture were positive, 36 culture results were yeast, 32 results were Gram-negative bacteria, and 5 results were Gram-positive bacteria. The most common organisms were *pseudomonas* (9 isolates), *Acinetobacter baumannii* (5), *E.coli* (4), *klebsiella* (4),

Staphylococcus aureus (3), *Enterococcus* (1) and *Serratia* (1). Throat cultures were conducted for 4 cases, 1 throat culture was positive and it was *klebsiella* spp. As shown in Table 4, none of the 19 nasal cultures was positive, while 10 (58.8%) rectal culture were positive, the most common organisms were *Klebsiella* (2 isolate), *pseudomonas* (1) and *E.coli* (1). Furthermore 21 (44.6%) out of 47 swab cultures from different body site were positive. The most common organisms were *pseudomonas* (6 isolates), *Klebsiella* (4), *E.coli* (3), *Staphylococcus* spp (2).

3.7.3 Secondary BSIs

A total of 23 cultures were considered to be related to BSIs and recorded as secondary BSIs, 18 BSIs were considered as secondary BSIs came from urine infection, five BSI were considered as secondary BSIs came from respiratory tract infection.

3.8 Admission from other Hospitals

A total of 23 blood cultures were performed for patients (each patient one culture) admitted from other hospitals, which represents 1.5% out of the total 1495 cultured samples. The hospitals were Alrazi hospital (12 blood cultures), Ibn Sina hospital (4), Rafidia hospital (3), Al-Shifaa hospital (2), Al-Amal hospital (1), An-Najah hospital (1).

3.9 Outcome Details (ALOS, Mortality, Discharged)

The study includes 1190 patients (here we are talking about the number of patients, not the number of blood culture samples), 142 patients were included in the infected group, 1048 patients were included in the non-infected group.

ALOS was recorded for all patients. ALOS for all patients suspected to have BSIs in the study was 7 days. ALOS for infected patient in the study was 9.6 days which was higher than ALOS for non-infected patients was 6.5 days. Thus, there was increase in ALOS for the infected patients compare with the non-infected patients. Through testing the data and using T-test, there was statistically significant differences in favor of the infected group (P=0.000).

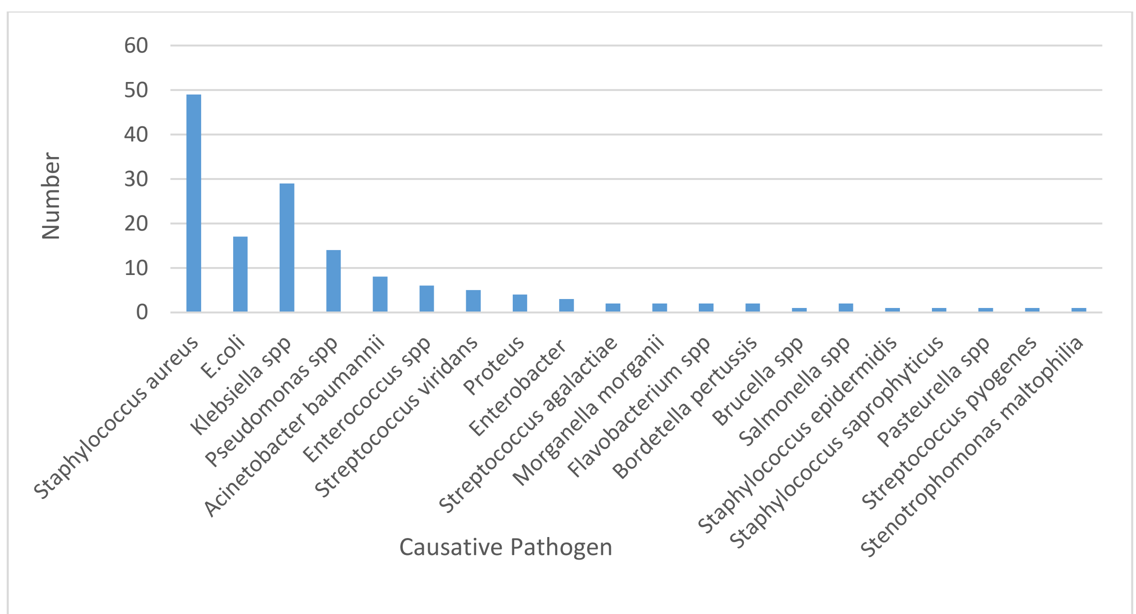
During the study period 156 (13.1%) patients were died out of the total 1190 patients in the study. Among those 156 patients, 32 patients were diagnosed with BSI. On the other hand, 110 with BSI were discharged or transferred from the hospital.

3.10 Microbiological Profile, Sensitivity and Resistance

Among 152 isolated pathogens from BSI cases, 66(43.4%) were Gram-positive bacteria, 85 (55.9%) were Gram-negative bacteria, and only 1 (0.7%) was yeast. The causative agents of BSI are shown in Figure 1 bellow After removal of duplicate, the most commonly detected pathogen was *Staphylococcus aureus* (32.4%), followed by *Klebsiella* spp (19.2%), *Acinetobacter baumannii* (5.3%), *Enterococcus* spp (3.8%), *Streptococcus viridans* (3.3%) *Proteus* spp (2.6%) and *Enterobacter* spp (2%). A very low percentage of detection was (1.3%) found for *Streptococcus agalactiae*, *Morganella morganii*, *Flavobacterium* spp, *Bordetella pertussis*, *Salmonella* spp. Furthermore, one pathogen was detected for 6 bacterial types, which were *Staphylococcus saprophyticus, Pasteurella* spp*, Streptococcus pyogenes, Stenotrophomonas maltophilia, Staphylococcus epidermidis and Brucella* spp (Table 11 in the Appendix).

Figure 1

Causative Pathogens of BSI



Causative pathogen that were not sensitive to at least one antibiotic in three or more antibiotic classes were called MDROs (84). A total of 11(7.3%) bacteria were MRSA, 7 (4.6%) bacteria were ESBL and 8 (5.3%) bacteria were CRE and 34 (22.5%) bacteria were MDRO. A total of 60 (39.7%) out of the total 151 bacterial isolates possessed different resistance phenotypes.

The most effective antibiotics were vancomycin and colistin (100% each) and were followed by teicoplanin (98.4%). Alarming resistant rates were found for a number of commonly used antibiotics. Erythromycin resistance rate was the highest (70%) followed by amoxicillin clavulanic acid combination (69.5%), cefuroxime (60.4%), co-trimoxazole (54%) and ceftazidime (50%). Although percentage of resistance to cefixime, fosfomycin, tetracycline and piperacillin was 100%, the results were not considered important due to the limited number of cases (Table 12 in the Appendix).

A comparison of antibiotic resistance rates between Gram-positive and Gram-negative bacteria was carried out. Resistance to amikacin antibiotic among in Gram-negative bacteria (25%) was significantly higher (P=0.031) than that of Gram-positive bacteria (8%). Resistance to amoxicillin clavulanic acid combination antibiotic among Gram-negative bacteria (74%) was significantly higher (P=0.012) than that of Gram-positive (20%), these results was illustrated in Table 9 in the Appendix.

3.11 Infected Group and Non-Infected Group

The study included 1495 samples examined by blood culture, 152 (10.2%) samples possessed positive results and were included into infected group, while 1343 (89.8%) samples were negative and were included in non-infected group.

3.11.1 Difference Regarding Age and Gender (Hypothesis One)

The results in Table 5 illustrate the difference between infected group and non-infected group regarding gender. The BSI was detected in 76 out of 783 (9.7%) males and in 76 out of 712 (10.7%) females. The infection rate in females was found to be insignificantly higher (P= 0.587) than males.

The results show that the highest percentage of BSI rate was 16%, which was found in patients with the age ranged between 40-59 years, followed by 14.4% in patients with the age 19-39 years, the lowest infection rate was recorded among patients less than 1 month (5.1%). The results in the Table 5 show that by using chi-square test, there is a significant difference between the infected group and non-infected group, the number of non-infected groups of patients were a significantly (P =0.000) higher than number of infected cases in all age ranges.

Table 5

Difference between Infected Group and Non-Infected Group Regarding Gender and Age Data

Variable	Category	Infected group N (%)*	Non-infected group N (%)	P-value
Gender	Male	76(9.7)	707(90.3)	0.587
	Female	76(10.7)	636(89.3)	
Age	Less than 1 month	19(5.1)	351(94.9)	0.000
	1 month- 2 years	19(7)	251(93)	
	2 - 18 years	7(5.8)	114(94.2)	
	19 -39 years	11(14.4)	65(85.6)	
	40 - 59 years	25(16)	131(84)	
	More than 60 years	71(14)	431(86)	

*Infection rate among corresponding group

BSI rate among patients with age range more than 60 years (14%) was significantly higher than that of patients ranged less than one month (5.1%; P=0.000). BSI rate among patients with age range more than 60 years (14%) was significantly higher than that of patients ranged 2-18 years (5.8%; P=0.014). BSI rate among patients with age range 40- 59 years (16%) was significantly higher than that of patients ranged less than 1 month (5.1%; P=0.000). BSI rate among patients with age range 40-59 years (16%) was insignificantly higher than that of patients ranged 19-39 years (14.4%; P=0.683). BSI rate among patients with age range 1 month- 2 years (7%) was insignificantly higher than that of patients less than 1 month (5.1%; P=0.183). BSI rate among patients with age range 40- 59 years (16%) was insignificantly higher than that of patients ranged more than 60 years (14%; P=0.423).

In the present study, regarding age groups, the results show that about a half (47%) out of the total 152 of positive samples were recorded for patients aged more than 60 years, and about quarter (23.6) out of total positive samples were recorded for patients aged less than 2 years (Table 5), in other words 70.6% out of 152 positive results were recorded for theses age ranges, so its recommended to increasing focus and interest in health care in these age groups.

By comparing the study samples frequency and percentage, the results show that 33.4% out of all blood culture specimens (1495) were done for patients aged more than 60 years, and 42.7% of all samples were done for patients less than 2 years, in other word

76.1% of suspected BSIs were done for these age ranges. The least common age group for suspected BSIs was the age between 19-39 years (Table 1).

3.11.2 Difference Regarding Inpatient or Outpatient, and Ward Data (Hypothesis Two)

Table 6 bellow show that the highest infection rate (25%) occurred at Dialysis ward, followed by Internal ward (14.4%), while the lowest infection rate (5.2%) occurred in NICU ward. The results show that by using chi-square test there is a significant difference between the infected group and non-infected group, the number of non-infected groups of patients were significantly (P =0.000) higher than number of infected cases in all wards.

Table 6

Difference between Infected Group and Non-Infected Group Regarding Ward and Patients Classification in Hospital

Variables	Infected group N (%)[1]	Non-infected group N (%)[2]	P- value
Ward			
Pediatric	24(6.7)	334(93.3)	0.000
NICU	18(5.2)	329(94.8)	
Internal	80(14.4)	472(85.6)	
ICU	18(11.8)	134(88.2)	
Dialysis	6(25)	18(75)	
surgery	6(9.7)	56(90.3)	
Patients Classification			
Inpatient	146 (10.1)	1296 (89.9)	0.861
Out patient	6 (11.3)	47 (88.7)	

[1] infection rate among corresponding group

[2] percent of non-infected patient in corresponding group

BSI rate among patients in dialysis ward (25%) was significantly higher than pediatric ward (6.7%; P=0.008). BSI rate among patients in dialysis ward (25%) was significantly higher than NICU ward (5.2%; P=0.002). BSI rate among patients in internal ward (14.4%) was significantly higher than that of NICU (5.2%; P=0.000). BSI rate among patients in internal ward (14.4%) was insignificantly higher than surgery ward (9.7%; P=0.437).

The results show that out of the total 152 positive results, about half of positive results in infected group (52.6%) came from internal wards, 30.9% of positive results were recorded in internal women ward, and 21.7% were recorded in internal men ward. The results show that the lowest number of positive blood cultures came from surgery and dialysis wards (Table 6).

Regarding the infection rate among inpatient and outpatients are shown in Table 6, the results show that BSI (11.3%) among outpatient was insignificantly higher from that among inpatients (10.1%; P=0.861).

3.11.3 Difference Regarding Chronic Infections, Diagnosis, Signs and Symptoms (Hypothesis Three)

In the present study, the most frequently recorded chronic disease in infected group was HTN (47 cases), followed by DM (45 cases) as shown in Table 7. The highest infection rate was recorded in hemodialysis (22%), followed by DM (14%). BSIs among diabetic patients (14%) was significantly higher than BSIs among non-diabetic patients (9%; P=0.012), BSIs among hypertension patients (13.1%) was significantly higher than BSIs among non-hypertension patients (9%; P=0.036). BSIs among dialysis patients (22%) was significantly higher than BSIs among non-dialysis patients (9.5%; P=0.000). BSIs among non-cancer patients (10.2%) was insignificantly higher than BSIs among cancer patients (8.5%; P= 0.525).

Table 7

Difference between Infected Group and Non-Infected Group Regarding Chronic Diseases

Chronic disease	Infected group N (%*)	Non-infected group N (%)	P- value
Diabetes mellitus (DM)	45 (14)	277 (86)	0.012
Hypertension (HTN)	47 (13.1)	310 (86.9)	0.036
Hemodialysis	17 (22)	60 (78)	0.000
Cancer	7 (8.5)	75 (91.5)	0.525

*percent of positive BSIs in each category

In the present study, Table 8 shows that the most common signs and symptoms for BSI patients (infected group) was acute pain, which was found in 67 (44%) out the total 152 infected samples, followed by fever 54 (35.5%) and cough 39 (25.6%). In contrast, the least signs and symptoms of patients were grunting and bradycardia, which represent

less than 1 sample for each one. Frequency of chills (10%) among infected group was significantly higher (P= 0.047) than that (5.7%) among non-infected group.

Table 8

Difference between Infected Group and Non-Infected Group Regarding Diagnosis, Signs, and Symptoms

Signs, and symptoms	Total	(%)	Infected group N (% of infected)	Non-infected group N (% of non-infected)	P-value
Fever	591	39.5	54 (35.5)	537 (40)	0.261
Chills	92	6.2	15 (10)	77 (5.7)	0.047
Weakness and dizziness	191	12.8	24 (16)	167 (12.4)	0.254
SOB, other respiratory symptoms	311	20.7	36 (23.6)	275 (20.5)	0.378
Acute pain	589	39.3	67 (44)	522 (38.9)	0.238
Cough	462	28.5	39 (25.6)	423 (31.5)	0.128
Vomiting	289	19.3	31 (20.3)	258 (19.2)	0.755
Diarrhea	93	6.2	13 (8.5)	80 (6)	0.218
Decrease oral intake	216	14.4	24 (15.7)	192 (14.3)	0.646
Tachycardia or tachypnea or both	140	9.3	12 (7.8)	128 (9.5)	0.495
Grunting	16	1	1 (0.6)	15 (1)	0.598
Bradycardia	19	1.2	1 (0.6)	18 (1.3)	0.472
Diagnosis					
COPD	81	5.4	9 (6)	72 (5.4)	0.787
Prematurity	102	6.8	5 (3.2)	97 (7.2)	0.066
Chronic kidney disease	59	3.9	19 (12.5)	40 (3)	0.000
Jaundice	33	2.2	1 (0.6)	32 (2)	0.168
Anemia	22	1.4	0 (0)	22 (1)	0.111
Clostridium difficile infection	5	0.3	1 (0.6)	4 (0.3)	0.470
Liver diseases	17	1.1	2 (1.3)	15 (1.1)	0.833
IHD	27	1.8	6 (3.8)	22 (1.6)	0.048
CVA	21	1.3	3 (1.9)	18 (1.3)	0.537
Total			152	1343	

Patients' diagnosis is also shown in Table 8. The most common diagnosis of 152 infected patients was CKD 19 (12.5%) followed by COPD 9 (6%). In contrast, the least for patients were jaundice, anemia, *Clostridium difficile* infection. Among patients diagnosed with chronic kidney disease, the percentage of infected group (12.5%) was significantly (P=0.000) higher than that of non-infected group (3%). Similarly, percentage of infected group (3.8%) was significantly (P=0.048) higher than that of non-infected group (1.6%) among IHD.

3.11.4 Difference Regarding Antibiotic Used

Ceftriaxone was the most commonly used antibiotic (32.8%) for infected group, followed by vancomycin (30.9%) and meropenem 38 (25%). On the other hand, rifampicin and cefuroxime were the least used antibiotics (Table 13 in the Appendix).

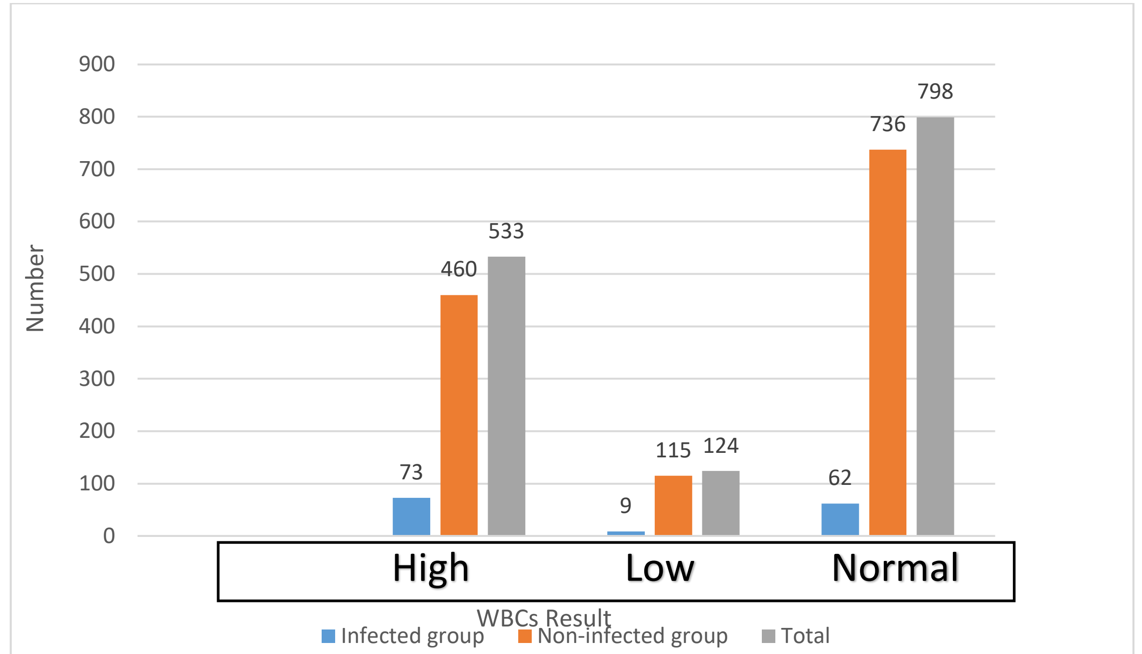
3.11.5 Regarding Inflammatory Marker Results (Hypothesis Four)

Comparison of inflammatory marker results indicated that there is a significant difference between the infected and the non-infected groups of patients with regard to positive CRP results (P= 0.000). In more details, positive CRP was found in 129 (84.8%) cases out of 152 infected group, this was significantly higher than percentage of CRP positive result (67.9%) among non-infected group (P=0.000).

Furthermore, there is a significant difference (P=0.001) between the infected and the non-infected groups of patients with regard to WBCs count. Figure 2 show that 82 (57%) samples were recorded as abnormal WBCs count out of the total 144 WBCs tests in the infected group. Abnormal WBCs count cases included high WBCs count (50.7%) and low WBCs count (6.3%). On the other had 575(44%) samples possessed abnormal WBCs count out of the total 1311 WBCs tests in the non-infected group.

Figure 2

WBCs Results in Infected Group and Non-Infected Group



3.11.6 Difference Regarding Previous Presence of Infection Source, Other Requested Sample Culture (Hypothesis Five)

Among the infected group of the present study, 36 cultured samples were for patients previously diagnosed with UTI and 42 cultured samples for patients with previous chest problem diagnosis However, among 165 patients who were previously diagnosed with UTI, 21.8% were associated with positive blood cultures, which was significantly (P= 0.000) lower than that (78.2%) of non-infected group. Similarly, higher percentage (89.2%) of previously diagnosed chest problem was found among non-infected cases, but without significant association (P=0.666).

3.11.7 Patient Admission from Other Hospital (Hypothesis Six)

In the present study, out of 23 patients admitted from other hospitals no patients were recorded in the infected group and 23 patients were recorded in non-infected group and there were no significant differences (P=0.103).

3.11.8 Difference Regarding Patient Outcome, LOS, Mortality (Hypothesis Seven)

A total of 32 (22.5%) out of the total 142 patients were recorded with the outcome of death in the infected group. Furthermore, statistical analysis revealed the mortality rate

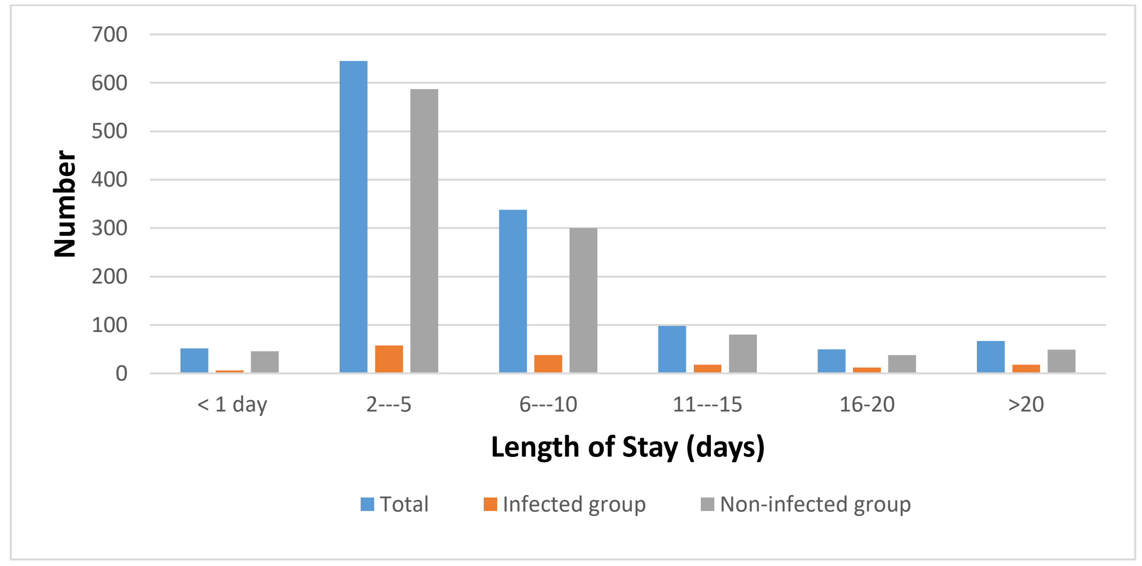
among infected group (22.5%) was significantly higher (P=0.000) than that of non-infected group (11.8%).

By using independent T-test there is a significant difference between the infected and the non-infected groups of patients regarding duration of stay in the hospital, because infected group have higher mean (mean=9.6, ST=8.93) compared to non- infected group (mean=6.5, ST=6.42), (P= 0.000). The results in Figure 3 show that the most recorded period was 2-5 days (58 cases) followed by 6-10 days' period (38 cases) in infected group.

By calculating the infection rate among LOS period, the highest infection rate was recorded in the period more than 20 days (26.8%), followed by the period 16-20 days (24%).

Figure 3

Difference between Infected Group and Non-Infected Group Regarding LOS Data



3.12 Research Hypothesis

1-There is a significant difference at a level of 0.05 related to the development of BSIs and patients' age and gender.

The results in the Table 5 show that there are no significant differences between the infected and the non-infected groups of patients with regard to gender, because the P-value is more than 0.05. Although, the infection rate in females (10.7%) was slightly higher than males (9.7%), there was no significance association (P=0.587).

The results also show that there were 152 positive cultured samples and 1343 negative cultured samples. The results in the Table 5 show that there is a significant difference between the infected and the non-infected groups of patients in age ranges because the P-value is less than 0.05.

2**-** There is a significant difference at a level of 0.05 related to the development of BSIs and patient origin (inpatient or outpatient, ward) in hospital.

The results show that there are no significant differences between the infected and the non-infected groups of patients with regard to patients' admissions because P-value was more than 0.05. The results show that 146 (96.3%) cultured samples of total 152 positive results were recorded for inpatients admissions in the infected group and 1296 (96.5%) cultured samples were recorded for inpatients admissions in the non-infected group.

The second part of hypothesis is about patients' ward. The results in the Table 2 show that there is a significant difference between the infected and the non-infected groups of patients with regard to wards because the P-value is less than 0.05 (P=0.000).

3- There is a significant difference at a level of 0.05 related to the development of BSIs and medical history, chronic diseases, and signs and symptoms.

Table 3 shows that there are significant differences between the infected and the non-infected groups of patients with regard to DM, HTN, and hemodialysis because the P-value is less than 0.05.

The results also show that there are no significant differences between the infected and the non-infected groups of patients with regard to cancer diagnosis, because P-value was more than 0.05.

Regarding signs, symptoms, and diagnosis, the results in the Table 8 show that there are significant differences between the infected and the non-infected groups of patients with regard to chills, CKD, IHD because the P-value is less than 0.05.

4- There is a significant difference at a level of 0.05 related to the development of BSIs and increase WBCs count and CRP level.

The results show that there are significant differences between the infected and the non-infected group with respect to CRP results, because the P-value is less than 0.05. where 129 (84.9%) positive results were recorded in the infected group and 888 (67.9%) positive results were in non-infected group.

The second part of hypothesis was about WBCs results. There is a significant difference between the infected and the non-infected group of patients with regard to WBCs results. In more detail, the results show that 73 (48%) cultured samples of the total 152 positive results were recorded for patients with high WBCs in the infected group, 9 (5.9%) cultured samples for patients with low WBCs count were recorded in the infected group, 62 (40.8%) cultured samples for patients with normal WBCs count were recorded in the infected group.

5- There is a significant difference at a level of 0.05 related to the development of BSIs and previous presence of infection source, and other requested sample culture.

The results show that there are significant differences between the infected and the non-infected groups of patients with regard to previous UTI diagnosis, because the P-value is less than 0.05.

The results also show that there are no significant differences between the infected and the non-infected groups of patients with respect to previous chest problem, infection (pneumonia), bronchitis, bronchiolitis, respiratory distress, or respiratory failure, because P-value is more than 0.05.

The results show that there are significant differences between the infected and the non-infected groups of patients with regard to positive urine cultured samples, because the P-value is less than 0.05.

Results show that there are no significant differences between the infected and the non-infected groups of patients with respect to positive sputum, swab, and rectal cultured samples, because P-value is more than 0.05.

6- There is a significant difference at a level of 0.05 related to the development of BSIs and patient admission from other hospital.

The results show that there are no significant differences between the infected and the non-infected group with regard to patient admission from other hospital, because P-value is more than 0.05. The results show that no patients were recorded in the infected group and 23 patients were recorded in non-infected group.

7- There is a significant difference at a level of 0.05 related to the development of BSIs and the outcome of the patients in terms of length of hospital stay, and mortality.

The results show that there is a significant difference between the infected and the non-infected groups of patients in relation to mortality outcome, because the P-value is less than 0.05.

The results show that there is a significant difference between the infected and the non-infected groups of patients with regard to LOS, because the P-value is less than 0.05.

ALOS was calculated for each patient in the study, the results show that ALOS in the study was 7 days for all patients. ALOS for the infected patients (9.6 days) was significantly higher compared to non-infected patients (6.5 days; P=0.000).

Chapter Four

Discussions and Conclusions

4.1 Overview

During the present study there was collection of many data related to the patients for whom blood culture tests were requested. The data included risk factors associated with BSIs, some chronic diseases, signs and symptoms, microbial etiology of BSIs, antibiotic susceptibility profile, patient's outcome in hospital, and the treatment regimen in the hospital.

This data can be used to draw perceptions of the medical reality with regard to BSIs. The collected data, recommendations and observations will form a basic building block in the development of the medical sector, and will give an opportunity to improve the health reality and services provided to patients in all of the West Bank.

4.2 Incidence and Microbiological Profile of BSIs.

The incidence of a disease or condition is the proportion of people who were infected by the disease within a particular population over a certain time period and it considered an essential word in epidemiology (85).

The sample during research period included 152 (10.2%) positive blood culture termed as infected patient group, and 1343 (89.8%) negative blood culture termed as non-infected group.

The study shows that the incidence for BSIs was 132 cases per 100000 per year. In a review of population-based studies conducted in 2013, involving determination of incidence of BSIs, few studies published since the 1970s have covered all BSI etiologies and reported rates between 80 to 189 per 100 000 per year (23).

Eight positive samples were considered as duplicated specimens, so they were subtracted from the total of positive results (160 cases) and 152 positive blood culture cases remained.

A retrospective observational study published in 2019 and conducted by Nannan Panday *et al* (86) for 7 months in a large European teaching hospital to evaluate blood

culture epidemiology and efficiency on patient age 18 years and older. This study was conducted on 3890 samples of blood culture, the study showed that 290 samples were positive, which represent 7.5% of the studied samples. A prospective observational study conducted in India and published in 2022, the study was performed for 6 months in Theresa hospital (Hyderabad). The study showed that 122 (23.4%) positive blood culture*s* were recorded among the total 522 blood culture test, which were included in the study (87).

A research was conducted during two years (2019 and 2020) in Indonesian hospital about blood culture epidemiology before and during the COVID-19, the study showed that positive rates were 19.5%, 20.9% in 2019, 2020, respectively. The research found that 70.8% out of the total positive blood results were recorded for Gram-negative bacteria, in contrast, 15.6% were recorded for Gram-positive bacteria. On the other hand, the most common Gram-negative bacteria were *E.coli, Klebsiella pneumonia,* and *Acinetobacter* spp, the most common Gram- positive bacteria were *Staphylococcus aureus* and *Enterococcus*, (88).

In the present study, out of the 152 positive blood culture, 85 (55.9%) samples were recorded Gram-negative bacteria, 66 (43.4%) samples were recorded Gram-positive bacteria, 1 (0.7%) sample was recorded fungi. In addition, the most common Gram-negative bacteria were *Klebsiella* spp (36 isolates), *E.coli* (17), *Pseudomonas* spp (14), *Acinetobacter* spp (8). On the other hand, the most common Gram-positive bacteria were *Staphylococcus aureus* (49 isolates), *Streptococcus* spp (8), and *Enterococcus* spp (6).

4.3 Discussion of the Study Hypothesis and Objectives

4.3.1 First Hypothesis

In the present study, the analysis of the data for the first hypothesis regarding gender indicate that there is no a significant difference at a level of 0.05 related to the development of BSIs. The infection rate in females (10.7%) was found to be insignificantly slightly higher (P= 0.587) than males (9.7%).

A retrospective cohort study was conducted by Cohen *et al* (89) and published in 2013. The study was conducted to investigate the relationship between BSIs and gender, and it was including 200348 patients, the result showed that men were more likely to develop

bloodstream and surgical site infections than women. Another prospective study published in 2022 and conducted in Norway, the study included 64040 patients, 46.8 % of them were males. According to this study, men were more likely than women to get BSIs and die from them (90). Uslan (91) carried out a study in Minnesota and published it in 2007. This study was a retrospective cohort one, the study showed that males were more likely than females to get BSI, which occurs more frequently as people get older.

The analysis of the data for the first hypothesis regarding patients' age ranges indicates that there is a significant difference at a level of 0.05 related to the development of BSIs. The highest frequency of BSI was in the age range more than 60 years (14%) and it was significantly higher than that of patients ranged less than one month (5.1%;P=0.000). More attention is needed in the health care for patients aged less than 2 years and more than 60 years.

According to population-based surveillance study conducted in Canada and published in 2021, older people frequently develop BSIs, which are a leading cause of death (92). Age increases the likelihood of BSIs, especially in males (93). A population based surveillance conducted in the health care system in Finland and published in 2012, the study showed that the rate of BSIs increase for patients over 65 years old and under 1 year, and more prevalent in male patients than in female individuals (94).

4.3.2 Second Hypothesis

The analysis of the data for the second hypothesis was regarding patients' ward. There is a significant difference at a level of 0.05 related to the development of BSIs in different wards, because P-value is less than 0.05.

In the present study, BSIs among dialysis patients (22%) was significantly higher than BSIs among non-dialysis patients (9.5%; P=0.000). It appears that dialysis patients were at high risk for infections due to the use of different devices and catheter, lowering immunity, and they were exposed to different NIs.

A systematic review and meta-analysis conducted by Raoofi *et al*, to evaluate the frequency of infections acquired in hospitals, the results showed that the highest infection rate were found in the ICU, neonatal, and transplant units of hospitals. A research was conducted by Suzuki *et al* to investigate the prevalence of BSIs in

hemodialysis patients, the research published in 2016, the results showed that compared to general population, hemodialysis patients had 26 times increased risk to acquire infection.

The analysis of the data for the second hypothesis regarding patients' admission indicates that there is no significant difference at a level of 0.05 related to the development of BSIs and patient classification to inpatient or outpatient in hospital, because P-value is more than 0.05.

A research was conducted by Laupland *et al* and published in 2005, to evaluate the importance of conducting blood culture tests for outpatients, the results showed that blood cultures were more commonly negative. In the present study, BSI rate among patients in dialysis ward (25%) was significantly higher than pediatric ward (6.7%; P=0.008). BSI rate among patients in dialysis ward (25%) was significantly higher than NICU ward (5.2%; P=0.002).

4.3.3 Third Hypothesis

There is a significant difference at a level of 0.05 related to the development of BSIs in relation to chronic diseases, signs and symptoms.

In the present study, there is a significant difference between DM, HTN, and hemodialysis and development of BSIs, because P-value is less than 0.05 for each one of them. This may be attributed to the fact that these chronic disease patients have different clinical conditions and exposed to different medical procedures.

Frequencies of DM, HTN, cancer diagnosis, and hemodialysis chronic diseases among the studied patients were evaluated. In our study 29.6% out of the total 152 positive results were recorded for DM patients, 30.9% of the positive results were recorded for HTN patients, 11.1% of the positive results were recorded for dialysis patients.

BSIs among diabetic patients (14%) was significantly higher than BSIs among non-diabetic patients (9%; P=0.012), BSIs among hypertension patients (13.1%) was significantly higher than BSIs among non-hypertension patients (9%; P=0.036). BSIs among dialysis patients (22%) was significantly higher than BSIs among non-dialysis patients (9.5%; P=0.000).

In parallel, Stoeckle *et al* (74) found that BSIs were more common in diabetic patients than in non-diabetic patients in a four years' study, the study showed that BSIs were 4.4 times more likely to occur in diabetic patients. A prospective study was conducted on BSIs in cancer patients in 2016 to assess clinical features in Mexico City. The study showed that ineffective antimicrobial therapy and multidrug resistance (MDR) development correlated with greater risk of death due BSIs(71).

Sheng *et al* (95) who conducted and published a research in 2022 to assess the changes on immune system in hypertension patients who infected with SARS-CoV-2, the results showed that, HTN associated with different infections, increased the risk of complications and mortality rate in severe infections.

According to CDC there were increased probability of different infections in dialysis patients due to frequent access to the bloodstream using different devices as needles or catheters, the results showed that more than 14,000 BSIs cases were recorded in 2020 in USA and the most common organism was *Staphylococcus aureus,* the probability to get *Staphylococci* BSIs in dialysis adult patient were 100 times more likely in comparison with non-dialysis adult patient (96).

Different signs, symptoms, and diagnosis were followed and recorded for patients in this study, to find any significant association with BSIs. There is a significant difference of frequencies of chills, CKD, and IHD in infected group (patients with BSIs) in comparison to non-infected group, there are no significant differences between the infected and the non-infected groups of patients with regard to fever, weakness, dizziness, SOB, DOB, apnea, dyspnea, hypoxia, asphyxia, acute pain, cough, vomiting, diarrhea, decrease feeding or oral intake or loss of appetite, tachycardia, tachypnea, COPD, liver disease, *Clostridium difficile* infection, CVA and prematurity, because P-value was more than 0.05.

In the present study, the most common signs and symptoms for infected group were acute pain (44%), followed by fever (35%), and cough (25.6%), while chills among BSI patients (10%) was significantly higher (P=0.047) than non-infected patients (5.7%). In a prospective cohort study carried by Holmqvist *et al* (97) in emergency ward and published in 2020, the results showed that chills were significantly associated with bacteremia (P=0.009).

4.3.4 Antibiotic Profile that was Used for Suspected BSIs

The results in Table 13 show that ceftriaxone (32.8% of infected group) was the most common antibiotic used for infected group, and the least common antibiotic used was rifampicin and cefuroxime (0.6% for each one). The results in Table 10 also show that ceftriaxone (31%) was the most common antibiotic used for all suspected BSIs patients, followed by ampicillin (26.5%). On the other hand, rifampicin (0.1%) was the least common antibiotic used for all suspected BSIs patients (infected and non-infected). Vancomycin was the best antibiotic for Gram-positive isolates, while meropenem was the best antibiotic for treatment of Gram-negative isolates, these results agree to results of a prospective descriptive study, conducted on neonatal septicemia in Gaza city in 2005 (76). Other studies regarding antibiotics are shown in empirical treatment section and literature review studies.

The data of the causative pathogen and susceptibility profile regarding sensitivity and resistance to antibiotics, constitute a basic building block for antibiotic stewardship programs, and to choose the appropriate empirical treatment (98).

4.3.5 Fourth Hypothesis

In the present study, there were 129 (84.8%) positive CRP results out of total 152 positive results in the infected group and 888 (66.1%) positive CRP results were in non-infected group. The results show that there is a significant difference at a level of 0.05 related to the development of BSIs and positive CRP results, because P-value is less than 0.05.

According to Anush *et al* (99) who used sequential organ failure assessment (SOFA) score, which was based on recording six variables that represent six organ systems, the results showed that the level of CRP was a more significant indicator of outcome in patients admitted with sepsis. The CRP level increases after infections, it may be increased in viral infections, but the highest increase occurred in bacterial infections (100).

The results show that there is a significant difference between the infected and the non-infected groups of patients in WBCs results, because P-value is less than 0.05. The results also show that 13.7% out of the total 533 cultured samples with high WBCs results were associated with BSIs, and 7.2% out of the total 124 cultured samples with

low WBCs were associated with BSIs. In other word 50.7% out of BSIs were associated with high WBCs result and 6.3% out of BSIs were associated with low WBCs result.

High white blood cell counts, or leukocytosis, can signify a number of illnesses, including infections, inflammation, injuries, and immune system problems. Leukocytosis is often detected using CBC test (101). Leukocytosis or increased WBCs level is considered an indication for infections (102).

4.3.6 Fifth Hypothesis

In the present study, out of total 165 UTI cases, 36(21.8%) BSIs were recorded. In addition, 42 (10.8%) BSIs were found among 389 patients with chest infection or complication cases. The results show that there is a significant difference at a level of 0.05 related to association of BSIs and UTI diagnosis, because P-value is less than 0.05.

The germs that caused the UTI can invade bloodstream. Urosepsis is the name of this condition, and it can be fatal disorder, urosepsis occurs when an untreated UTI progresses from patient urinary system to his kidney (pyelonephritis) and results in sepsis, malfunction of the kidneys as an example of organ failure, a severe drop in blood pressure caused by septic shock, which can raise the death probability (103).

Regarding the following up of chest infection (pneumonia), bronchitis, bronchiolitis, respiratory distress, or respiratory failure, the results in our study show that there are no significant differences between the infected and the non-infected groups of patients with regard to these chest problems and complications, because P-value is more than 0.05.

By following other requested sample culture, the results show that there are significant differences between the infected and the non-infected groups of patients in relation to positive urine culture samples, because the P-value is less than 0.05. In more details, 36 (23.7%) out of 152 BSIs were recorded for patients with positive urine results and this was significantly (P= 0.004) lower than those with positive urine culture but negative BSI (75.8%).

A matched case-control study was conducted on urinary tract-related BSIs risk factors; the study showed that the probability of secondary BSIs was 70% in neutropenic cases, and the most recorded microorganism, which pass from urinary tract to blood stream

was *Enterococcus* spp (104). In the present study, the most frequently pathogen for secondary BSIs was *klebsiella* spp.

In the present research, by following other requested sample cultures, the results show that there are no significant differences between the Infected and the non-infected groups of patients with regard to positive sputum, swab and rectal samples.

4.3.7 Sixth Hypothesis

In the present study, by following the admission data of study population from other hospital, the results show that no patient was recorded in the infected group and all the 23 patients were recorded in non-infected group. The results show that there are no significant differences between the infected and the non-infected groups of patients with regard to patient admission from other hospital, (P-value >0.05).

4.3.8 Seventh Hypothesis

In this hypothesis by following up the patient's outcome in term of mortality, the results show that 32 (22.5%) patients out of the total 142 patients were recorded with the outcome of death in the infected group. The analysis of the data for the seventh hypothesis indicate that there is a significant difference between the infected and the non-infected groups of patients with respect to mortality outcome, because P-value is less than 0.05.

A significant global hazard to public health is posed by BSI. About 2 million cases of BSIs happen each year in North America and Europe are linked to 250,000 deaths, making BSIs the main cause of infection-related mortality (105). Regarding different studies for the outcome of BSIs in term of mortality, the studies showed that the mortality rate of BSIs range between 4-41.5% (98,106).

Another part of this hypothesis was to follow up the study population LOS, the results show that by using independent-T test to compare the mean value between the two groups, there is a significant difference between the infected and the non-infected groups of patients regarding duration of stay in hospital, because the P-value is less than 0.05. In more detail, that ALOS for infected patient in the study was 9.6 days. ALOS for non-infected patients was 6.5 days. So that there is increase of LOS for BSIs patients.

The increasing LOS for patients at hospital lead to increase the probability of acquired different serious infections and complications, and increase financial burden on patients himself and health system (107).

A systematic review and meta-analysis study was published in 2020 to investigate the effect of HA-BSIs on LOS, the study contained more than 20 study in systematic review and 13 studies in meta-analysis. The results showed that ALOS was 4-28 days, between 1.43% and 24% of people died. So that mortality, LOS, and healthcare costs are significantly impacted by HA-BSIs (108).

4.4 Bacteriological Profile.

In the present study, the results show that the most common pathogens were Gram-negative bacteria, which represents 55.9% out of the total 152 positive results, 43.4% were Gram- positive and just one positive result was yeast.

Regarding the type of causative agent and after removal of duplicated results, the results showed that the most common pathogens were *Staphylococcus aureus* (32.4%), followed by *klebsiella* spp (19.2%). Regarding different resistance phenotypes, the results show that 39.7% out of the total positive results were bacteria possessing different phenotypes of resistance. Furthermore, 7.3%, 5.3%, 4.6%, and 22.5% of positive results were for MRSA, CRE, ESBL or MDROs, respectively.

Regarding microbiological and susceptibility profile, the most effective antibiotics were colistin, vancomycin, teicoplanin, ertapenem, doxycycline, and amikacin, respectively. On the other hand, the highest bacterial resistance rates to antibiotics were against cefixime, amoxicillin clavulanic acid combination, cefuroxime, and co-trimoxazole (trimethoprim/sulfamethoxazole), respectively.

4.5 Research Limitation.

In scientific research there were no complete or perfect studies, limitations of the study differ from one to another study, in this study six different limitations have been dealt with.

1-The first limitation was shortage of time, which resulted in a shorter data gathering period. If more information was collected, will lead to an increase in the power of the study.

2-The hospital does not have a specialized department with regard to the management of infectious diseases, there is one employee, who divides his work at hospital between nursing and infection control, and he does not possess full time to follow up on the various hospital departments with regard to infection control and prevention.

3-The following of blood culture result takes more than three days to follow up, Gram stain result after one to two days indicate the presence and morphology of organism, primary result after three days, the final reports take more than five days especially for negative results.

4-This was the first study regarding BSIs at the north of west bank in general and especially Jenin governmental hospital, and this was the reason for the lack of information regarding to the subject of the study, which required diligence and long thinking on a professional and scientific basis in some points.

5-There is great difficulty in obtaining information, there is no dedicated place to enter the information system in the hospital, where access to the information system requires the presence of a user account and a password. This requires the existence of a place designated for the purposes of scientific research and data collection, and the existence of an account designated for this purpose.

6-There is no recorded or follow up for anaerobic bacteria in pediatric who are less than 13 years old age, due to the use of only one pediatric bottle (BACTEC Ped medium), which is used for aerobic and facultative anaerobes culture. However, this is not expected to have considerable effect on results because aerobic and facultative anaerobic pathogens are typically responsible for BSI in younger people, and BSIs with obligate anaerobic bacteria are less common to occur (20).

7-The limited number of BSI caused by fungi may reflect insufficiently equipped laboratory or trained staff for monitoring fungal growth in blood culture, especially the bacterial rapid growth may obstacle the detection of slow growing fungal one in concomitant bacterial and fungal infection.

4.6 Strength of the Study

The hospital contains a laboratory equipped and qualified to deal with samples in correct and scientific methods within agreed work protocols with the Palestinian ministry of health. The laboratory contains an experienced staff.

The study period lasted for four months, on a daily basis, there was a follow-up of patients' data for each case separately, and recording of data on a daily basis documented in special records and statistical software that were used to analysis the data statistically in order to answer the hypotheses of the study.

There was cooperation from all members of the medical staff and a clear facilitation of the data collection process, a clear scientific methodology was used and the ethics of scientific research were preserved.

4.7 Conclusion

This study contained multiple data related to the BSIs and some factors and variables related to it. In this study, a similar rate of BSIs incidence for global reality was found and there were many requests blood cultures for examination. The study identified some risk factors related to the disease and their impact on it. Further studies and over longer periods of time may be needed to identify other factors.

There was a clear effect and relationship between the BSIs and the increase in the number of deaths in the hospital, and there was a clear relationship between the disease and increase of LOS in hospital, this was reflected in the increase in the consumption of antibiotics and the increase in the financial burden, and increases the exposure of the patient residing in the hospital to infectious diseases and its complications.

The data, which were collected in this study help in understanding this disease more and help in developing strategies to deal with it. The study can be considered as the beginning of other studies based on it. The aim is to establish a health system based on scientific foundations to limit the spread of the disease in the future.

There are no previous studies on this topic in our reign to make a comparison, to determine the change of incidence rate of BSIs, the change in risk factors, the changes in the causative agent, the development of antibiotic resistance. This study opens the way for other researches regarding BSIs in the coming years.

4.8 Recommendation

1- BSIs are a type of NIs, which needs continuous follow-up through training programs for medical staff and HCWs, controlling diseases, preventing their spread, and breaking the cycle of disease, achieves ideal health care and decrease the incidence of disease in the next years.

2- Conducting awareness programs and educating patients, especially patients with DM, HTN and dialysis, as it was found that there is a relationship between these diseases and the occurrence of the BSIs. More attention is needed in the health care of patients aged less than 2 years and more than 60 years.

3- Emphasis should be made on conducting blood tests for patients to monitor the WBCs count and CRP as inflammatory markers. In addition, blood culture samples from patients during high temperatures should be obtained to increase the opportunity to early detect the pathogen.

4- Adhere to the rules of the process of withdrawing blood for culture, practice and good hand hygiene. Put on the proper personal protective equipment's (PPE) depends on whether the patient needs to be isolated or there is a risk of being exposed to body fluids, to decrease contaminated results and maintaining the safety of the medical staff and preventing the acquisition of infection.

5- Work to find and develop isolation rooms for infected patients in the wards, and train a specialized staff to deal with these rooms in order to reduce the occurrence of a large spread of pathogens such as cases of *Acinetobacter baumannii* and *Clostridium difficile.*

6- Identification of patients at risk for nosocomial infections, hand hygiene and hand washing compliance, control measures, observance of conventional precautions to prevent transmission, and attempts to lower VAP, SSI, and CAUTI rates, which are examples of infection related to secondary BSIs.

7- Continuous developing for antibiotic stewardship program, observation for antibiotics' resistance, reduction of antibiotic consumption, commitment and compliance with requesting susceptibility profile before treatment.

The following general suggestions might be made in order to lower the incidence of BSIs in hospitals:

1- Following the right methods and protocols based on accurate science for cleaning and sterilizing furniture, surfaces, and rooms will help the hospital maintain its standards for cleanliness and sterility and lowering the risk of infections related to patient care. In addition, there should be an activation of the follow-up role and documentation of the follow-up processes through infection control checklists.

2- Improving infection preventive methods for those at risk of disease, such as those who have weaker immune systems, dialysis, chemotherapy, or go through major surgery.

3- The availability of sufficient amounts of the required hospital devices, as well as efficient and suitable disinfectants and hygiene supplies for cleaning. In addition, work to develop the sterilization department and ensure that the process of disposing of medical waste was carried out in proper way.

4- Supporting quick patient visits, and putting protocols in place to reduce big crowds of patients and visitors inside the hospital.

5- Developing the relationship between patients and medical staff, boosting hospital confidence, and promoting patients to inform about any new complain.

6- Ensuring that healthcare professionals receive the appropriate instruction and training on hand hygiene and methods for preventing infections, as well as encouraging them to follow the recommended practices.

7- Adopting the appropriate preventative measures to lower the frequency of infections in the future. Conducting periodic investigations to assess the incidence of infections in the hospital and increasing interest in antibiotic resistance topics in terms of data recording, especially ESBL, CRE, MRSA and others.

List of Abbreviations

Abbreviation	Meaning
ALOS	Average Length of Stay
BSIs	Bloodstream Infections
CA	Community-Acquired
CAUTI	Catheter Associated Urinary Tract Infection
CDC	Centers for Disease Control and Prevention
CKD	Chronic Kidney Disease
CL	Central-Line
CLABSI	Central Line-Associated Bloodstream Infection
CLSI	Clinical and Laboratory Standards Institute
CoNS	Coagulase-Negative Staphylococcus
COPD	Chronic Obstructive Pulmonary Disease
CRBSIs	Catheter-Related Bloodstream Infections
CRE	Carbapenem-Resistant Enterobacteriaceae
CRP	C-Reactive Protein
CSF	Cerebrospinal fluid
CVA	Cerebrovascular Accident
CVC	Central Venous Catheter
CVCs	Central Venous Catheters
DIC	Disseminated Intravascular Coagulation
DM	Diabetes Mellitus
DOB	Difficult of Breath
ESBL	Extended Spectrum Beta Lactamases
ESR	Erythrocyte Sedimentation Rate
EU/EEA	European Union /European Economic Area
FUO	Fever of Unknown Origin
GBS	Group B Streptococcus
HA	Hospital Acquired
HAIs	Hospital Acquired Infections
HAIs	Healthcare-Associated Infections
HCA	Health-Care Acquired
HCAIs	Healthcare-Associated Infections
HTN	Hypertension

ICU	Intensive Care Unit
IHD	Ischemic Heart Disease
IRB	Institutional Review Board
KPC	Klebsiella pneumoniae Carbapenemase
LCBSI	Laboratory Confirmed Bloodstream Infection
LOS	Length of Stay
MDR	Multidrug-Resistant
MDROs	Multidrug-Resistant Organisms
MRSA	Methicillin-Resistant Staphylococcus aureus
MSICU	Medical Surgical Intensive Care Unit
NICU	Neonatal Intensive Care Unit
NIs	Nosocomial Infections
NTS	Non-Typhoidal Salmonella
PPE	Personal Protective Equipment
SIRS	Systemic Inflammatory Response Syndrome
SOB	Shortness of Breath
SPSS	Statistical Package for the Social Sciences
SPSS	Statistical Package for Social Science
SSI	Surgical Site Infection
UTI	Urinary Tract Infection
VAP	Ventilator-Associated Pneumonia
VREF	Vancomycin-Resistant Enterococcus faecium
WBCs	White Blood Cells

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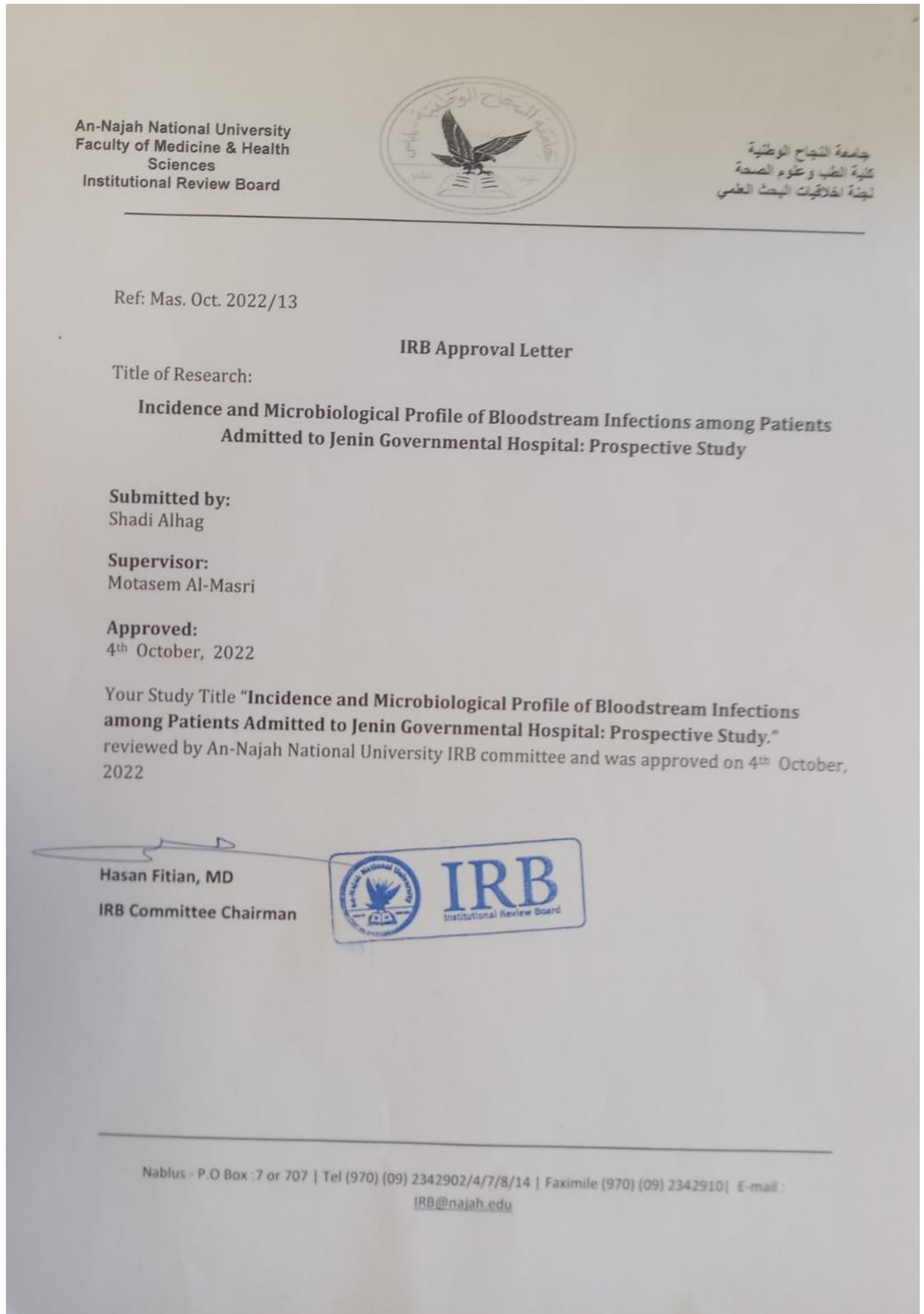
Appendices

Appendix A

Institutional Review Board (IRB)



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

جامعة النجاح الوطنية
كلية الطب وعلوم الصحة
لجنة اخلاقيات البحث العلمي

Ref: Mas. Oct. 2022/13

IRB Approval Letter

Title of Research:

Incidence and Microbiological Profile of Bloodstream Infections among Patients Admitted to Jenin Governmental Hospital: Prospective Study

Submitted by:
Shadi Alhag

Supervisor:
Motasem Al-Masri

Approved:
4th October, 2022

Your Study Title "**Incidence and Microbiological Profile of Bloodstream Infections among Patients Admitted to Jenin Governmental Hospital: Prospective Study.**" reviewed by An-Najah National University IRB committee and was approved on 4th October, 2022

Hasan Fitian, MD

IRB Committee Chairman

IRB
Institutional Review Board

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

Appendix B

An official book, Facilitating A researcher's Task

State of Palestine
Ministry of Health
Education in Health and Scientific Research Unit

دولة فلسطين
وزارة الصحة
وحدة التعليم الصحي والبحث العلمي

Ref.: ………………
Date:………………

الرقم: ……………………
التاريخ: ……………………

الأخ مدير عام الادارة العامة للمستشفيات المحترم،،،
تحية واحترام،،

الموضـوع: تسهيل مهمة بحث

يرجى تسهيل مهمة الطالب: شادي عادل يوسف مصلح- ماجستير مكافحة وضبط العدوى - جامعة النجاح، لعمل بحث بعنوان:

" Incidence and Microbiological Profile of Bloodstream Infections among Patients Admitted to Jenin Governmental Hospital: Prospective Study"

حيث سيقوم الطالب بجمع بيانات خاصة بالبحث من ملفات المرضى عينة الدراسة، مع الالتزام بعد التعرض للمعلومات الشخصية للمرضى، وذلك في:

- مستشفى جنين

مع العلم أن مشرف الدراسة: د. معتصم المصري.

على ان يتم الالتزام بالمحافظة على اخلاقيات البحث العلمي وسرية المعلومات.
على ان يتم الالتزام بجميع تعليمات واجراءات الوقاية والسلامة الصادرة عن وزارة الصحة بخصوص جائحة كورونا، وتحت طائلة المسؤولية. وابراز شهادة التطعيم قبل دخول مرافق وزارة الصحة.
على ان يتم تزويد الوزارة بنسخة PDF من نتائج البحث، التعهد بعدم النشر لحين الحصول على موافقة وزارة الصحة.

مع الاحترام،،

د. عبد الله القواسمي
رئيس وحدة التعليم الصحي والبحث العلمي

نسخة: نائب الرئيس للشؤون الأكاديمية المحترم/ جامعة النجاح

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Appendix C

Additional Tables and Figures

Table 9

Frequencies of Susceptibility Profile Results for the Study Sample Regarding Gram Stain Type

Sensitivity Profile	Gram Negative		Gram Positive		P-value
	S/T	R/T (%)	S/T	R/T (%)	
Amikacin	61/81	20/81 (25)	35/38	3/38 (8)	0.031
Amoxicillin+Clavulanic acid	14/54	40/54 (74)	4/5	1/5 (20)	0.012
Gentamicin	49/77	28/77 (36)	33/53	20/53 (38)	0.941
Cefepime	12/19	7/19 (37)	0/1	1/1 (100)	0.209
Cefixime	0/7	7/7 (100)	-------	-------	
Cefotaxime	34/63	29/63 (46)	4/4	0/4	0.072
Cefoxitin	-------	-------	37/50	13/50 (26)	
Ceftazidime	27/56	28/56 (52)	1/1	0/1 (0.0)	0.313
Ceftriaxone	35/63	28/63 (44)	4/4	0/4 (0.0)	0.081
Cefuroxime	17/45	28/45 (62)	2/3	1/3 (33)	0.322
Meropenem	66/83	17/83 (20.4)	3/4	1/4 (20)	0.828
Ofloxacin	12/24	12/24 (50)	-------	----------	
Colistin	26/26	0/26 (0.0)	-------	----------	
Ciprofloxacin	44/72	28/72 (39)	20/38	18/38 (47)	0.391
Levofloxacin	18/28	10/28 (36)	4/5	1/5 (20)	0.492
Aztreonam	36/65	29/65 (45)	--------	---------	
Ertapenem	47/56	9/56 (16)	2/2	0/2 (0.0)	0.537
Clindamycin	-------	-------	32/58	26/58 (45)	
Erythromycin	-------	-------	17/57	40/57 (70)	
Rifampicin	--------	-------	39/50	10/50 (22)	
Teicoplanin	-------	-------	63/64	1/64 (2)	
Piperacillin +Tazobactam	53/81	28/81 (35)	2/2	0/2 (0.0)	0.307
Doxycycline	10/11	1/11 (9)	18/23	5/23 (22)	0.365
Co-trimoxazole	22/49	27/49 (55)	18/40	22/40 (55)	0.992
Tetracycline	0/1	1/1 (100)	-------	-------	
Penicillin G	7/9	2/9 (20)	3/4	1/4 (25)	0.913
Piperacillin	-------	-------	0/2	2/2 (100)	
Imipenem	24/34	10/34 (30)	2/2	0/2 (0.0)	0.367
Fosfomycin	0/1	1/1 (100)	-------	-------	
Vancomycin	-------	-------	64/64	0/64 (0.0)	

Table 10

Antibiotics Used for Suspected BSIs

Antibiotic	Number of specimens	Percentage (%)
Ceftriaxone	463	31
Ampicillin	396	26.5
Gentamicin	265	17.7
Meropenem	227	15.2
Piperacillin+ tazobactam	205	13.7
Cefotaxime	192	12.8
Ceftazidime	101	6.7
Vancomycin	229	15.3
Azithromycin	172	11.5
Levofloxacin	168	11.2
Ciprofloxacin	27	1.8
Clindamycin	8	0.5
Amikacin	36	2.4
Metronidazole	35	2.3
Rifampicin	1	0.1
Colistin	36	2.4
Fluconazole	46	3.2
Nystatin	19	1.3
Cefuroxime	12	0.8
Augmentin	15	1.0
Teicoplanin	7	0.4
Adcef (cefdinir)	8	0.5
Total	1495	100

Table 11

Causative Agent of BSI

Causative Agent (Bacteria)	**Frequency (%)**
Staphylococcus aureus	49 (32.4)
Klebsiella spp	29 (19.2)
E.coli	17 (11.2)
Pseudomonas spp	14 (9.2)
Acinetobacter baumannii	8 (5.3)
Enterococcus spp	6 (3.8)
Streptococcus viridans	5 (3.3)
Proteus	4 (2.6)
Enterobacter	3 (2)
Streptococcus agalactiae	2 (1.3)
Morganella morganii	2 (1.3)
Flavobacterium spp	2 (1.3)
Bordetella pertussis	2 (1.3)
Brucella spp	1 (0.6)
Salmonella spp	2 (1.2)
Staphylococcus epidermidis	1 (0.6)
Staphylococcus saprophyticus	1 (0.6)
Pasteurella spp	1 (0.6)
Streptococcus pyogenes	1 (0.6)
Stenotrophomonas maltophilia	1 (0.6)
Total results	151

Table 12

Susceptibility Profile Results for the Positive Results

Antibiotic	S: Sensitive		R: Resistance	
	N	%	N	%
Amikacin	96	80.6	23	19.4
Amoxicillin +Clavulanic acid	18	30.5	41	69.5
Gentamicin	82	63	48	37
Cefepime	12	60	8	40
Cefixime	0	0	7	100
Cefotaxime	38	56.7	29	43.3
Cefoxitin	37	74	13	26
Ceftazidime	28	50	28	50
Ceftriaxone	39	58.2	28	41.8
Cefuroxime	19	39.5	29	60.4
Meropenem	69	79	18	20
Ofloxacin	12	50	12	50
Colistin	26	100	0	0
Ciprofloxacin	64	58.2	46	41.8
Levofloxacin	22	67	11	33
Aztreonam	36	55	29	45
Ertapenem	49	84.5	9	15.5
Clindamycin	32	55	26	45
Erythromycin	17	30	40	70
Rifampicin	39	78	11	22
Teicoplanin	63	98.4	1	1.6
Piperacillin +Tazobactam	55	66.2	28	33.8
Doxycycline	28	82	6	18
Co-trimoxazole	40	45	49	54
Tetracycline	0	0	1	100
Penicillin G	10	77	3	23
Piperacillin	0	0	2	100
Imipenem	26	72.2	10	27.8
Fosfomycin	0	0	1	100
Vancomycin	64	100	0	0

Figure 4

Age Distribution of BSIs

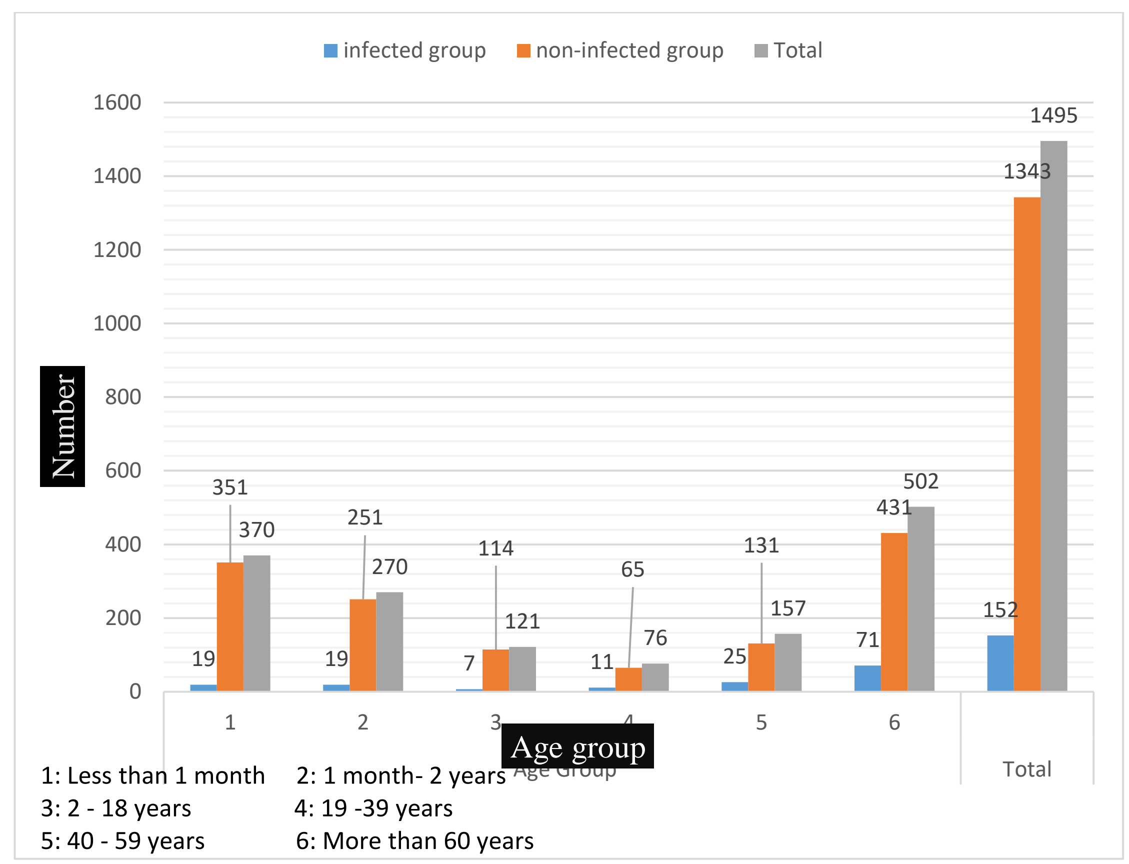

Table 13

Antibiotic Used for Treatment of Infected Group and Non-Infected Group

Antibiotic used	**Infected group** **N (% of infected)**	**Non-infected group** **N (% of non-infected)**
Piperacillin +Tazobactam	30 (19.7)	175 (13)
Ampicillin	14 (9.2)	382 (28.4)
Cefotaxime	10 (6.5)	182 (13.6)
Ceftazidime	11 (7.2)	90 (6.7)
Gentamicin	10 (6.5)	255 (19)
Cefuroxime	1 (0.6)	11 (0.8)
Ceftriaxone	50 (32.8)	413 (30.7)
Meropenem	38 (25)	189 (14.1)
Vancomycin	47 (30.9)	182 (13.6)
Azithromycin	15 (10)	157 (11.7)
Levofloxacin	17 (11)	151 (11.2)
Amikacin	5 (3.2)	31 (2.3)
Metronidazole	3 (2)	32 (2.4)
Fluconazole	11 (7.2)	35 (2.6)
Colistin	12 (7.8)	24 (1.8)
Rifampicin	1 (0.6)	0 (0)
Clindamycin	3 (2)	5 (0.4)
Ciprofloxacin	5 (3.2)	22 (1.6)
Total	152	1343

Figure 5

Difference between Infected Group and Non-Infected Group Regarding Antibiotic Used for Patients

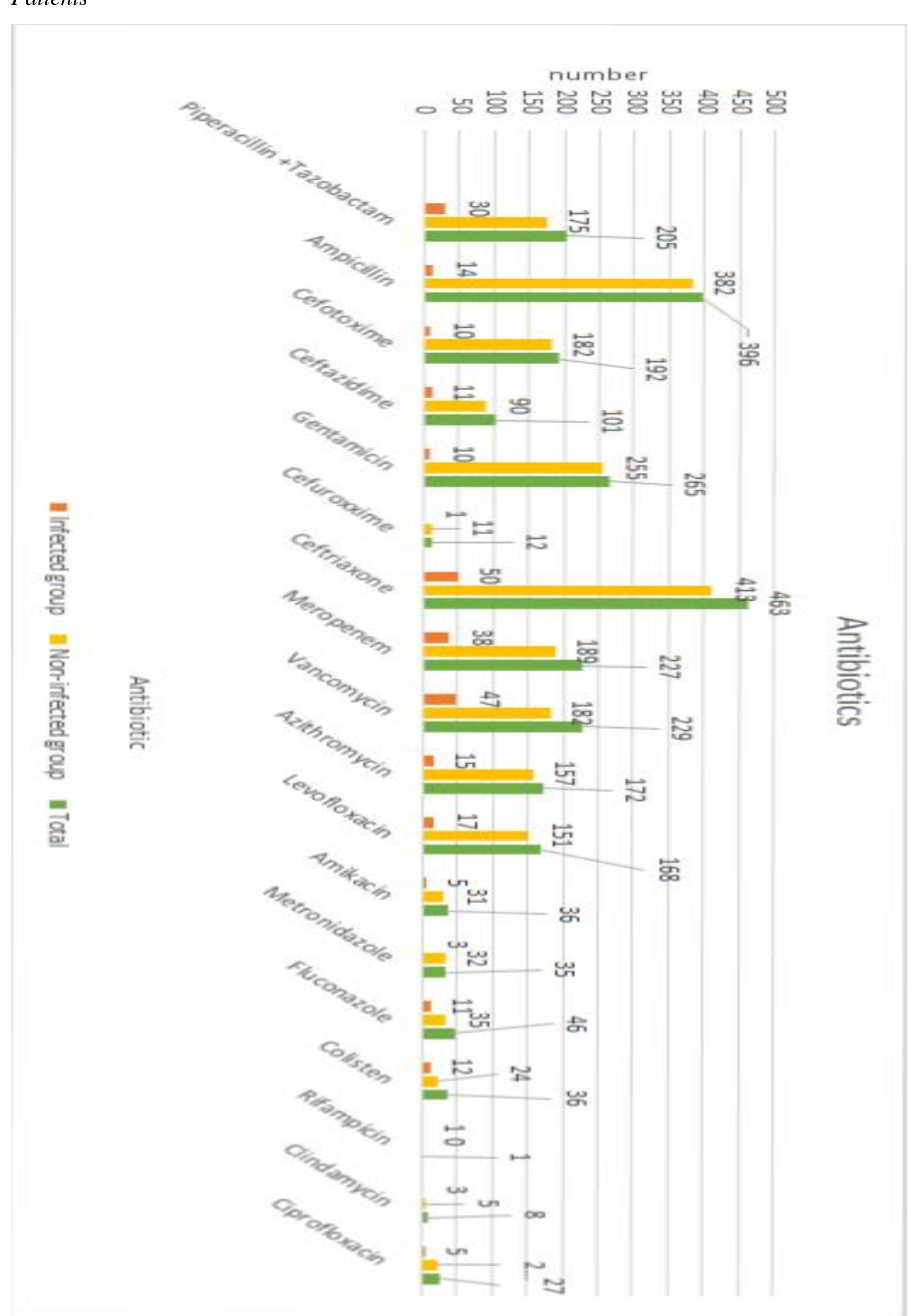

Table 14

Susceptibility Profile Results for the Study Sample Regarding E.coli spp

Antibiotic	Frequency (Total =17)	
	S	R
Amikacin	15	1
Amoxicillin+Clavulanic acid	11	6
Gentamicin	11	4
Cefepime	2	1
Cefixime	0	2
Cefotaxime	11	6
Cefoxitin		
Ceftazidime	6	3
Ceftriaxone	11	5
Cefuroxime	6	8
Meropenem	15	1
Ofloxacin	1	2
Colistin	1	0
Ciprofloxacin	8	6
Levofloxacin		
Aztreonam	12	3
Ertapenem	15	1
Clindamycin		
Erythromycin		
Rifampicin		
Teicoplanin		
Piperacillin +Tazobactam		
Doxycycline		
Co-trimoxazole	9	5
Tetracycline		
Penicillin G		
Piperacillin		
Imipenem	2	0
Fosfomycin		
Vancomycin		

Table 15

Susceptibility Profile Results for the Study Sample Regarding S.aureus spp

Antibiotic	Frequency (Total =49)	
	S	R
Amikacin	34	3
Amoxicillin+Clavulanic acid		
Gentamicin	27	20
Cefepime		
Cefixime		
Cefotaxime		
Cefoxitin	36	13
Ceftazidime		
Ceftriaxone		
Cefuroxime		
Meropenem		
Ofloxacin		
Colistin		
Ciprofloxacin	17	17
Levofloxacin		
Aztreonam		
Ertapenem		
Clindamycin	26	23
Erythromycin	13	36
Rifampicin	38	11
Teicoplanin	49	0
Piperacillin +Tazobactam		
Doxycycline	12	3
Co-trimoxazole	16	20
Tetracycline		
Penicillin G	5	1
Piperacillin		
Imipenem		
Fosfomycin		
Vancomycin	49	0

Table 16

Susceptibility Profile Results for the Study Sample Regarding Pseudomonas spp

Antibiotic	Frequency (Total =14)	
	S	R
Amikacin	11	2
Amoxicillin+Clavulanic acid		
Gentamicin	11	2
Cefepime	8	1
Cefixime		
Cefotaxime		
Cefoxitin		
Ceftazidime	10	3
Ceftriaxone		
Cefuroxime		
Meropenem	13	1
Ofloxacin	6	3
Colistin	4	0
Ciprofloxacin	13	1
Levofloxacin	9	1
Aztreonam	7	7
Ertapenem		
Clindamycin		
Erythromycin		
Rifampicin		
Teicoplanin		
Piperacillin +Tazobactam	12	2
Doxycycline	5	0
Co-trimoxazole		
Tetracycline		
Penicillin G	2	1
Piperacillin		
Imipenem	11	2
Fosfomycin		
Vancomycin		

Table 17

Susceptibility Profile Results for the Study Sample Regarding Klebsiella spp

Antibiotic	**Frequency (Total =29)**	
	S	**R**
Amikacin	21	6
Amoxicillin+Clavulanic acid	7	22
Gentamicin		
Cefepime	1	3
Cefixime	0	3
Cefotaxime	14	15
Cefoxitin		
Ceftazidime	4	11
Ceftriaxone	14	15
Cefuroxime	10	13
Meropenem	22	7
Ofloxacin	3	5
Colistin	9	0
Ciprofloxacin	14	14
Levofloxacin	4	6
Aztreonam	12	10
Ertapenem	21	8
Clindamycin		
Erythromycin		
Rifampicin		
Teicoplanin		
Piperacillin +Tazobactam	16	12
Doxycycline	7	0
Co-trimoxazole	8	14
Tetracycline		
Penicillin G	4	1
Piperacillin		
Imipenem	5	4
Fosfomycin		
Vancomycin		

جامعة النجاح الوطنية

كليـــــة الدراســـــــات العليــــــا

معدل حدوث المرض والتنوع الميكروبولوجي لعدوى مجرى الدم ضمن المرضى الذين يدخلون إلى مستشفى جنين الحكومي: دراسة مستقبلية استطلاعية

إعداد

شادي عادل يوسف مصلح

إشراف

د. معتصم المصري

قدمت هذه الرسالة/الأطروحة استكمالا لمتطلبات الحصول علي درجه الماجستير في برنامج مكافحة وضبط العدوى، من كلية الدراسات العليا، في جامعة النجاح الوطنية، نابلس- فلسطين.

2023

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الملخص

مقدمة- تحدث عدوى مجرى الدم (BSIs) عندما تدخل مسببات الأمراض إلى الدورة الدموية، مما يؤدي إلى مضاعفات خطيرة، زيادة استهلاك المضادات الحيوية، زيادة مدة الإقامة في المستشفى، وزيادة معدل الوفيات. وتعتبر معدلات الإصابة الكبيرة المبلغ عنها في جميع أنحاء العالم تحديًا للصحة العالمية.

الأهداف- تحديد مدى حدوث التهابات مجرى الدم، توضيح توزيع استخدام المضادات الحيوية، دراسة الملف الميكروبيولوجي، حساسية المضادات الحيوية، ارتباطها بمقاومة المضادات الحيوية، توضيح المصدر المسبب.

تصميم الدراسة والمنهجية - الدراسة عبارة عن دراسة مستقبلية استطلاعية لمدة أربعة أشهر أجريت في الفترة من أكتوبر 2022 إلى فبراير 2023 في أقسام مختلفة في مستشفى جنين الحكومي في شمال الضفة الغربية لفلسطين. اشتملت الدراسة على ما مجموعه 1495 عينة لـ 1190 مريضا.

النتائج - أظهرت الدراسة أن معدل الإصابة بـعدوى مجرى الدم كان 132 لكل 100000 سنويا، أظهرت الدراسة أن معدل الإصابة بـعدوى مجرى الدم كان 10.2% ضمن 1495 حالة متوقعة، فيما يتعلق بنوع العامل الممرض في الدراسة الحالية، 55.9% من النتائج الإيجابية كانت سلبية الجرام و43.4 % كانت إيجابية الجرام، وكانت البكتيريا سالبة الجرام الأكثر شيوعًا هي *Klebsiella* الكليبسيلا (19.2% من مسببات الأمراض المكتشفة)، *E.coli* الإشريكية القولونية (11.2%)، *Pseudomonas* السيدومنوناس الزائفة (9.2%). بالإضافة إلى ذلك، كانت *S. aureus*المكورات العنقودية الذهبية (32.4%) هي البكتيريا إيجابية الجرام المعزولة في الغالب. تم اكتشاف أنواع أخرى من البكتيريا إيجابية الجرام بشكل أقل تكرارًا مثل المكورات

*Streptococcu*s spp (5.3%) و(3.8%) *Entercoccu*s spp المكورات المعوية. كان العامل الممرض الأكثر عزلة لمرض BSI الثانوي هو *Klebsiella* الكليبسيللا. ومن بين البكتيريا المعزولة، كان 40% منها يمتلك أنماطًا ظاهرية مختلفة للمقاومة. كان هناك ارتباط كبير بين تطور BSIs ومرض السكري (P = 0.012) (DM)، وارتفاع ضغط الدم (P = 0.036) (HTN)، وغسيل الكلى (P = 0.000). كان السيفترياكسون (32.8%) هو المضاد الحيوي الأكثر شيوعًا المستخدم للمجموعة المصابة وكان المضاد الحيوي الأكثر شيوعًا (31%) المستخدم لجميع حالات BSI المشتبه فيها. كان المضاد الحيوي الأكثر فعالية المستخدم ضد البكتيريا إيجابية الجرام هو الفانكومايسين (100%). وكان المضاد الحيوي الأكثر فعالية المستخدم لسلبية الجرام هو الكوليستين (100%). علاوة على ذلك، تبين أن المجموعة المصابة لديها إقامة أطول بكثير في المستشفى (9.6 أيام) مقارنة بالمجموعة غير المصابة (6.5 أيام؛ P = 0.000). أولئك الذين اصيبوا BSIs كان لديهم معدل وفيات أعلى بكثير (22.5%) (P = 0.000) من معدل الوفيات لدى المجموعة غير المصابة (11%).

الخاتمة والتوصيات - ينبغي بذل جهود حثيثة لتطوير سياسات وبرامج مكافحة العدوى داخل المستشفيات. يجب أن يكون هناك تطوير لبرنامج الإشراف على المضادات الحيوية بسبب ارتفاع معدل اكتشاف البكتيريا المقاومة.

الكلمات المفتاحية: عدوى مجرى الدم، البيانات الديموغرافية، علامة الالتهاب، مقاومة المضادات الحيوية، العامل المسبب للمرض.