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Laboratory Practices and Antimicrobial Resistance in a Florida Hospital

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Walden University
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Abstract

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MPH, Silliman University, 2014

BSMT, Silliman University, 1995

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

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Abstract

Antibiotic resistance is a health threat affecting millions of Americans. Microorganisms develop resistance to antibiotics, rendering them useless for treating infections. The purpose of this quantitative study was to assess the associations between sample processing time and antibiotic resistance and is based on the health belief model. A retrospective specimen tracking activity of data from November 2019 to November 2020 was obtained by random sampling of 246 bacterial cultures. One hundred ninety-six (80%) samples were processed on time, and 50 (20%) were delayed; 167 (68%) samples were determined to have the presence of antimicrobial resistance (AMR), and 79 (32%) with no resistance to antibiotics. The data analysis plan for the study on lab practices and antimicrobial resistance included binary and multiple logistic regression. The time for culture set-up was found to have a statistically significant association with AMR. There was a 56% decreased odds of reporting AMR on samples set-up within 30 mins compared to more than 30 mins, $OR = 0.44$, 95% CI = [0.44, 0.80], $p = 0.007$. The findings were preserved even after adjusting for other times associated with the overall order of processing samples, adjusted $OR = 0.46$, 95% CI = [0.25, 0.85], $p = 0.012$. There was a non-significant 30% increased odds of reporting AMR on the time for the final reporting of results. The positive social change implication of the study is that laboratory leaders would design a better laboratory process for setting up cultures within 30 minutes and consequently to report final culture results on time, to prevent unnecessary antibiotic prescribing, reducing patient's hospital stay and the financial burden from treatment and hospitalization.

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Dedication

My greatest inspiration for the achievement of this scholarly endeavor are the men and women behind the scenes in the care of patients: the medical laboratory scientist, specifically the infectious disease microbiologist, and all laboratory assistants. Working so hard with all patient samples to immediately report results to physicians for the accurate diagnosis and treatment of patients. The research study was also intended to impart knowledge and understanding of the importance of sample processing time. Moreover, for the clinical laboratories to continue studying ways to improve laboratory services. Also, I am dedicating this study to the youth to understand the importance of the laboratory in the care of patients and for the desire for more individuals to become clinical laboratory professionals.

Acknowledgments

The fulfillment of this doctoral journey comes from the support of my husband, Jesu Trias, and my mother, Perla Sy. It was a life-changing process, and the challenge was bearable with their support. To my two brothers, sisters-in-law, my nephews, Milo and Leo Sy, and our Fettuccine. My family was my source of joy and inspiration. They were always there with me, canceling every vacation to not leave me alone working on my dissertation. To my research committee, Dr. Hadi Danawi as chairperson, Dr. Harrison Ndetan as the second member, and the URR, Dr. Peter Anderson, for their guidance and expertise in research. To the University of Florida Health Jacksonville laboratory, which is my work home, for allowing me to use the microbiology laboratory data for the Chapter 4 of my study. To the IRB of the hospital, to Mr. Noel Gomez, the informatics supervisor of the laboratory. To the laboratory director, Mr. Fredrick Schumann, and to my co-laboratory educator, Ms. Ezra Mae Magaya, for the support. And lastly, to Dr. Dianne Halstead and Baptist Health Jacksonville microbiology department for the inspiration and love for infectious diseases. They were instrumental to me in pursuing a Ph.D. degree and studying the laboratory's role in antimicrobial resistance. And lastly, to my God of strength, wisdom, and knowledge. I held unto thee throughout this education journey for the service of others.

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Chapter 1: Introduction to the Study

Introduction

The use of antibiotics in the United States offers life-saving medical advances. Millions of Americans receive and rely on antibiotics for complicated bacterial and fungal infections. However, people are dying of diseases where effective antibiotic treatments are unavailable. It was estimated that about 47 million or 30% of antibiotics are prescribed each year for infections that do not need antibiotics (Centers for Disease Control and Prevention [CDC], 2019). The practice worsens the side effects of antibiotics and the development of antibiotic resistance (AR). The CDC (2019) also states that at least 1.7 million Americans each year get an infection that develops into sepsis. Without effective antibiotic treatment, it could rapidly lead to death due to tissue damage and organ failure.

Data from the CDC (2019) showed that antibiotics are also essential during surgical procedures, organ transplants, and cancer care. People undergoing common medical procedures, including 1.2 million women undergoing cesarean procedures, need antibiotics. All patients undergoing other complex surgeries, such as organ transplants, are at risk for surgical site infections. Thirty million people with chronic illnesses such as diabetes are also at a higher risk for infection because of their weakened immune system (CDC, 2019). Also, more than 500,000 dialysis patients and around 650,000 cancer patients are often at risk of developing an infection, and antibiotics are necessary to protect and treat these patients (CDC, 2019). I conducted this study assessing multidrug resistant microorganisms isolated from samples submitted for bacterial culture to

determine the association between the number of cases of AMR in a Florida hospital and the processes of handling samples in the laboratory.

I examined processes in the clinical laboratory and the contribution to AMR cases in hospitals to understand infection control prevention and lessen the financial hospital burden. The lab sample processes would improve the reporting of antibiotic testing results to physicians, limiting the overprescribing of broad-spectrum antibiotics. The processes included the prompt handling of culture and antibiotic sensitivity testing samples. There are technologies that can be used for the quick testing of samples, such as molecular tests and matrix-assisted laser desorption-time of flight (MALDI-TOF); however, because of the expense of new technology in bacterial identification, they were not part of the study.

Little is known about how the samples are handled in the clinical laboratory and whether the processes and procedures greatly affect the number of AMR cases in hospitals. I determined the association between laboratory practices as they relate to the cases of AMR in a Florida hospital. I obtained the data for the study retrospectively from the University of Florida Health Jacksonville laboratory's information systems for 1 year, from November 2019 to November 2020.

Background

Clinical and microbiology testing is important for the effective fight against AMR. The process includes timely collection and transport, setting up of the samples for bacterial culture, identifying the resistant microorganism and antibiotic sensitivity testing of the identified microorganism, and monitoring the impact of maintenance of the

measures for the control of AMR (Jackups, 2020; Jimenez et al., 2020). Early detection contributes to preventing the dissemination of resistant bacteria and implementing appropriate infection control measures, such as isolation of AMR-positive patients, environmental disinfection, appropriate management of waste, and healthcare workers to wear personal protective clothing, including masks, gloves, gowns when caring for patients (Rocco et al., 2019; Rump et al., 2020). Ning et al. (2016) mentioned the importance of patient identification and communication of multidrug resistant organisms (MDRO). Misidentification or mislabeling of samples during specimen collection and throughout the process is crucial in preventing treatment errors because of the wasted time fixing the errors, such as recollection of samples, repeating all procedures, amending the results, and reporting back to the providers.

There are several processes in identifying bacteria; when the samples are received in the microbiology laboratory, a gross examination of the specimens is performed. The examination includes the presence of mucus or blood and any other significant impressions of the sample and must be documented for correlation with bacterial growth (Forbes et al., 1998). Another way of determining the quality of the sample is through direct microscopic examination; for example, a sputum sample can be rejected when seen microscopically as saliva rather than sputum through the quantitation of the number of white blood cells in the specimen (Forbes et al., 1998; Jorgensen et al., 2015). Moreover, according to Forbes et al. (1998), microscopic examination of specimens, such as using stains (e.g., gram stains, acid-fast stains), will aid the clinicians in an early indication of the patient's infection. Furthermore, the microscopic result can guide the extent of culture

workup of the specimen, for a microbiologist to only focus on the predominant organism that is causing the infection and not the other normal bacterial flora mixed in the sample.

Microbial culture allows microorganisms to grow and reproduce by using various types of culture media that contain nutrients for the growth of bacteria and other chemicals used to inhibit other organisms and allows the selective growth of specific organisms. For example, the blood agar plate (BAP) culture media contains nutrients that will allow the growth of all microorganisms except for the *Haemophilus spp*., which only grows in media with special factors (e.g., X and V factors). Also, BAP can distinguish the organisms by its hemolytic reaction to blood; it shows complete or beta hemolysis, partial or alpha hemolysis, and no hemolysis or gamma. For example, *Staphylococcus aureus* shows complete hemolysis compared to other *Staphylococcus spp.* (Jorgensen et al., 2015; Berkowitz, 2016; Locke, 2013). Inoculation for culture is done using an inoculating loop that would transfer a number of organisms throughout the culture plate by streaking, allowing a semi-quantitative determination of the number of organisms growing on the culture. When the organisms are growing all over the plate, it is quantitated as heavy growth, then the medium as moderate growth, and if the growth is just on the first quadrant or first side of inoculation, it is light growth. The incubator for growing the culture must have a controlled temperature (Jorgensen et al., 2015; Tille, 2016). Most microorganisms grow and multiply at a temperature between 35^{o}C to 37^{o}C; however, other organisms such as *Campylobacter spp.* would only grow at 42^{o}C. Environmental conditions are also essential for the culture of organisms; most organisms grow in the presence of air or oxygen (aerobes). However, some organisms cannot

survive in the presence of oxygen (anaerobes), and some survive with a small amount of oxygen and carbon dioxide (capnophilic) (Jorgensen et al., 2015; Tille, 2016). Therefore, the laboratory needs to know the sample's source to assess the cultured media's environment and temperature for the growth of the suspected resistant microorganism.

Rapid identification of microorganisms using the latest technologies is being utilized in microbiology laboratories. Patel (2016) stated that the technologies are helpful to clinicians for the quicker and more appropriate interpretation of bacterial identification and to improve patient care. Moreover, next-generation sequencing (NGS), a molecular procedure, revolutionized the clinical practice and its usefulness in healthcare settings to detect numerous microorganisms from several anatomic sites. Polymerase chain reaction (PCR), sometimes called molecular photocopying, is a fast and inexpensive test to amplify segments of DNA. The National Human Genome Research Institute (2020) stated that PCR is a valuable tool in most laboratories to detect bacteria and viruses, perform DNA fingerprinting, and diagnose genetic disorders. According to the *Fast Facts on U.S. Hospitals, 2021* (n.d.), there are 6,090 hospitals in the U.S., and in the advent of the SARS-CoV-2 virus, most hospitals implore using a molecular test such as the PCR test. The College of America Pathology (CAP) (2021), a clinical laboratory accrediting body, includes molecular testing or PCR on its accreditation checklist and accredits hospital laboratories based on the functionality of the PCR test. These are whole-genome sequencing and phenotypic antimicrobial sensitivity testing. It is used to determine MDROs such as the carbapenemase-producing *Enterobacterales*. The molecular diagnostic procedures include detecting resistant bacteria in positive blood cultures,

gastroenteritis for stool pathogens, meningitis and encephalitis from Cerebrospinal Fluid (CSF), and urinary tract infection (UTI) from urine samples. The challenges in using NGS are the lack of standardized definitions and quality control metrics and the limited availability of the test because of the expense and lack of sequencing platforms. The expense limitation must be considered, especially in low-resource health facilities (Lesho et al., 2016). The MALDI-TOF and Mass spectrometry (MS) used in the microbiology laboratory only takes a few minutes to identify an organism from a pure culture compared to the traditional identification method. It also reduces the time it takes to report bacterial identification results to clinicians is important to consider (Rocco et al., 2019); however, the gold standard for bacterial identification is still culture or cultivation of bacteria. The potential resistant microorganisms that are included in the research study are Carbapenem-Resistant *Acinetobacter (*CRA), *Candida auris*, Carbapenem-resistant *Enterobacterales* (CRE), *Clostridioides difficile*, *Neisseria gonorrhoeae,* Vancomycin-resistant *Enterococcus* (VRE), *Pseudomonas aeruginosa*, and Methicillin-resistant *Staphylococcus aureus* (MRSA).

The study on the cases of AMR in the Florida hospital employed clinical informatics experts and developed tools for quicker reporting of results and comprehensive guidelines for effective laboratory tests (Jackups, 2020). The intervention of constant communication and training of health caregivers and electronic identification technologies significantly lower the cases of sample misidentification. Tacconelli et al. (2018) mentioned the importance of surveillance in controlling AMR and the data

obtained from hospital laboratories. Inaccurate surveillance data can delay the translational approach to the control of AMR and the treatment of patients.

Although researchers have investigated the issue of AMR, the topic of lab practices and AMR has not been explored in this way. The study focused on the instances wherein the laboratory had delays in reporting results to physicians for the prompt treatment of specific antibiotics to patients. The possible predictors were the time the specimen was transported to the laboratory, the time the samples were processed for testing, the time multi-drug resistant organisms (MDRO) were identified in culture, the time antibiotic sensitivity testing (AST) results were reported, and the time final results were reported. According to Jacobs et al. (2019), one of the gaps in the control of AMR was that the general medical community was less familiar with the diagnostics and educational framework required for a productive laboratory workforce.

Sautter and Halstead (2018) stated the importance of the laboratory's role in improving patient outcomes on MDRO infection. However, no data showed the effects of pre-analytic, analytic, and post-analytic laboratory practices in control and prevention. There were limited data on the challenges and barriers in integrating the clinical laboratory's role in the containment of AMR from the transport, cultivation, identification, and reporting of antibiotic resistance results. Most researchers have discussed the technologists' role in the identification of AMR organisms but not in the process of events, from sample collection to reporting of results, and this is the reason why this research study was needed to determine whether there was an association between the laboratory's handling of samples suspected of AMR.

Problem Statement

The situation or issue that prompted my AMR research was that the health threat affects at least 2.8 million Americans, with more than 35,000 deaths each year (CDC, 2020). Any person can be infected with MDRO at any stage of life, and most of those are people receiving health care and people with a weakened immune system (Florida Department of Health [FL-DOH], 2021). The CDC (2020) also stated that AMR infections threaten modern medicine; without antibiotics, patients with infections acquire sepsis and tissue damage, organ failure, and death. Hospitalized patients undergoing surgery, those with chronic diseases such as diabetes, organ transplant, dialysis care, and cancer patients on chemotherapy need effective antibiotics to protect and prevent infections.

Moreover, AMR as a social problem, affects the economy. Treatment cost for community and hospital-onset AMR infections in the United States was estimated at $4.6 billion in 2017 (Nelson et al., 2021). Healthcare professionals, including laboratory microbiologists/medical technologists, are crucial in controlling antimicrobial resistance. In most microbiology laboratories, reporting culture results will take 48 hours or longer, especially identifying complex organisms and the process for antibiotic sensitivity testing (AST). The expected time the results are released will make physicians prescribe broad-spectrum antibiotics. The over and under-prescribing antibiotics can destroy normal bacteria and allow antibiotic-resistant microorganisms to multiply (Landecker, 2016).

Infections caused by AMR are difficult to treat and have a high mortality rate. The number of cases of AMR was the study's dependent variable, in which the number of

organisms showing resistance to at least three groups of antibiotics is accounted as a case. The independent variables in the research study on AMR in hospitalized individuals were based on pre-analytical, analytical, and post-analytical determination. The pre-analytic factors were the time the specimen was transported to the lab and the time in setting up the samples for bacterial culture. The time in identifying and testing for antimicrobial sensitivity, which were analytical factors, and the time in reporting results was post-analytical.

In this study, I examined whether the samples arrived on time, were set up on time, whether the multidrug resistant microorganisms were identified within 24 hours, whether antibiotic sensitivity testing was reported at 48 hours, and whether the time of result completion contributed to the number of AMR cases in a Florida hospital. There was a lack of studies conducted to determine the association between the time of the transport of samples to the laboratory, the time in setting up for culture and growing of bacteria in the samples, the time in the identification of the significant organism, the time in testing for antibiotic sensitivity, and the time in reporting of results, in relation to the cases of antibiotic resistance in hospitals.

Purpose of the Study on Antimicrobial Resistance

The purpose of this quantitative study on AMR cases was to examine the association between (a) the time the sample was transported in the laboratory, (b) the time the sample was set-up on culture media to grow the bacteria, (c) the time in the identification of bacteria, (d) the time in testing for antimicrobial sensitivity as analytical factors, and (e) the time in reporting AST results as post-analytical factors, which were

the independent variables, and the diagnosis of AMR cases in a Florida hospital as the dependent variable.

Research Questions and Hypotheses on Antimicrobial Resistance

Research Question 1 (RQ1): Is there an association between the time samples are transported to the laboratory and AMR cases in a Florida hospital?

Null Hypothesis ($H_0$1): There is no association between the time samples are transported to the laboratory and AMR cases in a Florida hospital.

Alternative Hypothesis (H_a1): There is an association between the time samples are transported to the laboratory and AMR cases in a Florida hospital.

Research Question 2 (RQ2)**:** Is there an association between the time samples are set-up for culture in the laboratory and AMR cases in a Florida hospital?

Null Hypothesis ($H_0$2): There is no association between the time samples are set-up for culture in the laboratory and AMR cases in a Florida hospital.

Alternative Hypothesis (H_a2): There is an association between the time samples are set-up for culture in the laboratory and AMR cases in a Florida hospital.

Research Question 3 (RQ3): Is there an association between the time microorganisms are identified in culture and AMR cases in a Florida hospital?

Null Hypothesis ($H_0$3): There is no association between the time microorganisms are identified in culture and AMR cases in a Florida hospital.

Alternative Hypothesis (H_a3): There is an association between the time microorganisms are identified in culture and AMR cases in a Florida hospital.

Research Question 4 (RQ4): Is there an association between the time antibiotic sensitivity testing is reported and AMR cases in a Florida hospital?

Null Hypothesis ($H_0$4): There is no association between the time antibiotic sensitivity testing is reported and AMR cases in a Florida hospital.

Alternative Hypothesis (H_a4): There is an association between the time antibiotic sensitivity testing is reported and AMR cases in a Florida hospital.

Research Question 5 (RQ5): Is there an association between the time the final culture results are reported and AMR cases in a Florida hospital?

Null Hypothesis ($H_0$5): There is no association between the time the final culture results are reported and AMR cases in a Florida hospital.

Alternative Hypothesis (H_a5): There is an association between the time the final culture results are reported and AMR cases in a Florida hospital.

Research Question 6 (RQ6): Is there an association between the time of specimen transport, culture set-up, identification of microorganisms, antibiotic sensitivity test, time when culture results are reported, and AMR cases in a Florida Hospital?

Null Hypothesis ($H_0$6): There is no association between the time of specimen transport, culture set-up, identification of microorganisms, antibiotic sensitivity test, time when culture results are reported, and AMR cases in a Florida Hospital.

Alternative Hypothesis (H_a6): There is an association between the time of specimen transport, culture set-up, identification of microorganisms, antibiotic sensitivity test, time when culture results are reported, and AMR cases in a Florida Hospital.

Theoretical Framework and Study Variables

The theories and concepts that I used to ground this study were the health theory that focuses on an individual's actions in AMR: the health belief model (HBM). HBM theory focuses on individuals' actions and behaviors. Practitioners and researchers use the HBM to identify a person's health behavior background to design effective health behavior interventions (Glanz et al., 2015). The HBM can predict people's actions in preventing, detecting, and controlling AMR.

The number of AMR cases from hospitalized patients in the United States was perceived from individual practices (Jackups, 2020). Microbiology laboratory testing conducted by laboratory personnel was vital for diagnosing and treating patients infected with AMR organisms. Jackups (2020) also mentioned that diagnostic errors from laboratory testing could result in over-prescribing or under-prescribing antibiotics and longer hospital admission due to unnecessary antibiotic treatment.

The challenges in staffing and the lack of funds in the clinical lab have a role in the containment of AMR, according to Jacobs et al. (2019). Also, pre-analytical and analytical errors are misidentification or mislabeling of crucial samples, resulting in erroneous lab findings, diagnosis, and treatment (Ning et al., 2016). Moreover, a post-analytical error, such as an error in reporting results and the lack of a laboratory information system (LIS), also plays a part in delays in reporting results to physicians.

The time in sample transport and setting up for culture was perceived to affect the reporting of AMR results on time. Any delay in transporting and setting up samples can destroy cells and bacteria, resulting in the missed determination of MDRO. The analytical

identification of AMR organisms was a perceived susceptibility, wherein there was a perception of contracting the disease or a positive result on the presence of AMR in the samples (Witte, 1992). According to LaMorte (2018), individuals have different vulnerabilities and severity of infections or illnesses. Any delay in reporting results was a perceived barrier in the early diagnosis and treatment of patients. LaMorte (2018) also stated that barriers or impediments were inconvenient, time-consuming, unpleasant, dangerous, and costly. The barriers all lead to the severity of the patient's illness and the worsening of hospitalization expenses.

I obtained the data for this study from the LIS, using dashboards to pull the number of samples submitted for bacteriological culture to identify antibiotic-resistant microorganisms. I used the stamped time from the collection, transport, receiving, and setting up of the samples for culture, identification, AST set-up and reading, and the overall time track from the LIS. I generated a year of data from November 2019 to November 2020 and conducted a statistical analysis.

Table 1

Theoretical Framework of the Study.

Health Belief Model Constructs	Study Variables	Variable Nature and Coding Scheme
	Independent/predictor variables	
Perceived Severity (Pre-Analytical determination)	The time of specimen transported to the lab. *Samples arrived in the lab more than two to four hours after collection.*	Categorical: Dichotomous Coding: 0 – More than 2-4 hours 1 – Within 2-4 hours
Perceived Severity (Pre-Analytical determination)	The time for setting up samples for culture. *The samples sit in the laboratory's receiving area for more than 30 minutes.*	Categorical: Dichotomous Coding: 0 – More than 30 mins 1 – Within 30 mins

Perceived Susceptibility (Analytical determination)	The time in the identification of organisms in culture. *The bacterial identification is delayed for more than 24 hours after the samples are set up.*	Categorical: Dichotomous Coding: 0 – More than 24 hrs 1 – Within 24 hrs
Perceived severity (Analytical determination)	The time antibiotic sensitivity testing (AST) is set up. *The antibiotic sensitivity testing is delayed 48 hrs after the sample is set up.*	Categorical: Dichotomous Coding: 0 – More than 48 hrs 1 – Within 48 hrs
Perceived Barriers and Perceived Severity (Post-Analytical determination)	The final time results are reported *Final results are reported for more than three days.*	Categorical: Dichotomous Coding: 0 – More than 72 hrs 1 – Within 72 hrs
	Dependent/outcome variable	
Perceived Benefits (Post-Analytical determination)	Cases of AMR in a Florida hospital *Identified cases of AMR organisms in a Florida Hospital.*	Categorical: Dichotomous Coding: 0 – Absence of AMR organism 1 – Presence of AMR organism

Nature of the Study on Antimicrobial Resistance

This study employed a retrospective cohort using data from the LIS, which shows the time the bacterial culture was ordered until the results were reported. To determine the association between the time of specimen handling and the diagnosis of cases of AMR in a Florida hospital, a retrospective cohort on cases of resistant microorganisms isolated from samples submitted to the laboratory for culture identification and antibiotic sensitivity testing was used for the planned research design from the Florida hospital, a government-subsidized hospital of Northeast Florida. The data was obtained from the

clinical laboratory specimen tracking systems. The time samples were delivered to the laboratory, the time in growing bacteria using culture media, the time in reading the cultures for bacterial identification, the time in the setting up of antibiotic sensitivity testing, and the time in reporting final results to the providers were all associated with the number of cases of AMR in a Florida hospital.

Definition of Terms on Antimicrobial Resistance

Antimicrobials or Antibiotics: are medical interventions of infections that involve eradicating infectious microorganisms by inhibiting or killing their growth. Depending on the type of target organism, it is also known as antibacterial, antifungal, antiparasitic, or antiviral.

Antimicrobial Resistance (AMR) or Antibiotic resistance (AR): results from altered cellular physiology of microorganisms. The result is a partial or complete loss of the effectiveness of antibiotics or standard treatment for resistant microorganisms is rendered ineffective. Infections persist and increase tendencies to spread the infection.

Antibiotic sensitivity testing (AST): determines whether the bacteria of concern express resistance to the antimicrobial agent that is a potential choice for managing infection.

Clinical Laboratory Standards Institute (CLSI): the standard used by clinical laboratories to improve testing outcomes and maintain accreditation. In microbiology, it is the breakpoint for determining whether a microorganism is sensitive or resistant to the antibiotic.

Medical Errors: are serious health problems and a leading cause of death in the U.S. The two types of errors are errors of omission and errors of commission. Omission errors occur when actions are not taken, such as when samples for microbiological cultures are not processed immediately. The error of commission occurs when wrong actions are taken, for example, using the wrong culture media used to grow bacteria and test for sensitivity to antibiotics.

Multidrug-resistant organisms (MDRO): are the type of bacterial resistance that predominates in hospitals, wherein bacteria acquire resistance to one or more antimicrobial agents. Microorganisms that are resistant to three antibiotic classes are used to treat infections.

Resistance mechanisms: are the microorganism's defense strategy, wherein a certain DNA creates specific resistant genes that can change over time, resulting in more resistant infections. The resistant organisms can also share their resistance genes with other microorganisms not exposed to antibiotics.

Sample phases of testing:

Pre-analytical testing: the first phase in laboratory processes, which includes handling specimens before they are received in the laboratory. Important errors such as identification and specimen handling occur at this phase allowing problems or errors to happen further in the later phase of specimen analysis.

Analytical testing: is the second phase of sample processing, the actual laboratory testing; it involves processes that ultimately provide testing results.

Post-Analytic testing: the final phase of sample processes in the laboratory and ends with the final result and reporting of results to clinicians or providers.

Time: the duration of a sample for bacterial identification and antibiotic sensitivity testing is processed in the clinical laboratory. It is appointed or fixed minutes or hours for a process to adhere to the required turnaround time for the final culture results to be reported to the clinical providers.

Assumptions

I acquired the data used for the research study on the diagnosis of AMR cases from the Florida hospital timeline records of samples ordered for bacterial culture. The data were the time physicians placed the orders, the time the samples were collected, and the time of transport and receipt to the laboratory. Also, the time the samples were cultivated to special culture media, the time when microbiologist tests and interprets the culture growth, the time antibiotic sensitivity was tested on the organisms, and the time the final report was reported to the ordering provider. There were assumptions about the role of the laboratory in improving patients' prognosis and treatment of AMR organisms, as mentioned by Sautter and Halstead (2018); however, no data were presented from their study. Sautter and Halstead's assumptions made me decide to study the times in handling samples for microbiology culture for the identification of bacteria and testing for the appropriate antibiotics, for the prompt treatment of patients using the correct antibiotic and not with broad-spectrum antibiotics.

Scope and Delimitations

The scope of the study as presented above, the data on the time the specimens were collected, the time it was received in the laboratory, the time the samples were set-up to culture media to allow the growth of microorganisms, to the time the cultures were read by microbiologist, to the time antimicrobial sensitivity testing was performed, and the time the results are reported to the physician. All samples from admitted adult patients submitted to the laboratory for bacterial culture were included in the data collection and analysis for the association between sample handling and the number of AMR cases in a Florida hospital. The samples include urine, blood, superficial and internal wound, sputum, and other lower respiratory samples such as bronchoalveolar lavage, tracheal aspirate, and pleural fluid. Also, stool, tissues, and other body fluids received in the laboratory were included in the sampling and data analysis. These samples were collected, analyzed, and reported within the same year. These organisms must resist multiple antibiotic groups or be pan-resistant to all available antibiotics. The samples for bacterial cultures that were excluded from the study were from young pediatric patients aged between zero to twelve years of age. Also, organisms identified with sensitivity results showing sensitivity to antibiotics were excluded from the study. The study's biggest challenge in antibiotic resistance from hospitals was access to clinical laboratory data. To be granted access to the data was to request permission from UF Health Jacksonville hospital’s ethics committee or the hospital’s institutional review board (IRB). When access to data was approved, all samples submitted for culture from November 2019 to November 2020 were checked for the times from ordering to

reporting of results, and results were checked on whether the organisms isolated from culture were resistant to antibiotics.

Limitations

The possible limitation of the retrospective cohort data sampling on AMR cases in the Florida hospital was that some rare antibiotic-resistant organisms were not captured in the one year allocated for the study, from November 2019 to November 2020. Available data might not be appropriate for the study, or the data does not have the needed information for the research study. Not all relevant information was available for analysis. Moreover, some data were unavailable as it was not recorded in the past. For example, resistant organisms, which were not determined in the past because of the lack of testing technology, have not created a program to capture the data. Also, according to LaMorte (2016), in retrospective cohort studies, because it is recorded in the past, there is a frequency of absence of data on confounding factors. Such as when hospitalized patients' data are mixed with outpatient results or results from the community. Therefore, there were no means to compare previous results on whether there was truly a significance in the number of cases of AMR in hospitals due to the phases of sample handling. Biases in retrospective cohort studies include a differential loss to follow-up on issues. The results cannot be repeated and compared to the gold standard since the study was done in the past.

To address the limitation of the unknown potential confounders that were not included in the sampling, the "need to improve the comparability of the intervention and control groups" is necessary (Kim, 2017, p.13). The methods include the design phase,

which includes restriction and matching of data. However, restriction or inclusion can limit the generalizability of the study and cannot be used for other populations. Matching of data was done by making a like-to-like comparison. Other methods to address the limitation in the data analysis phase include stratification, regression, and propensity score. Stratification would divide the datasets into homogenous subgroups and conduct a subset data analysis. Regression would estimate the association of each variable after adjusting the effects of the other variables. According to Kim (2017), if the data analysis greatly differs, the difference in baseline characteristics of the variables must have a substantial effect on the outcome. The propensity score method to address the limitation of a retrospective cohort study was to work on larger samples to attain the distribution balance of the observed covariates.

Significance

This study was significant because the quantitative results on AMR provided vital information locally, within the clinical laboratory, and in the medical community. The findings contribute to the knowledge of the number of MDRO or AMR organisms cases in the Florida hospital and allow public health organizations, and health professionals, particularly laboratorians, to develop strategies to process the sample as quickly as possible. The clinical laboratory used new technologies (e.g., MALDI-TOF) that directly identify the causative agent of infection, faster determination of resistance strains by the antibiotic sensitivity test, and report accurate results to physicians to prevent antibiotic prescribing errors. Moreover, the research study has the potential for positive social change in the general community, as it can provide key information on AMR infections

that are harming admitted patients in hospitals. Finally, the information allowed healthcare agencies to develop AMR control and prevention approaches to reduce hospitalization's financial burden.

Summary

The first chapter elaborated on the purpose of the study in the laboratory practices in handling samples for the association of the cases of antibiotic-resistant organisms in the Florida hospital. It was mentioned that the independent variables were the four common factors or steps before results were reported to providers. The dependent variable was the number of AMR cases, affecting millions of Americans yearly and leading to death (CDC, 2019). Aside from the statement on the epidemiology and the prevalence of the disease in the U.S., the role of the laboratory, as stated by Sautter and Halstead (2018), was a reason for overprescribing or underprescribing broad-spectrum antibiotics to patients. However, no data showed that the clinical laboratory greatly influences the number of cases of AMR; therefore, there was a gap in knowledge from the statement of Sautter and Halstead (2018).

As a social problem, AMR was also mentioned as more individuals were hospitalized, and the treatment cost for the disease is estimated at billion dollars, as stated by Nelson et al., 2021. AMR affects the country’s economy and could result in a significant financial burden. The study's main purpose was to quantitatively analyze data obtained retrospectively from a cohort of secondary longitudinal data. Six hypotheses and research questions were listed based on the study variables. The health belief model was the basis for building the theoretical framework of the proposed quantitative research.

The patient population included in the research study were all adults and older pediatric patients admitted to the hospital. All sources of samples that were tested and have MDRO isolated were also included in the data analysis. The possible limitation of the study was missing some information and data, which could not be captured within the time or year allotted to acquire the data.

In Chapter 2, a comprehensive literature review on AMR cases in the US and searching for peer-reviewed literature on laboratory processes and tests are undertaken. According to Lai (n.d.), researchers and authors use literature review to create a foundation to justify their research and present current topics. The Walden University library and other websites for peer-reviewed are good sources for literature searches. The rationale of the theories of the study on AMR, as described in Chapter 2, provided the rationale of the health belief model theoretical framework on the association of AMR cases and the laboratory's processes in handling samples suspected of MDRO.

Chapter 2: Literature Review on Antimicrobial Resistance

Introduction

AMR has been a health threat to millions of Americans, with deaths that are in the thousands. The disease can infect any individual at the age stage of life, especially the most vulnerable, such as patients in the hospital undergoing surgery, patients with chronic diseases (e.g., diabetes, hypertension), patients with cancer, and undergoing chemotherapy. Infections caused by AMR are hard to treat because of the limited antibiotic resources and thus result in a high mortality rate. AMR affects the nation's economy as people infected with resistant microorganisms tend to be admitted longer in the hospital, and alternative antibiotics are more expensive and have side effects (CDC, 2019; Jimenez et al., 2020).

My goal for this study was to assess the association of the time in the processing of specimens sent to the laboratory for AMR testing, making physicians resort to prescribing broad-spectrum antibiotics, which are not specific to the resistant organism and can destroy another normal organism that is beneficial to the body. The results from the laboratory would only be wasted since broad-spectrum antibiotics have already been prescribed to the patients. The focus of the study was to determine sample processing delay from the laboratory workers. The study involved checking the date and time when samples are processed, from when physicians placed the orders to the date and time when results are reported back to the physician. Also, to focus on the number of delays from the laboratory, to create positive social change in the awareness of the existing problem,

and recommend guidelines or policies that will change the habit or culture that has been erroneously practiced.

Literature from different sources mostly states the prevalence of AMR in healthcare institutions and the community. In this study, I assessed bacterial threats based on clinical impact on the patients, the number of incidences, how quickly the organism was transmitted from one person to another, whether effective antibiotics were available, whether there were barriers for prevention and control, and the economic impact on AMR infection. The study involved hospitalized or admitted patients diagnosed with AMR based on the antibiotic sensitivity results obtained from the clinical microbiology laboratory.

Chapter 2 of the study included a list of search engines and databases on the significant, relevant, and latest research studies on AMR and showed the scope of the literature in terms of search year and current peer-reviewed literature. The literature review described the methodology for isolating and identifying resistant microorganisms, antibiotic sensitivity testing, and other constructs of interest in AMR. The theoretical framework and synthesized studies related to the research questions were also presented in Chapter 2. Lastly, the summary and conclusion will describe the literature gaps and provide transitional materials to connect the gap with the methods described in Chapter 3.

Literature Search Strategy

Terms for searching literature review on laboratory practices and antimicrobial resistance:

1. *Antimicrobial resistance*

2. *Antibiotic resistance and USA*
3. *Antimicrobial resistance, Clinical laboratory, and Hospital*
4. *Antimicrobial resistance and Laboratory Practices*
5. *Drug resistance*
6. *Drug resistance in bacteria/microorganisms*
7. *Antibacterial agents*
8. *Microbial sensitivity tests*
9. *Medical Errors, Laboratory Errors*

The peer-reviewed literature was from publication dates 2016 to 2022. The databases were MEDLINE with full text, Academic search complete, CINAHL Plus with full text, PubMed, Sage Journals, and ProQuest Health & Medical Collection.

Table 2

Literature Search Summary of the Study.

Search Term	Database	Publication Date	Results (Peer-reviewed)
Antimicrobial Resistance Florida	CINAHL Plus with Full Text	2016 – 2021	104
	PubMed		45
	MEDLINE with Full Text		823
	Sage Journals		2326
Antimicrobial Resistance Clinical Laboratory	CINAHL & MEDLINE with Full Text	2016 – 2021	1119
	PubMed		9324
	Sage Journals		2523
Drug-Resistant Organism USA	ProQuest Health & Medical Collection	2016 – 2021	944
	PubMed		8790
	Sage Journals		2065

Antimicrobial Resistance Laboratory Processes	MEDLINE with Full Text	2016 – 2022	1140
Laboratory Errors	MEDLINE with Full Text Academic Search Complete CINAHL Plus with Full Text	2016 – 2021	390 383 100
Medical Errors in hospitals	MEDLINE with Full Text Academic Search Complete CINAHL Plus with Full Text	2016 – 2021	116 72 58
Retrospective Study Antimicrobial Resistance Hospitals	MEDLINE with Full Text Academic Search Complete Directory of Open Access Journals	2019 – 2022	389 212 183

Theoretical Foundation on Antimicrobial Resistance

The HBM was developed by the U.S. Public Health Service in the year 1950 to explain the failure of individuals to participate in disease detection and prevention programs (Glanz et al., 2015). Two major approaches were developed under the HBM: stimulus-response and cognitive theories. The stimulus-response theory states that reinforcements and consequences affect the physiological drive of people. It does not require mental processing or thinking and reasoning, and it is an automatic behavior of individuals (Glanz et al., 2015). In my research study on the determination of laboratory processing time in handling samples for AMR organisms, the actions of lab employees were also assessed on whether they automatically or immediately processed the samples and whether results were promptly reported for the accurate treatment of patients, prevent complications, and longer hospitalization.

The Cognitive theory operates by “influencing expectations rather than directly influencing behavior.” The critical components of the cognitive theory are thinking, reasoning, expecting, or hypothesizing; all value expectancies and individual values are the outcome of the expectation (Glanz et al., 2015, p. 75). In my research study, laboratory workers handling the samples were reinforced and expected to work on samples immediately when received in the laboratory.

The expected routine processing of samples by lab workers starts with receiving specimens, and then the lab assistant immediately delivers the sample(s) to the microbiology department, and the microbiology technologist immediately set-up the sample on culture media and loads it into incubators. Microorganisms are identified within 18 to 24 hours, then sensitivity testing is performed within 72 hrs, and results are reported to clinicians. Physicians and other healthcare providers expect the samples to be processed immediately in the lab so results are reported on time, and patients are treated with specific antibiotics, not broad-spectrum antibiotics.

The HBM relates to the research questions of the association of AMR to the time in sample processes in the clinical laboratory by following the theory's key concepts: perceived severity, perceived susceptibility, perceived barrier, and perceived benefits. Perceived severity can be applied during the pre-analytic stage of sample processing by determining the number of times the samples arrive in the laboratory more than 2 hours after collection and the number of times the samples have been sitting at the receiving section for more than 30 mins. Perceived severity can also be applied during the analytical stage to determine how often antibiotic sensitivity testing was reported more

than 3 days after sample collection. Perceived susceptibility applies during the analytic testing phase in identifying the name of the resistant microorganisms through a culture that harms patients in hospitals. Perceived barriers when the final or complete results were not reported on time for the treatment of patients against antibiotic-resistant organisms. The last concept related to the research question was perceived benefits, wherein the value of time in handling samples for antimicrobial resistance was used for public awareness of the importance of timeliness and the prompt treatment of patients for infection control and prevention.

Knowledge on Antimicrobial Resistance

The National Institute of Health [NIH] (2021) defined antibiotics as medicines used to treat diseases caused by bacteria or fungi by controlling or destroying growth. The common infections treated with antibiotics are urinary tract infections (UTIs), strep throat, whooping cough, and sepsis, a life-threatening condition caused by bacteria. Antibiotics are not recommended for treating sinus and ear infections as these infections usually get better on their own. Antibiotics are not a treatment of choice for virus infections such as influenza, COVID-19, and HIV. According to the CDC (2021b) and mentioned by Ali et al. (2021), antibiotics are a life-saving treatment for patients with infections but have little effect on patients without infection, putting them at risk for antibiotic side effects, which include adverse drug reactions, secondary infection, and resistance to antibiotics.

There are minor and severe side effects of using antibiotics. Diarrhea, nausea, rash, and yeast infection are minor side effects. Serious side effects are *Clostridiodes*

difficle infection that causes diarrhea and damages the colon. Other serious antibiotic effects are allergic reactions that are life-threatening and AMR. The CDC (2021b) has stated that many antibiotics are prescribed unnecessarily and not used inappropriately, threatening the antibiotic medication's effectiveness. The common mistake of taking antibiotics is not finishing the full dose, resulting in the recurrence of the infection. Another mistake is a delay in taking the antibiotics, sharing the antibiotics with others, and using someone else's antibiotic prescription. The three ways of taking antibiotics are orally, topically, and intravenously. By mouth for liquid, pills, and capsules; topically with ointment, cream, spray, and drops for ear and eye infections; and intravenous for complicated infections such as sepsis and bacteremia (CDC, 2021; Roger et al., 2019).

Person, Time, and Place Epidemiology of Antimicrobial Resistance

Person

Human, animal, and environmental health are connected and consider antibiotic resistance (AR) a One health challenge. The advocacy of the one health challenge is only to prescribe antibiotics when necessary, when the drugs are needed for infection, and to prevent sepsis. Because AR is difficult to treat, healthcare costs have considerably increased; infections with AMR require more toxic and expensive treatment, follow-up visits to healthcare providers, and extended hospital stay (Hassoun-Kheir et al., 2020). Atif et al. (2021) mentioned that inappropriate use of antibiotics could prolong hospital admissions, increase the cost of treatment, the need for additional antibiotics that usually have side effects and are much more expensive, and adverse outcomes to patients and the development of antibiotic resistance. Kamenshchikova et al. (2021) stated a higher risk of

acquiring AMR in people admitted to hospitals. AMR is more problematic in clinical settings than in public with its biomedical nature and mechanism. Although the U.S. saw a reduced number of deaths from AMR in the year 2021, with a 30% reduction of patients admitted to hospitals, and an 18% overall reduction in the number of cases of AMR infections, the CDC (2021) still states the need to protect against AR organisms, especially during COVID-19 pandemic.

AMR affects anyone at any age, mostly people with weakened immune systems. The CDC (2019) stated that AMR jeopardizes modern medicine's advancement as patients who undergo special procedures such as joint replacement, organ transplantation, and cancer therapy are at risk of infection and thus require effective antibiotics against multidrug-resistant organisms (MDRO). According to the CDC (2021), the estimated national cost of treating infections caused by multidrug resistant organisms commonly found in healthcare is more than $4.6 billion annually. The World Health Organization (WHO, 2021) stated that there was a shortage of antibiotics classified as innovative for treating AMR infection, affecting the economy of countries, especially the healthcare systems. The cost of AMR to the economy significantly affects the productivity of patients and healthcare workers as hospitalization is prolonged and the need for more intensive and expensive care.

Time

AMR microorganisms can resist antibiotics that are used to treat life-threatening infections. In 2017, the number of cases of AMR in the United States was estimated at more than 2.8 million, and 35,000 people died of the disease. AMR is a global health and

developmental threat declared by the WHO (2021) as one of humanity's top 10 health threats. The CDC (2021) is concerned about the emergence and spread of community-acquired AMR infections that can put more people at risk and make it more difficult to identify, contain, and threaten the progress made in protecting hospital patients.

Place

AMR was determined as one of the greatest health threats of our time. Around the world, including in the United States of America, people are dying due to the emergence, spread, and uncontrolled infections of organisms resistant to most antibiotics. The CDC categorized 18 AMR microorganisms as urgent, serious, and concerning. As a result of overtreatment with antibiotics is the occurrence of *C. difficile*, which has an estimated number of cases of 223,900 and deaths of 12,800. According to the WHO (2021), the emergence and spread of AMR are alarming and rapidly spreading, and thus also termed “superbug.”

The common cause of hospital-acquired infections (HAI) is the failure of healthcare workers to practice hand hygiene and poor and unsterile technique in placing foleys and catheters (Rodziewicz et al., 2021). These HAI can be misdiagnosed when samples are improperly handled in the clinical laboratory. Rodziewicz et al. (2021) also mentioned that the common misdiagnosed infections are acute pyelonephritis, appendicitis, cellulitis, osteomyelitis, pneumonia, and urinary tract infection (UTI). The bacterial threats that are mentioned by the CDC (2019) are assessed based on clinical impact on the patients, the number of incidences, how quickly the organism is transmitted

from one person to another, whether effective antibiotics are available, whether there are barriers for prevention and control, and the economic impact on AMR infection.

Atif et al. (2021) revealed that physicians prescribe broad-spectrum antibiotics as empiric therapy. The practice of empiric prescribing leads to inappropriate antibiotic use and, subsequently, to antibiotic resistance. Moreover, Atif et al. (2021) stated that doctors prescribed antibiotics to almost all hospitalized patients as a prophylactic measure to counteract nosocomial infections. Nair et al. (2019) also revealed that doctors prescribe antibiotics to avoid superinfections.

Mechanism of Resistance of Antimicrobial Resistant Microorganisms

The mechanism of resistance is driven by a combination of microorganisms' exposure to antibiotics, the spread of resistance from the organisms, and the constant presence of the resistance in the environment or patients (Berkowitz, 2016; Locke, 2013). Infections are untreatable when bacteria and fungi carry the resistant genes that make antibiotics ineffective for treatment (Berkowitz, 2016). The creation of resistance strains continues to spread when the resistant genetic information is passed from one bacterium to another through mobile genetic processes (Forbes et al., 1998). Jorgensen et al. (2015) explain how bacteria and fungi evade antibiotics: they restrict access to its cell wall, destroy the antibiotic with bacterial enzymes, change its target site for the specific drug, and remove antibiotics using cellular pumps. The two most common broad-spectrum antibiotics used for immediate infections are cephalosporins and carbapenems, a β-lactam class of antibiotics that destroys bacteria by binding with bacterial protein to prevent cell wall formation (Jorgensen et al., 2015).

However, some bacteria, such as *Enterobacterales*, produce toxic enzymes called extended-spectrum beta-lactamase (ESBL), which breaks β-lactam antibiotics. Carbapenem antibiotics destroy ESBL-producing bacteria when second-generation cephalosporins antibiotics are rendered useless. In addition, carbapenem-resistant strains are also rising and destroying antibiotics (Jorgensen et al., 2015; Kettani Halabi et al., 2021). Consequently, physicians are losing antibiotic options to treat patients with complicated infections. There are four known Carbapenemase resistant enzymes in Carbapenemase resistant *enterobacterales* (CRE); these are *K. pneumoniae* carbapenemase (KPC), Oxacillanase-48 (OXA-48), New Delhi Metallo-beta-lactamase (NDM), Verona integron-encoded Metallo-beta lactamase (VIM) (Jorgensen et al., 2015; Tille, 2016).

Concept of the Creation of Antimicrobial Resistance

The use of secondary and third-line antibiotic treatment for multidrug resistant microorganisms is unreliable and can potentially harm patients due to the side effects of antibiotics, such as organ failure, and would prolong care and recovery. Eventually, all treatment options are exhausted. Consequently, antibiotics are not the only way of controlling the spread of AMR and treatment, but containment and other preventive methods, such as accurately diagnosing patients by producing fast and accurate laboratory results.

According to Shebl & Mosaad (2019) and Zhi-wen et al. (2015), the slow identification of bacterial agents in patients with critical infections leads to prescribing broad-spectrum antibiotics and their overuse. They also mentioned that the prescribing

dilemma of resistant organisms to all available antibiotic agents would only be susceptible to more toxic, older types of antibiotics, which leaves physicians with less effective treatment alternatives.

Transmission of Antimicrobial Resistance

The CDC (2019) states that most AMR microorganism transmission occurs from person to person in the hospital from other infected patients via caregivers or by using medical devices such as catheters that are pathways for bacteria to get inside the body. MDRO organisms can thrive on bedrails, sinks, and toilets and can be a source of infection for hospitalized individuals who are mostly immunocompromised (CDC, 2019). Abera et al. (2021) mentioned that hospitalization further exposed patients to infections through contamination from the healthcare environment, using medical devices (e.g., stethoscopes, blood pressure cuffs), hospital gowns, bed rails, bed linens, bedpans, and urinals. Also, Abera et al. (2021) stated that risk factors associated with the spread of AMR are a history of antibiotic use, concurrent or recurrent infections, longer hospitalization duration, catheterization and surgery, and immunosuppression as a result of a certain type of diseases such as HIV, cancer, and diabetes. Delivery and transfer of known AMR-infected patients and travel are also ways for the AMR bacteria to be spread to other patients in different medical facilities in the U.S. and other countries through international travel.

Common Antimicrobial Resistant Microorganisms in Hospitals

According to the CDC (2019), the organisms causing the most health burden in hospitals are Carbapenem-resistant *Acinetobacter baumanii* (CRAB), Carbapenem-

resistant *Enterobacterales* (CRE), *Candida auris*, ESBL-producing *Enterobacterales*, Methicillin-resistant *Staphylococcus aureus* (MRSA), multidrug resistant *Neisseria gonorrhoeae*, *Pseudomonas aeruginosa*, and Vancomycin-resistant *Enterococcus*. The stated antibiotic-resistant microorganisms are the focus of the study on AMR cases in a Florida hospital.

Carbapenem Resistant *Acinetobacter* (CRA)

This bacterium is common in hospitalized patients in the intensive care unit, where critical patients are managed, leading to severe infection in immunosuppressed patients (Rodziewicz et al., 2021). CRA can survive on surfaces for long, contaminating equipment and surfaces in health facilities. Carbapenemase enzymes are produced by *Acinetobacter*, making them more resistant to antibiotics and difficult to treat. Infection control measures and clinical surface disinfection are needed to control the spread of CRA (Lv et al., 2019). The estimated number of hospitalized patients due to CRA infection was 8,500 in 2017, with an estimated death of 700 and an attributable healthcare cost of two hundred and eighty-one million dollars (CDC, 2019).

Candida Auris

The yeast is an emerging resistant yeast first isolated in Asia in 2009. Outbreaks from healthcare facilities are easily spread to hospitalized patients. Some individuals can carry it without causing the infection, but they spread the resistant yeast to vulnerable and immunocompromised patients. The yeast is difficult to identify and is commonly misidentified as other species of *Candida* (CDC, 2019b). The development of real-time

PCR methods aids in accurately and rapidly identifying *C. auris*. There were at least 323 cases of *C. auris* in the U.S. in 2018 (CDC, 2019).

Carbapenem-resistant *Enterobacterales* (CRE)

Patients at risk of getting infected with CRE take long courses of antibiotics, and those requiring medical devices. According to the CDC (2019), CRE is a major concern in healthcare because it leaves fewer effective antibiotics and fewer toxic options for patients. The two most common resistant bacteria in the *Enterobacterales* group are *Escherichia coli* (EC) and *Klebsiella pneumoniae* (KP). According to Rodziewicz et al. (2021), EC is the most common cause of UTI, and KP causes the most pneumonia, UTI, wound infection, and meningitis in hospitalized patients. In 2017, 13,100 cases of CRE were estimated in hospitalized patients in the U.S., with 1,100 deaths and expenditure of a hundred-thirty million dollars (CDC, 2019; Rodziewicz et al., 2021).

C. difficile

This organism is rarely resistant to antibiotics; however, infections with *C. difficile* are due to taking antibiotics for other diseases, manifesting in life-threatening diarrhea (CDC, 2019; Rodziewicz et al., 2021). It is considered the most common healthcare-associated infection (HAI), and the most severe cases are seen in adult patients (CDC, 2019). For example, antibiotic fluoroquinolones can disrupt the balance of microorganisms in the gut, creating a *C. difficile* strain, ribotype 027, that causes serious gastrointestinal infections. Therefore, the most important strategy to decrease *C. difficile* infection is to discourage the overuse of antibiotics. Two hundred twenty-three thousand

nine hundred estimated cases of *difficile* infection were seen in hospitalized patients, with 12,800 deaths, with an estimated cost of one billion dollars (CDC, 2019).

***Neisseria gonorrhoeae*.**

It is an emerging resistant organism with only ceftriaxone as the last recommended treatment. A sexually transmitted disease (STD) can lead to ectopic pregnancies and infertility. Also, having gonorrhea increases the risk of getting infected or transmitting HIV, and it can cause neurological and cardiovascular problems when the disease spreads in the blood (CDC, 2017; CDC, 2019; Springer & Salen, 2021). Routine screening, timely diagnosis, and prompt treatment are the ways to control drug-resistant *N. gonorrhea* effectively. The CDC (2019) reported 550,00 estimated drug-resistant *N. gonorrhea*, with 1.14 million infections per year. The annual discounted lifetime direct medical cost is 133.4 million dollars.

Vancomycin-resistant *Enterococcus* (VRE)

It is a common healthcare-associated infection (HAI) affecting the urinary tract, bloodstream, and surgical sites (Levitus et al., 2021). Thirty percent of *Enterococcus* HAI are Vancomycin-resistant. Patients admitted to intensive care units (ICU), long-term care hospitals, and those undergoing cancer therapy and organ transplants are most at risk for VRE (CDC, 2019). In 2017, the estimated number of cases of VRE in U.S. hospitals was 54,500, with 5,400 deaths, and the attributable healthcare cost was 539 million dollars (CDC, 2019). *Enterococcus* species have become one of the leading causes of nosocomial or hospital-acquired infection. Significant rates of Vancomycin-resistant *enterococcus* were identified as high in children with a history of chronic illness and

those who underwent invasive treatment procedures (Abera et al., 2021; Levitus et al., 2021).

Pseudomonas Aeruginosa

Multidrug resistant *P. aeruginosa* is causing many types of HAI, including urinary tract infection (UTI), pneumonia, bloodstream infection or septicemia, and surgical site infection (SSI). It occurs in hospitalized patients with compromised immunity, such as patients with chronic lung disease. It is multidrug resistant since it is resistant to almost all antibiotics, including Carbapenem drugs (Pang et al., 2019). The CDC (2019) reported estimated cases of multidrug resistant *P. aeruginosa* at 32,600, deaths of 2.700, and healthcare costs of 767 million dollars.

Methicillin-resistant *Staphylococcus Aureus* (MRSA)

A very common organism that is causing HAI. MRSA can lead to difficult to treat infection due to its resistance to many types of antibiotics. The CDC has seen a significant change in infection rate due to infection control measures, including screening patients upon admission, tracking MRSA infection, and emphasizing hand hygiene (CDC, 2019; Siddiqui & Koirala, 2021).

Importance of Laboratory Diagnostic Tests

Transport and storage of samples should follow the clinical laboratory standard institute (CLSI); for example, urine samples for culture and sensitivity testing are recommended to test urine within two hours from collection. If testing within two hours is impossible, the urine sample should be stored at 4^{o}C and analyzed for 24 hours (Dolscheid-Pommerich et al., 2016). Another critical aspect of lab testing is the time

interval from sample collection to analysis. Sample stability during storage is also the focus of the preanalytical stage of sample handling (Dolscheid-Pommerich et al., 2016). For the appropriate treatment of antibiotics to patients by providers, prompt and accurate results from the laboratory play a huge part in the process. The laboratory performs a crucial role in identifying resistant organisms and providing essential data and correct antibiotics for the treatment of patients. Continuous improvement in laboratory automation has become part of the standard examination of samples submitted for AMR organism testing. According to Dolsnscheid-Pommerich et al. (2016), preanalytic specimen requirements must be enforced to avoid false laboratory results and interpretations.

Hospital workers' commitment and the hospital administrations' support to successfully adopt and implement stewardship in the fight against AMR in the U.S. (Tahir, 2021). Reliable diagnostics tools are important for identifying resistant organisms, and according to Wolk (2021), consistency in reporting specimen stains and culture results is necessary to diagnose and treat patients with severe infections quickly. It is also important for infection control to prevent the spread of an emerging infectious agent. The CDC (2019) mentioned that diagnostic tools are as important as fighting and destroying AMR bacteria with antibiotics.

The study of Mponponsuo et al. (2021) revealed that using rapid molecular tests resulted in cost-saving compared to the conventional culture tests, as the length of stay and cost per day of hospitalization was lowered because laboratory results are released quicker, and immediate treatments were given. Moreover, quality diagnostic tools were

essential for the accurate and rapid identification of resistant organisms, to reduce unnecessary use of antibiotics, or were given appropriately if the patient truly needs them. The diagnostics tool also supports public health tracking of resistant microorganism threats by reporting infection trends. Overall, the tools provide information to laboratorians, providers, and epidemiologists to choose the best treatment for AMR organisms, infection control, and prevention.

Medical and Laboratory Errors

Rodziewicz et al. (2021) stated that approximately 400,000 hospitalized patients experience preventable harm each year. Medical errors account for over $4 billion annually and cost approximately $20 billion annually. Approximately 100,000 people die each year in hospitals and clinics. Documented medical errors relevant to AMR cases include diagnostics, medication, infections, systems failures, and healthcare technology. Also, according to Rodziewicz et al. (2021), missed diagnosis and treatment errors are common in outpatient settings, and surgical errors are common in hospitals. The overall misdiagnosis rate is approximately 10% to 15%. The three stages of laboratory sample processing include preanalytical, analytical, and post-analytical. Evidence shows that most laboratory errors happen during the preanalytical stage; Al Saleem & Al-Surimi (2016) stated that preanalytic errors include incorrect test orders, mislabeling of samples, and the wrong sample collected to the overall delay in sample processing and reporting results. This study will highlight missed diagnoses of AMR and treatment errors due to the delays in the laboratory processing of samples. The antibiotics for treatment are selected based on culture and sensitivity results; however, the lack of trust by doctors in

the timely laboratory results compels prescribing broad-spectrum antibiotics to patients (Atif et al., 2021). According to Al Saleem & Al-Surimi (2016), preventable medical errors adversely affect patient safety and waste resources. Laboratory errors as a patient safety issue is a goal of the Joint Commission (2021); it is their first international patient safety goal (IPSG).

Methods for the Detection of Antimicrobial Resistant Microorganisms

Antimicrobial sensitivity testing (AST)

AST uses bacterial cultures to determine whether an organism is sensitive or resistant to a group of antibiotics. An organism can be regarded as multidrug resistant or pan-resistant through AST testing on antibiotics used by a microbiology laboratory. The Kirby-Bauer disk diffusion is a method of testing the antibiotic sensitivity of microorganisms. The interpretation of resistance is based on the Clinical Laboratory Standard Institute (CLSI) guideline (CDC, 2019; Shebl & Mosaad, 2019; Zhi-wen et al., 2015).

Biochemical Testing

Biochemical testing is used to classify bacteria using different proteins or sugars. Microorganisms are identified through reactions observed from the chemical components. Examples of reactions are bacterial motility, turbidity and cloudiness, and the presence of bubbles (Jorgensen et al., 2015).

Culture

A laboratory procedure that allows the cultivation of bacteria to identify resistance. The routine culture method is used for growing the organisms from the

samples. Culture media are incubated for 24 hours at 37^{o}C, and if there is no growth, the culture plates are reincubated for a total of 48 hours (Fahim, 2021). Microorganisms isolated are recognized by their colony morphology, gram stain, and biochemical tests (Fahim, 2021; Jacobs et al., 2019)

Matrix-Assisted Laser Desorption Ionization-time of Flight (Maldi-Tof) Mass spectrometry

Mald-Tof is a rapid and sensitive way of microbe identification. It is economical in cost and labor (Singhal et al., 2015).

Molecular Diagnostic Tests

Molecular testing offers faster pathogen identification and antibiotic sensitivity results than conventional culture identification, and the cost-effectiveness of the rapid molecular diagnostics test for MDRO compared with conventional testing was determined as the test saves microbiology time and resources (Mponponsuo et al., 2021). Nucleic Acid Amplification (NAAT) uses DNA and RNA-specific targets to detect multidrug-resistant organisms. The Whole Genome Sequencing (WGS) identifies the genetic sequence of a pathogenic organism related to a known database. WGS provides a detailed DNA profile of the bacteria and identifies resistant genes.

Process and Timeline for Culture and Sensitivity Testing

1. Specimen collection and sample set-up for AMR testing with blood samples.
    1.1. Ten milliliters (ml) of blood sample are collected aseptically and added to a culture bottle with 25 ml brain heart infusion (BHI) broth.
    1.2. Deliver to the laboratory within four hours.

1.3. Receive at the sample receiving area of the laboratory.

1.4. Deliver to the microbiology department of the laboratory.

1.4.1. Culture bottles incubated for a total of five days.

1.4.2. Positive blood culture bottle(s) are re-cultured using plated culture media.

1.4.2.1. Gram stain results reported to providers.

1.4.2.2. Culture plates incubated for 18 to 24 hours at 37ºC.

1.4.2.3. Bacterial colonies are identified and tested for biochemical reactions.

1.4.2.4. Preliminary results reported, and cultures reincubated for another 24 hours.

1.4.3. Antibiotic sensitivity testing (AST) procedures are set-up.

1.4.3.1. The AST is incubated for 18 to 24 hours at 37ºC.

1.4.3.2. AST results read, and final results reported.

2. Specimen collection and sample set-up for AMR testing with urine samples

2.1. Ten ml of mid-stream catch urine is voided into a sterile cup.

2.2. Deliver to the laboratory within two hours of collection.

2.3. Receive at the sample receiving area of the laboratory and deliver to the microbiology department.

2.4. Inoculated on culture media using one microliter (µl) inoculating loop.

2.5. The culture is incubated for 18 to 24 hours at 37ºC.

2.6. Colony morphology and biochemical testing are used to identify AMR microorganisms.

2.7. Preliminary results reported. Culture reincubated for another 24 hours.

2.8. AST is set-up and incubated for 18 to 24 hours at 37^{o}C.

2.9. AST results are read, and final results are reported to providers.

3. Specimen collection and set-up of other samples (e.g., sputum, wounds, fluids, tissues, biopsies).

3.1. Deliver to the laboratory within four hours of collection.

3.2. Receive at the receiving area of the laboratory.

3.3. Deliver to the microbiology department.

3.4. Samples plated into culture media.

3.5. Samples gram stained and read under the microscope and reported.

3.6. Culture media with inoculated samples are incubated for 18 to 24 hours at 37^{o}C.

3.7. Culture is read after 24 hours, and biochemical tests are done.

3.8. Preliminary results reported. Reincubated for another 24 hours.

3.9. AST set-up and incubated for 24 hours.

3.10. AST read and final results reported.

The overall processing of samples delivered to the laboratory would depend on the testing site and how specimen processing and testing were performed as the specimen arrives. Whenever multiple specimens were delivered to the laboratory simultaneously, priority must be given to critical samples such as cerebrospinal fluid (CSF), blood, fluids, and tissues. Some microbiology laboratories also practice batch set-up of samples. For a typical culture, processing samples from the delivery to the laboratory to the time the culture and AST results are completed will take up to 72 hours (Tille, 2013).

Antimicrobial sensitivity testing can be performed in several ways, such as using the antibiotic disc, an antibiotic strip, and concentrated liquid antibiotic infiltrated into plastic cards. Kirby Bauer disk diffusion uses 3 to 5 pure bacterial colonies homogenized in 5 ml of normal saline. The turbidity of the suspension is adjusted and comparable to 0.5 McFarland standard. The suspension was swabbed evenly onto a Mueller Hinton agar and allowed to dry for 5 minutes; then, antibiotic discs are applied on the surface of the culture media. The diameter of the zone of inhibition is measured using a caliper and interpreted as sensitive, resistant, and intermediate based on the CLSI. Quality control parameters must meet the CLSI guidelines. The quality of the media must be checked for sterility by incubating at 37^{o}C for 24 hours; the gram stain and other biochemical reagents are checked with known standard strains of organisms such as the *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 25923.

Tracking Antimicrobial Resistance Data

The laboratory information management system (LIMS) supports data quality management activities to monitor turnaround time, the number of samples tested, workflow, and the number of significant results, including antibiotic-resistant microorganisms (Turner et al., 2021). The CDC used electronic health data to gather national estimates from U.S. acute-care hospitals. The use of databases to determine the number of cases of AMR in hospitals quantitatively. The CDC uses health-related germs to assess the threat level of microorganisms to humans. Healthcare facilities track AMR through information technology (IT) systems and instrument manufacturers' database tracking. In 2018 the CDC antimicrobial-resistant (AR) laboratory network detected

resistant organisms every four hours, and with an estimated number of 160,000 and 2,238 alerts, the public needs awareness. Also, almost 13,000 organisms were detected in healthcare facilities. Dolscheid-Pommerich et al. (2016) stated that hospital and laboratory records are valuable data sources and studies conducted for one year.

An example of laboratory data is Gram-negative enteric organisms, common infectious agents resistant to multiple antibiotics. Moreover, rapid molecular testing combined with electronic medical records (EMR) may advance the ability to identify MDRO cases and outbreaks rapidly and support quality improvement plans (Wolk, 2021). Microbiology laboratory results are used to identify infections in hospitalized patients, using a broader group of infection types from sterile and non-sterile sources such as blood, urine, and skin. The database system was a simple way of coding for antibiotic resistance compared to methods that utilized the International Classification of Diseases (ICD), which uses diagnosis codes or death certificate dates that likely under-report true antimicrobial resistance cases and deaths.

Managing the Problem on Antimicrobial Resistance

The U.S. has core actions to prepare for the emergence of resistant organisms worldwide: to reduce the spread of multidrug resistant (MDR) bacteria by preventing the spread of the disease. To appropriately use and reduce unnecessary use of antibiotics. To improve vaccine access and develop diagnostics technologists for quicker AR detection, prevention, and treatment. To improve data collection and data sharing on AMR cases. The CDC (2019) stated that U.S. hospital prevention programs had succeeded, as seen in the drop in the cases of AMR infection and deaths to 27% and 30%, respectively, from

2012 to 2017. However, the improvement would only be temporary when the vigilance and actions against AMR are not sustained. Tahir (2021) stated that the clinical microbiology laboratory plays a cardinal role in guiding the choice of antimicrobials to support successful patient outcomes and minimize the adverse impacts on healthcare costs. As mentioned during the State of the World's Antibiotics 2015, the overuse of antibiotics drives the evolution of antibiotic resistance. There is a direct relationship between the emergence and spread of antibiotic resistance and the use of antibiotics (Gelband et al., 2015; Tahir, 2021).

The threat of AMR is addressed by prevention of getting infected, early or rapid detection, effective antibiotics to slow the development of resistance, stop the spread of resistance, and improve antibiotic use and infection prevention in all settings (CDC, 2021c). Dolscheid-Pommerich et al. (2016) mentioned that preventing AMR is easier than treating the infection; therefore, it is always recommended to disinfect everything, and antibiotics should only be prescribed as necessary and sufficient duration treatment. Vaccination is an effective tool in preventing AMR infections. Known healthcare strategies to control the spread of AMR are to prevent device-related infections such as central line and urinary catheters to control the spread of AMR to other hospitals, early and aggressive detection, and appropriate use of antibiotics. To prevent the hospitalization of people, community strategies must also be done through vaccination, routine screening for known resistant organisms such as tuberculosis (TB) and gonorrhea, safe handling of food, and the practice of safe sex.

Moreover, healthcare workers must screen at-risk patients and alert other medical facilities when moving an AMR carrier patient. Health education to all for infection prevention and to control the spread of deadly microorganisms. Antibiotic prescribers should appropriately prescribe antibiotics and only be given to positive patients for harmful bacteria. To not prescribe antibiotics to patients with viral infections. The laboratory must be prompt in testing samples for accurate diagnosis and for physicians to prescribe specific antibiotics and not rely on broad-spectrum antibiotics that are most harmful to beneficial bacteria and trigger antibiotic resistance. Also, to report AMR cases isolated and send unusual microorganisms to the health department to identify and determine the appropriate treatment of infected patients.

Antimicrobial Resistance Testing Strengths and Weaknesses

Strengths

Several rapid tests have been developed over the past two decades, which reduce the turnaround time for the identification and sensitivity testing of resistant organisms compared to the traditional culture method (Tahir, 2021). The turnaround time of rapid diagnostic assays is between 0.2 to 2 hours. The current assays for detecting resistance markers include peptide nucleic acid fluorescent in situ hybridization, MALDI-TOF, real-time PCR, blood culture nucleic acid microarray, and multiplex nucleic acid amplification test. Also, laboratories must establish an alert system that promptly communicates high-risk infections to providers (Tahir, 2021).

The U.S. government is piloting activities to combat AMR domestically and internationally in coordination with other health sectors, public and private, from the

federal, state, and local health agencies. The U.S. Congress appropriated one hundred and sixty million dollars for AMR initiatives. The CDC allocated Fifty-nine state and local health departments at least three hundred million dollars to detect and prevent antibiotic-resistant microorganism threats. The CDC also invested millions in diagnostics, therapeutics, and innovations for ninety-six U.S. healthcare facilities.

Weaknesses

The CDC (2019) stated that the laboratory has gaps that allow AMR to spread as resistant organisms are constantly emerging. Laboratories in the U.S. need to implement new technologists and specialized strategies to improve AMR's rapid detection and reporting to providers. Moreover, according to the CDC (2019), delayed antibiotic therapy caused by the delay in the delivery of laboratory testing results increases the mortality rates of patients. Complications of multidrug resistant infection increase healthcare costs and morbidity rates (Dolscheid-Pommerich et al. 2016). It is strikingly endangering the U.S. healthcare systems creating a negative economic effect and therapeutic challenge to clinicians. According to Dolscheid-Pommerich et al. (2016), empirical antibiotics are often prescribed to patients before the culture and antibiogram results are released. Also, Turner et al. (2021) stated that barriers to reliable laboratory specimen processing information, such as the determination and documentation of the time the samples are received, set-up on culture media, identified, and resulted, are the lack of information technology (IT) and the high cost of commercial laboratory information management systems.

Remains to be Studied on Antimicrobial Resistance

The CDC (2019) recommended that laboratories expand their capabilities in detecting and identifying new and emerging AMR for containment and prevention efforts. Fahim (2021) stated that continuous monitoring of laboratory processes on the inevitable catastrophe threatening patients' lives and conducting more studies to have a complete picture of cases of antibiotic resistance before reaching a deadlock or uncontrolled AMR infections in patients. An example of a laboratory process that Dolscheid-Pommerich et al. (2016) use is a urine sample sitting for two hours and four hours without preservatives showing no significant difference when comparing results. However, if the laboratory does not follow the four-hour process, culture and AST results and patient treatment will be delayed. Also, blood culture samples at the specimen receiving area are not received and transported immediately to the microbiology laboratory to start incubating bacteria that cause sepsis or blood infection. Several laboratory processes have been ignored, resulting in patient complications on antibiotic resistance.

Study Design on Antimicrobial Resistance

A retrospective study was conducted on the cases of AMR for a year from November 2019 to November 2020. To determine instances that a sample for bacterial culture was delayed, from the collection of the sample to the transport to the laboratory, to the receiving and logging of the sample in the laboratory, to the time the sample was set-up for bacteriological culture, to the time when there was a delay in reading the culture and in the identification of the pathogenic organism, for the delay in setting up for

antibiotic sensitivity testing, and the overall delay in reporting the final results to the physician.

The goal was to understand the association of the naturally occurring variables, which cannot be manipulated. The type of quantitative study applied as the dependent variable was the occurrence or presence of antibiotic-resistant organisms in samples collected from patients admitted to the hospital. Burkholder et al. (2016) stated that correlational research could make predictions between two variables. Knowing the score of one variable can be used to predict the score of the other variables, and predictions are computed using statistical data.

Summary and Conclusion

Delay in diagnosis is the most common medical error. Most errors are due to system or process failure that needs to be changed for system improvement. The delay in reporting resistant organisms is a medical error in which the determination of the time in sample processing can be used as a means for positive social change. Part of the solution to the problem of AMR is to improve the processes in the clinical laboratory and create an improvement for patient AMR diagnosis and treatment. To keep a culture recognizing erroneous processes to support the fight against antimicrobial resistance.

The Joint Commission has introduced some patient safety goals that apply to the control of AMR cases, including correctly identifying the patient using at least two ways to improve the processing of samples and get results quickly to healthcare providers. To achieve quality improvement in controlling laboratory errors, as mentioned by Al Saleem & Al-Surimi (2016), emphasizes the importance of monitoring workflow and evaluation

of compliance by the laboratory personnel and is valuable in avoiding extra work of employees by fixing errors and controlling the indirect cost for the misdiagnosis and mismanagement of patients.

The third chapter on the study of AMR in a Florida hospital presents the research design and methodology. The data on the number of cases of AMR at the UF Health Jacksonville hospital was obtained through a retrospective study for one year, from November 2019 to November 2020. A nonprobability sampling method was used to obtain data for the study, and the study established a correlation with the time and prompt processing of samples for AMR determination. To examine the association between antibiotic-resistant cases and time in processing patient samples for bacterial culture and sensitivity testing. Five sample processes were examined, including the delivery and transport of samples, receiving and sample inoculation, reading of culture growth, testing using automated microbiology, set-up and reading of antibiotic sensitivity results, and the time the final results were verified and reported to clinicians or providers.

Chapter 3: Research Method

Introduction

The study on antimicrobial resistance and laboratory practices was used to examine the association between the time in the transport and delivery of samples, the time in the setting up for culture to grow the bacteria, the time when bacteria are identified, on the time when antibiotic sensitivity testing was done, and the overall time in the reporting of final results. Chapter 3 explained the research design used for the study to support the answers to the research questions. Random sampling was used to obtain the data. The target population and sample size were determined using a calculation tool to justify the effect size, alpha, and power levels. Constraints of time and resources were also explained, consistent with the research design choice.

The process of gaining access to the research data was requested with legal and ethical considerations. Ethical procedures for the study were thoroughly explained in writing to the hospital's IRB, where the data were obtained, and Walden University. When approval was received for data gathering, the laboratory provided the data. The data was then analyzed using the IBM SPSS version 28.0 software to test the hypothesis and answer the research questions.

Research Design and Rationale

The laboratory's research study on antimicrobial resistance and sample processes has five independent variables to determine the association between the number of known cases. The independent variables were (1) the time when the samples for bacterial culture are transported or delivered to the laboratory, (2) the time in setting up samples for

growth in culture, (3) the time in identifying bacteria using conventional culture, (4) the time in the setting up and reading antibiotic sensitivity testing, (5) the time in the reporting and charting bacterial culture results in the patient's chart for physicians to review and acknowledge as the basis for antibiotic prescribing to patients. The study's dependent variable was the cases of AMR in the Florida hospital.

The quantitative research study was performed on bacteriological culture samples received in the laboratory from November 2019 to November 2020. The study on AMR and laboratory processes was a retrospective study on samples submitted for culture to identify organisms resistant to antibiotics for the association between the cases of antimicrobial resistance in a Florida hospital and the laboratory's practices in processing samples and reporting results to antibiotic prescribers. The retrospective cohort study was taken from a large population, the prevalence of an outcome of interest was estimated, and 246 samples were tested.

The research on AMR and lab practices generally gather data, which was relatively inexpensive and only took a little time to conduct, as mentioned by Ader & Mellenbergh (1999), and offers an advantage in assessing the cases of previously known AMR infection by focusing on a period in which the data obtained were presumed to be significant. Moreover, the study aimed to establish positive social change to control processing delays of samples in the laboratory and help solve the problem of unnecessary antibiotic treatment by physicians.

Research Methodology

The target population for the research study on the cases of AMR in a Florida hospital and its association with laboratory practices were hospital admitted patients with samples submitted for bacterial culture and antimicrobial sensitivity testing. Included in the study were patient samples with positive cultures. The age definitions of the patients were adults 18 years old and above and older pediatric patients 10 years old to 17 years old. Patients 10 years old and below and negative cultures were excluded from the study.

According to Andrade (2020), a sample larger than the necessary numbers better represents the population and provides more accurate results. Therefore, the study's year samples were sufficient for the research study to display a statistically significant outcome. A smaller sample size than necessary would have insufficient statistical power to answer the research questions and be considered unethical. The sample size calculation requires assumptions on the expected means and standard deviations. The estimated sample size for the study was 246 based on a 95% confidence level, a 5% margin of error, and an 80% population proportion. 95% confidence interval and 80% population proportion were chosen because each sample represents the study population, and all the samples submitted for culture were included in the study. The margin of error was 5% because the time stamped on the sample processing was the actual time the samples were handled by laboratory workers.

The formula used for sample size computation was $n = z2 * p * (1 - p) / e2$, where the z-score is 1.96 for a confidence level (α) of 95%, the percentage or representative of the target population, *p* for the sample proportion of 80% which is expressed as a

decimal, and *e* for the margin of errors, which is also expressed as a decimal and indicates the extent of the output of the sample population, reflective of the overall population. Manual computation for the sample size of the study:

N = 1.96(2) x .80 x (1-.80)/.05(2)
= 3.84 x .80 x 0.2/0.0025
= 0.6144/0.0025
= 245.76 or 246

Sampling Procedure

The sampling method for the research study on AMR and laboratory practices was probability sampling to obtain data to address the research question. Choosing the cases from the Florida hospital represent cases from other hospitals in the United States or collectively represent the population. Also, with probability sampling, the sample size was large enough for representativeness and focused on the breadth of information generated before the study was started *(Laerd* Statistics, n.d.). AMR has been an ongoing problem in healthcare facilities, causing problems due to the over-treatment of broad-spectrum antibiotics. The study aided in the determination of ways that can improve antibiotic prescriptions, in which specimen handled by the clinical laboratory was assessed to determine whether it affects the cases of AMR. The data from the probability sampling were numerical, applying a mathematical formula to generate the sample size.

The specific sampling subcategory used for the research study was stratified random sampling. Only hospitalized adults and older pediatric individuals were included in the study. According to *Laerd* Statistics (n.d.), there is an equal chance of selecting a unit or patient from a particular group or stratum with stratified random sampling. The strength of stratified random sampling is that it reduces the potential for human bias and

provides a high representation of the studied population. For example, in the research study on AMR, all samples submitted from inpatients were included regardless of the patient's gender, the diagnosis, and the hospital unit where the patient was admitted.

Moreover, because stratified random sampling was a probabilistic method, the statistical conclusion from the collected data was considered valid. Stratified random sampling also provides greater precision than simple random sampling and uses a smaller sample, which saves time and money, and it was viewed as a superior method because of the potential to be evenly spread over the population. The limitations or weaknesses of the sampling method were that it could only be carried out if a complete list of cases was available. If there was a limited sample gathered, this could mean increasing the required sample size, which would mean increased costs and time to conduct the research. Furthermore, even if the cases of AMR were available, gaining access to the data was challenging because it was protected by privacy policies requiring a lengthy process to attain permission. However, as stated in *Laerd* Statistics (n.d.), stratified random sampling is one of the gold standards in sampling techniques, as samples or patients have an equal chance of being selected.

The samples or data for the study were acquired from the hospital's LIS, Epic Beaker. The patient must first be registered for information that includes the patient's name and demographics. The collection date and time were stamped on the patient's record using the positive patient identification approach (PPID), a combination of computer systems and hardware devices (Positive Patient Identification | Zebra, n.d.).

The laboratory's LIS accurately documents essential patient information throughout the entire care journey (Labcompare, 2013). The laboratory's LIS tracks each sample throughout the laboratory, from when the samples were received until the results were finalized and reported. The LIS that the Florida hospital uses is the Epic system, a healthcare software company that held 54% of patients in the U.S. and 2.5% worldwide in 2015 (Glaze, 2015). The time orders were placed to the time samples were collected and transported to the laboratory, the time samples were received in the laboratory, the time the samples were set up and incubated for the growth of the microorganisms, the time the culture was read, and the organisms identified, the time the cultured organisms were set up for AST, to the time the ASTs read were all stamped on Epic Beaker's specimen tracking system. The tracking time of cultures was all saved on an Excel spreadsheet and statistically analyzed on SPSS version 28 to determine whether processing time is associated with AMR cases.

Data Collection for Antimicrobial Resistant Cultures

Data collection is an important research process in which information is gathered and analyzed to offer a solution, evaluate the test results, answer the research questions, and eliminate the assumptions of the hypothesis testing. The two types of data collection are primary and secondary data collection. Primary data collection collects original data or gathers raw data from the source. Secondary data is gathering second-hand data or collecting existing data at no expense and it is easier to collect.

Secondary data collection was conducted for the quantitative research study on antimicrobial resistance associated with laboratory processes. The existing data from

November 2019 to November 2020 was obtained online through the laboratory's LIS. According to Johnston (2017), the advantage of using secondary data was that the information was easily accessible, and the accuracy of the data was very high, which strengthened the quality of the information for the study. However, some of the data and the evaluation of results were difficult to understand. In the hospital setting, the transfer of health data across stakeholders of the healthcare system is known as health information exchange (HIE) to improve the overall health outcome and quality of care (Sylvia, 2018). Secondary data from HIE expedites the research process and provides information necessary for research purposes. The LIS, where the data for the study was taken, was part of the health system's electronic health record (EHR). It is a longitudinal electronic record of a patient's health data generated from multiple hospital encounters (Sylvia, 2018).

The data on the research study on AMR at the hospital and laboratory processes in handling samples were obtained from the UF Health Jacksonville EHR. In order to get access to the data, approval from the hospital's IRB and the laboratory's administrator was obtained. When permission was received, access to the data was granted, and data collection commenced. The process starts with logging in to the Epic beaker, the hospital's LIS, to open the Epic dashboards and menus for generating data. The tracking time of the samples with the date and time transported and received at the laboratory, set-up on culture media, organism identified, antibiotics tested, and results reported were all documented and saved into an Excel spreadsheet.

Table 3

Sample Tracking Sheet for the Study

Sample No.	Culture Order	Sample Collection	Sample Received	Culture starts	ID Result	AST Read	Final Result
1							
2							
3							
4							
5							

Measurement of Variables

The variables for the quantitative research study on AMR and laboratory processes were the cases of AMR in a Florida hospital as the dependent variable. The dependent variable was the outcome or the presumed effect of the independent variables and was also known as the criterion variable in non-experimental and correlational research (Burkholder et al., 2016). The independent variables for the study were the determined time the microbiology culture was ordered, the time the sample is collected, the time the sample was delivered to the laboratory, and the time the sample was set-up for bacterial identification by the conventional culture reading, also the time when antibiotic testing was performed, and the time the AST was read, and the time the order was completed and reported to the provider. According to Burkholder et al. (2016), independent variables were the presumed factors that can cause a change in the studied phenomenon or situation. Independent variables were also the predictor variable commonly used in non-experimental correlational research (Burkholder et al., 2016).

The levels of measurement in the research study on AMR and laboratory processes in a Florida hospital were nominal. According to Burkholder et al. (2016), the level of measurement enables classification of things that share a common attribute. The categorical dichotomous measurement will reflect the multidrug resistant organism isolated from the samples submitted to the laboratory from November 2019 to November 2020. The coding scheme of the variables was 0 for not on time for the delivery of samples and 1 for on time in the delivery of samples to the laboratory.

The independent variables are the steps in handling specimens submitted to the laboratory for bacterial culture. Each step must be accomplished before proceeding to the next step or process in working on a sample. In other words, when the samples were delayed from the start, in the middle of the process, or at the end could all result in the overall delay in reporting results. Any delay in each step was assumed to affect the time the cultures and sensitivity results were reported to the physicians for the prompt treatment of specific antibiotics for the bacteria causing the infection. The dependent variable, the cases of AMR, was determined to have been affected by sample processing time. The effects of the variables could be determined with a retrospective study of samples submitted, processed, and resulted from November 2019 to November 2020.

Table 4

Study Variables and Coding Scheme of the Study.

Study Variables	Variable Nature and Coding Scheme
Independent Variables:	
Time the samples are transported to the laboratory.	Categorical: Dichotomous Coding: 0 – More than 2-4 hrs 1 – Within 2-4 hrs

Time the samples are set-up for culture in the laboratory.	Categorical: Dichotomous Coding: 0 – More than 30 mins 1 – Within 30 mins
Time in the identification of organisms by culture	Categorical: Dichotomous Coding: 0 – More than 24 hrs. 1 – Within 24 hrs
Time in antibiotic sensitivity testing (AST)	Categorical: Dichotomous Coding: 0 – More than 48 hrs 1 – Within 48 hrs
Time in reporting final culture results.	Categorical: Dichotomous Coding: 0 – More than 72 hrs 1 – Within 72 hrs
<u>Dependent Variable:</u> Cases of AMR in a Florida hospital	Categorical: Dichotomous Coding: 0 – Absence of AMR organism 1 – Presence of AMR organism

The software used to analyze the data was the IBM SPSS version 28.0. According to Kremelberg (2010), the IBM SPSS was preferable for entering data and charts and graphs, which was a preference for the research study on AMR and lab processes. Also, IBM SPSS uses syntax, saving time in entering data and making changes to the analyses (Kremelberg, 2010). IBM SPSS is fast in data manipulation and statistical procedures, a third of other nonstatistical programs. It is known to be the world's leading statistical software. SPSS enables users to dig deeper into the data making it a more useful tool than spreadsheets. Also, it is more effective than spreadsheets, standard multi-dimensional tools for analysts, and databases. Moreover, complex patterns and associations make sense when using SPSS, enabling users to make predictions and draw conclusions (SPSS Statistics - Overview, 2021).

Data Screening and Cleaning

An important aspect of a research study was how the data used for the study to cleaned and screened for erroneous data or the process of detecting and editing data that might be erroneous and could cause a confusing statistical analysis. The American Statistical Association recommends that data be a standard part of reporting statistical methods because it is rare to find data-cleaning method statements in some medical publications (Van den Broeck et al., 2005). The research of the number of cases of AMR entailed the use of data from the hospital; in other words, the results taken were from medical procedures and processes; thus, cleaning and screening of the data were appropriate for the study on AMR in the Florida hospital. According to Van den Broeck et al., 2005, data cleaning involves screening, diagnosing, and editing. Screening of data was checked for the lack and excess of data. Outliers and inconsistencies were also checked as unusual patterns in the data. The data was diagnosed for errors and some missing data. To determine whether the data were accurate and reflected the actual result as analyzed by the microbiologist or the time documented by the laboratory assistant receiving the samples.

The last process was editing to check whether the data needed to be corrected, deleted, or left unchanged. With the research study on AMR, the data taken from UF Health LIS were assessed to determine whether the number of cases of resistant microorganisms isolated from sample cultures was accurate. Also, the time shown on specimen tracking reflects when the laboratory receives, set-up for culture, bacterial growth identified, antimicrobial sensitivity tested, and reporting of results. Several ways

of screening data were used for research, first is to check whether the data entry program was validated. Checking of data was through the LIS system and employees' training and competency. Another method of data screening that can be applied to the research study on AMR was browsing quality control (QC) and instrument maintenance records, in which results would not be considered legitimate if the QC results were out of range.

Addressing Missing Data

Some data might be missing from the study for the research on AMR and laboratory specimen processing. According to Kang (2013), missing data reduces statistical probability, wherein the test would reject the null hypothesis when the results were false or incomplete. Also, biases could happen in the estimation of parameters, the sample's representativeness is reduced, and it can complicate the analysis of the study. Overall, if the research study has missing information, the validity of the research will be threatened and lead to invalid conclusions. As Rubin (1975) described, missing data can be missing completely at random (MCAR), wherein the missing data are not related to the specific value that is supposed to be obtained. Another type of missing data is missing at random (MAR), in which the probability of missing data depends on the set of observed responses and is not related to the specific data expected to be obtained. The last type of missing data is missing not at random (MNAR), which is usually problematic, and the only way to obtain an unbiased estimate is to model the missing data; then, the model would be incorporated into a more complex way of estimating missing information.

There are several techniques to handle missing data, which can be achieved by a well-planned research study and careful data collection. To collect the essential data, identify the possible problems that might occur during the data collection, and set a target of acceptable and unacceptable data. Also, the data collection site was monitored as closely in real-time as possible during the study. Data analysis methods were robust to problems caused by missing data and confident that violations of the assumptions produced little bias or distortion to the study's conclusions.

The missing data analysis applied to the study on AMR and laboratory practices was listwise or case deletion, the most common method of handling missing data. Data imputation preserved cases by replacing the missing data encountered during data collection and analyzed to complete the data. Listwise or case deletion was done by omitting the missing data and only analyzed the remaining data. However, according to Kang (2013), listwise deletion is not the right strategy for missing data if the sample is not too large. Therefore, for the research study on AMR in a Florida hospital, the year's worth of data was adequate, even if some data was missing, and the listwise or case deletion technique of handling data was appropriate for the study.

Research Questions

RQ1: Is there an association between the time samples are transported to the laboratory and AMR cases in a Florida hospital?

H_o1: There is no association between the time samples are transported to the laboratory and AMR cases in a Florida hospital.

H_a1: There is an association between the time samples are transported to the laboratory and AMR cases in a Florida hospital.

RQ2: Is there an association between the time samples are set-up for culture in the laboratory and AMR cases in a Florida hospital?

H_o2: There is no association between the time samples are set-up for culture in the laboratory and AMR cases in a Florida hospital.

H_a2: There is an association between the time samples are set-up for culture in the laboratory and AMR cases in a Florida hospital.

RQ3: Is there an association between the time microorganisms are identified in culture and AMR cases in a Florida hospital?

H_o3: There is no association between the time microorganisms are identified in culture and AMR cases in a Florida hospital.

H_a3: There is an association between the time microorganisms are identified in culture and AMR cases in a Florida hospital.

RQ4: Is there an association between the time antibiotic sensitivity testing is reported and AMR cases in a Florida hospital?

H_o4: There is no association between the time antibiotic sensitivity testing is reported and AMR cases in a Florida hospital.

H_a4: There is an association between the time antibiotic sensitivity testing is reported and AMR cases in a Florida hospital.

RQ5: Is there an association between the time the final culture results are reported and AMR cases in a Florida hospital?

H_o5: There is no association between the time the final culture results are reported and AMR cases in a Florida hospital.

H_a5: There is an association between the time the final culture results are reported and AMR cases in a Florida hospital.

RQ6**:** Is there an association between the time of specimen transport, setting up for culture, identification of microorganisms, antibiotic sensitivity test, and the time when culture results are reported and AMR cases in a Florida Hospital?

H_o6: There is no association between the time of specimen transport, setting up for culture, identification of microorganisms, antibiotic sensitivity test, and the time when culture results are reported and AMR cases in a Florida Hospital.

H_a6: There is an association between the time of specimen transport, setting up for culture, identification of microorganisms, antibiotic sensitivity test, and the time when culture results are reported and AMR cases in a Florida Hospital.

Data Analysis Plan

Statistical Tests for the Hypotheses

The statistical test that was used to test the hypothesis was multiple logistic regression (MLR), where two or more variables were used to predict the outcome of a response variable or explain the relationship between multiple independent variables, which serves as predictor variables, and a dependent variable that serves as a criterion variable (Frankfort-Nachmias & Leon-Guerrero, 2017). The outcome variable for the research study on AMR and laboratory processes was the AMR cases in a Florida hospital. The predictor variable was also quantitative: the number of occurrences of delay

in culturing samples for bacterial identification and sensitivity testing resulting in the delay in reporting results. There was more than one predictor variable in the study, and these processes included the time in the delivery of samples to the laboratory, time in receiving and logging of samples, time in setting up the specimen in culture media, time in the identification of resistant organisms from culture, and time in reading antibiotic sensitivity testing.

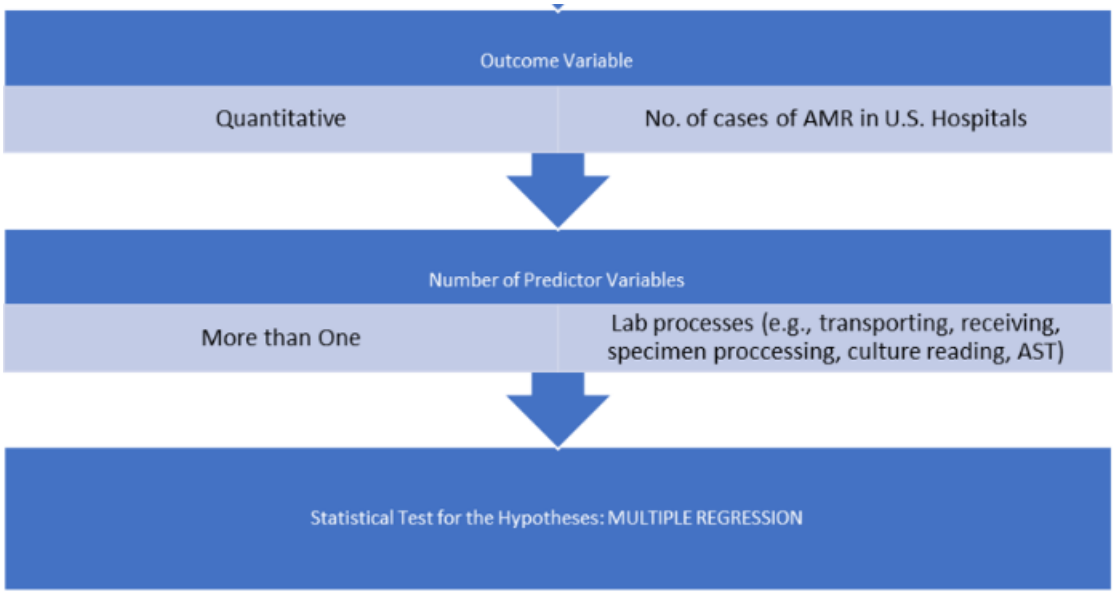
Moreover, according to Warner (2012), multiple regression expands the relationship between explanatory and single response variables, another term for independent variables which can be used interchangeably but with a subtle difference. When the variable is not affected by any other variable, it is independent. However, if it is affected by other variables, it is known as explanatory (Stephanie, 2015). The research on AMR and laboratory processes was explanatory because it involves several variables which would affect the outcome variable. For instance, there were some explanations or reasons for the delays, maybe the hospital tube system was down, or the transporter had to deliver other things to other departments. The response variable is also known as the dependent or the outcome variable, which would be affected by the explanatory or independent variables.

Furthermore, MLR predicts two or more variables to predict another to quantify the relationship between the variables. The variable that needs to be predicted or the outcome variable is binary, and the predictors are one or more variables. Thus, MLR applies to the study of laboratory practices and the number of AMR cases. Once again, MLR was used for prediction, for binary dependent variable, and when there are more

than one independent variable and no repeated measures. The predictor variables of the study, all the delayed laboratory sample handling, were predicted to affect the number of identified multiple antibiotic-resistant microorganisms isolated from samples taken from hospitalized patients.

Figure 1

Data Analysis Plan on Laboratory Processes and Antibiotic Resistance.



Assumptions to Multiple Logistic Regression

The multiple logistic regression (MLR) statistical assumptions for the research study on AMR and laboratory processes followed a linear relationship between the outcome and the predictor variables. The outcome variable would only have two outcomes as a dichotomous variable; moreover, the third type of MLR assumption used for the research on AMR and laboratory processes was independence, in which each variable is independent, and the value of a variable was not dependent on the other variables. There should be no multicollinearity. It is assumed that there will be no

multicollinearity in the data because, if so, the independent variables are highly correlated. When multicollinearity is present, the statistical significance and regression coefficient will be unstable and less trustworthy (Bodily, 2022). The assumption on the logistic relationships of the predictor and the outcome variables was not applied to the analysis since the variables were all categorical in nature. Moreover, there were no extreme outliers in the datasets.

Process for Testing and Assessing the Assumptions

The assumptions were assessed during risk qualification; in other words, assumptions during risk determination were tested before using the information collected. There was a greater related risk when the assumptions were wrong. The stability of the assumptions was also assessed to evaluate the potential for change in each assumption because the nature of assumptions was that they would change and would not remain stable (Creswell & Creswell, 2018). Moreover, the consequences of the assumptions were also assessed to evaluate the potential impact when the assumptions were proven invalid. Warner (2012) stated that the stability and consequences of assumptions are rated from one to ten, which results in a valid assumption and has a large impact. For the study on AMR and laboratory processes, the assumption that delay in the processing samples and the final reporting of resistant microorganisms and their sensitivity testing potentially result in the increasing numbers of AMR or multidrug resistant infections; so, risk qualification was performed to have the assurance that the assumptions were valid and created an impact to the research study.

Actions Taken if the Assumptions are Violated

Violations of the assumptions of the analysis of the research study on AMR impacts the ability to trust the results and validity of the research. According to Rummel (1998), data transformations such as square root transformation or natural log address the violations. However, once the data was transformed and analysis was conducted, it only interprets transformed variables and cannot interpret the results of untransformed variables.

Statistical Plan for the Research Questions

Descriptive Statistics

Frequency of distribution for the number of times bacterial culture samples were transported to the laboratory. The mean central tendency for the average times and how often samples were transported to the laboratory was determined. The degree of variability was calculated as to which nursing department has the most identified AMR organisms. Frequency distribution on the processing of samples after being received in the laboratory was also measured to determine the number of times samples were left not being handled for some time. The measure of central tendency on the average times that samples were left un-processed and the common time the medical laboratory assistants (MLA) forgot to deliver the sample to the microbiology department for sample processing. The degree of variation was measured on each sample handled by a particular MLA and the variation in the workload for a particular shift.

Variation on the time the organism grows, the time the microbiologist performs the bacterial staining and microscopic reading, and the time for biochemical testing to

confirm the pathogenic organism on the culture. Measures of variability, for example, on when the incubator or instruments were down and the number of samples loaded to the instrument, whether more or less than the average load on each shift. Antibiotic sensitivity testing (AST) was measured through variability. Variability in the time of setting the organism for AST by the microbiologist, the time the organism grows and reacts to the antibiotics, and the time the microbiologist reads the AST results. Reporting of final results was also measured as a frequency distribution. Normally bacterial cultures are completed between 48 and 72 hours; the frequency distribution of the study was measured as mean or average. Measures for variability were determined by the type of bacterial culture; for example, blood cultures were finalized at five days, cerebrospinal cultures were completed in three days, and some organisms were slow growers, which grows more than three days or rapid growers, that grows for only four hours.

Binary Logistic Regression

Binary logistic regression analysis of the data was measured using SPSS statistical analysis on the sample transport time from the different hospital units and the cases of AMR. Beginning with the MLAs receiving and delivering the samples to the microbiology department. The time pathogenic organisms were identified by the microbiologist, and reporting identified organisms within 24 to 48 hours of culture. Moreover, also measured was the time when AST was set up and the final time when the culture was done and reported back to the ordering physician. In SPSS, the Significance (Sig) or *p*-value and the Exp(B) or odds ratio were used to determine whether the data on sample handling and the cases of AMR in a Florida hospital were significantly different

from what was expected.

Multivariate Statistics

Multiple logistic regression (MLR) was performed on the data through stepwise regression analysis using SPSS version 28.0. First was determining the number of times samples were transported with delay. Then, adding the time for processing the sample for culture, the time to identify the microorganism from culture. The time in setting up the organism(s) for AST and for reading the antibiotic reactions to the time the final report was verified to be seen by the ordering physician. The overall time from the transport to the reporting of results was used to associate the number of cases of AMR in hospital-admitted patients. Multivariate variance analysis analyzed all the data, with one dependent and multiple independent variables.

Interpretation of Multiple Logistic Regression Results

Interpretation of results of the study on AMR using MLR tests on the hypothesis is based on a 95% confidence interval and a 5% margin of error. According to Creswell & Creswell (2018), the interpretation of results in quantitative research is used to conclude the research questions and hypothesis. The interpretation would involve extension descriptions of the results, statistical significance, confidence intervals, and effect sizes. Statistical significance testing reports that the assessment of the observed scores reflects a pattern rather than by chance. The statistical test was considered significant when the results were unlikely by chance, and the null hypothesis was rejected with a rejection level of "no effect" with a p-value ≤ 0.05.

Furthermore, practical evidence of the results was reported, including the confidence interval and the effect size. The confidence interval is the value that describes the uncertainty level of an estimated observed score and shows how good the estimated score will be. A 95% confidence interval indicates that 95 out of 100 times, the observed score is in range with the allowable score. The effect size identifies the strength of the conclusions on the relationships of the variables (Creswell & Creswell, 2018).

The study on AMR and laboratory processes in a Florida hospital was retrospective, and using the odds ratio in data analysis was appropriate. Daniel and Cross (2018) stated that a retrospective study was based on samples with the disease or the number of cases of AMR and the number of samples that were submitted and processed on time and compared to the samples without the disease or negative cases of AMR and delays in the processing of samples for culture. As defined by Daniel and Cross (2018), the odds ratio is the ratio of the probability of success or failure.

Table 5

Computation of Odds Ratio on Lab Processing Time and AMR.

Risk Factor	Absence of AMR (0)	Presence of AMR (1)	Total
Within the Required Time (1)	*A*	*b*	*a + b*
More than the Required Time (0)	*C*	*d*	*c + d*
Total	*a + c*	*b + d*	*n*

Equation 1

The formula for computing the Odds ratio on the cases of AMR and the laboratory process:

1. The odds of patients having AMR organisms

   = [a/(a + b)]/[b/(a + b)] = a/b

2. The odds of patients not having AMR organisms

   = [c/(c + d)]/[d/(c + d)] = c/d

Ethical Procedures

The institutional review board (IRB) is the committee that reviews and evaluates research proposals that involve patients. IRB was approved before collecting data for the research study, and if the research poses a risk to participants, modifications of the proposal were required prior to the approval of the IRB (Warner, 2012). For the research study on AMR and its association with laboratory processes, two IRBs were required, one from Walden University and one from the Florida hospital, to access patients' information and laboratory results. An informed consent and courtesy letter were sent to the clinical laboratory director, the medical director and supervisor of the microbiology department, the operations manager, and the laboratory's information technology (IT) supervisor. To let them be aware of the research study and explain how the data obtained would be used. The research ethics approval checklist will manage possible ethical concerns during the data collection. The ethical standards were fulfilled for data collection, including consent from Walden University and the Florida hospital. The steps of data collection were thoroughly explained to the IRB committee. I adhered to patient

confidentiality on the data collected, and the data were stored securely and only accessed by myself, and no patient names were shown on the report. The demographics presented were gender and age, the identified bacteria, and the stamped time for processing the samples for bacterial culture.

Patient confidentiality of the data obtained was a huge requirement and involved my medical laboratory scientist license, which can be rebuked following the Health Insurance Portability and Accountability Act of 1996 (HIPAA) privacy rule. Also, because the data collection uses electronic medical records (EMR), adherence to the Standards for Privacy of Individually Identifiable Health Information ("Privacy Rule") of the U.S. Department of Health & Human Services (2008), a national standard on the protection of health information was accomplished throughout.

Summary

The research study on AMR and laboratory processes in the Florida hospital adhered to the ethical standards for the confidentiality of data collected for statistical analysis. Sampling did not commence until approval was received from the Walden University IRB and Florida hospital. The data analysis was done using the IBM SPSS version 28.0 of the retrospective data on the number of resistant microorganisms and the times in submitting and processing samples. The retrospective study of the cases was done for one year, from November 2019 to November 2020. The laboratory workers' behavior in processing samples for microorganisms and antibiotic testing was observed and used as a tool for behavioral change. The study's target population were adults and older pediatric patients, 10 to 17 years old, admitted to the hospital during the specified

period. The sample size was 246 culture samples based on a 95% confidence interval, 80% population proportion, and a 5% margin of error. The probability sampling method generated sample data and addressed the research question. Specifically, stratified random sampling provided greater precision than random sampling and was appropriate for AMR sampling as most all target patients were selected. The data was drawn from the LIS computer software of the laboratory. There were missing data from the sampling, which created bias, complicated the analysis, and distorted the study's conclusion, the research study was well-planned, data collection was conducted carefully, and the listwise analysis was used to omit the missing data and only analyze the remaining data. In Chapter 4, the results of the study were presented to show whether the statistical analysis would reject or accept the null hypotheses and using the odds ratio to report the presence and absence of AMR at the Florida hospital.

Chapter 4: Research Results

Introduction

AMR infection is a health threat that affects millions of Americans and, with thousands of deaths each year, impacts vulnerable individuals, especially patients admitted to hospitals. Patients suffering from cancer and chemotherapy treatment, those undergoing surgery, on dialysis treatment for kidney failure, those with chronic disease, and those with untreatable infections are all prone to AMR infections (CDC, 2020).

The purpose of the research study on AMR and laboratory practices in a Florida hospital was to test whether there was an association between existing sample processing practices by the clinical laboratory and cases of AMR in the hospital. The determination included sample processing time from when the patient's provider makes the orders, time for sample collection by the nurse or healthcare worker, the time the specimen was transported to the laboratory, the time the specimen was set up for the culture of organisms, the time pathogenic organism was identified, the time for antibiotic sensitivity testing, and the time when the final result was sent to the patient care provider.

The six research questions and hypotheses used for the problem statement of the research study were the following:

RQ1: Is there an association between the time samples are transported to the laboratory and AMR cases in a Florida hospital?

H_o1: There is no association between the time samples are transported to the laboratory and AMR cases in a Florida hospital.

H_a1: There is an association between the time samples are transported to the laboratory and AMR cases in a Florida hospital.

RQ2: Is there an association between the time samples are set-up for culture in the laboratory and AMR cases in a Florida hospital?

H_o2: There is no association between the time samples are set-up for culture in the laboratory and AMR cases in a Florida hospital.

H_a2: There is an association between the time samples are set-up for culture in the laboratory and AMR cases in a Florida hospital.

RQ3: Is there an association between the time microorganisms are identified in culture and AMR cases in a Florida hospital?

H_o3: There is no association between the time microorganisms are identified in culture and AMR cases in a Florida hospital.

H_a3: There is an association between the time microorganisms are identified in culture and AMR cases in a Florida hospital.

RQ4: Is there an association between the time antibiotic sensitivity testing is reported and AMR cases in a Florida hospital?

H_o4: There is no association between the time antibiotic sensitivity testing is reported and AMR cases in a Florida hospital.

H_a4: There is an association between the time antibiotic sensitivity testing is reported and AMR cases in a Florida hospital.

RQ5: Is there an association between the time the final culture results are reported and AMR cases in a Florida hospital?

H_o5: There is no association between the time the final culture results are reported and AMR cases in a Florida hospital.

H_a5: There is an association between the time the final culture results are reported and AMR cases in a Florida hospital.

RQ6: Is there an association between the time of specimen transport, setting up for culture, isolation of microorganisms, antibiotic sensitivity test, and the time when culture results are reported and AMR cases in a Florida Hospital?

H_o6: There is no association between the time of specimen transport, setting up for culture, identification of microorganisms, antibiotic sensitivity test, and the time when culture results are reported and AMR cases in a Florida Hospital.

H_a6: There is an association between the time of specimen transport, setting up for culture, identification of microorganisms, antibiotic sensitivity test, and the time when culture results are reported and AMR cases in a Florida Hospital.

Chapter 4 provided the results of the statistical findings, answered the research questions, aligned with the purpose of the study, and the importance of conducting the study. The data used for the study were organized, so the information obtained was logical. Using an Excel spreadsheet and the SPSS software, the data showed the date and time of sample processing, beginning from when the cultures were ordered, the time when samples were collected, the time delivered to the laboratory, the time when set-up on culture media, when organisms were identified, and AST was done, and the final time when results were completed and reported.

The results from data collection were presented on tables, charts, and figures and individually explained to test the association between the independent variables of sample processing time and the dependent variable of the cases of AMR at the Florida hospital. The information presented in Chapter 4 was used in data statistical analysis to answer whether to reject or accept the null hypotheses and to answer the research questions.

Collection of Data

Data collection for the time tracking of samples for bacterial culture from the LIS Epic Beaker took 30 mins to an hour of database programming. It took 3 to 4 hours to download a year's worth of reports from November 2019 to November 2020. The informatics supervisor of the laboratory downloaded the generated data to an Excel spreadsheet. Deidentifying and removing patient identification for each culture report took another 3 to 4 hours. The data were saved into the laboratory administration's secured drive and accessible only by the laboratory's IT supervisor and myself. The total number of cultures reported from November 2019 to November 2020 was 32067, a combination of normal and negative results. The data were extrapolated on whether they were from patients admitted to the hospital or from outpatient clinics, filtered by the age of the patients, and removed all negative cultures from the list. Cultures growing resistant organisms were filtered out in Excel and organized by the type of resistant microorganism. The identified microorganisms were *Klebsiella pneumonia* ESBL, *Escherichia coli* ESBL, *Pseudomonas aeruginosa* Meropenem resistant, Vancomycin-

resistant *Enterococcus* (VRE), and Methicillin or Oxacillin resistance *Staph aureus* (MRSA).

The probability stratified random sampling was performed on the filtered data to obtain a sample size of 246. An Excel formula was used to convert the date and time for the sample handling from collection to final verification of results to either minutes, hours, or days. It took 35 hours or 1 week to filter the data within the Excel spreadsheet. Next was the creation and loading of the data to SPSS. Eleven variables were created: age, sex, specimen type, hospital unit, organism identification, and the six-sample processing time. Each processing time or independent variables were coded 1 for processing within the required time and coded 0 for processing beyond the acceptable time. It took 2 weeks, or 56 hours to convert each sample's date and time to minutes, hours, and days. The estimated total hours of data sampling were between 97 to 99 hours.

The discrepancy with the data was that the laboratory computer system (Epic Beaker) was unorganized since it showed two culture orders on one sample. When sensitivity testing was performed, the computer system triggered another test order or start time, appearing as another set of culture orders. The laboratory's IT supervisor programmed and organized the data to show both the original date and the time when the culture was ordered and the date and time when sensitivity testing was started in one culture order.

Also, the data presented were all the results for the year, including negative and positive cultures and cultures from outpatients, which made the extrapolation and filtering of the data tedious and completed beyond the planned time to obtain clean data.

Moreover, the conversion of the date and time to minutes, hours, and days for each of the data sets of the 246 culture samples took several hours, including the coding of each culture's processes. Furthermore, transferring the data from Excel to SPSS took several days. All the data was manually transferred, which took several days to complete.

The data on microbiological cultures from November 2019 to November 2020 consisted of 16 columns which included (1) test or culture order name, (2) organism isolated, (3) order date and time, (4) collection instant or the time samples were collected, (5) receiving info or the time samples were received in the lab, (6) lab task instant or the time samples were processed in the lab for bacterial culture identification and antibiotic testing, (7) preliminary instant was the time preliminary results were reported, (8) verified instant which was the final time when results were completed and reported, (9) total hours of the culture, (10) specimen source, (11) components for the type of antibiotic used for testing, (12) Value of the result of the antibiotic test, (13) interpretation of the antibiotic results, (14) department or hospital unit, (15) age of the patients, (16) gender or sex of the patient. As stated in Chapter 3, the sample inclusions and exclusions of the data collected that only hospital-admitted adults eighteen and above and older children aged between ten and seventeen years old were included in the study. Pediatric patients below 10 years old and all outpatient samples were excluded from the data sampling. The time variables were coded as to whether it was more than or within the allotted time of sample processing. The time difference between culture order and sample collection should be within an hour, and from collection to delivery and receiving in the laboratory should be within 2 to 4 hours. The processing of the specimen for

culture growth should be within 30 minutes from the time the sample was delivered to the laboratory. Preliminary results should be between 24 to 48 hours after culture set-up, and the final results should be within 72 hours or 5 days for blood cultures.

The samples from the Florida hospital from the probability stratified sampling represent the population with a sample size of 246 submitted for bacteriological culture from November 2019 and November 2020. With random sampling, there was an equal chance of selecting a sample from a particular hospital unit, focusing on the samples collected from the emergency department (ED), the intensive care unit (ICU) and critical care unit (CCU), the operating room, general medicine, and obstetrics and gynecology. In other words, the sample size is enough to focus on a breadth of information representing the population. Furthermore, as stated in Chapter 3, probability stratified random sampling is appropriate for the research study on antimicrobial resistance in hospitals because the potential for human bias was reduced, as mentioned that all samples sent for cultures had an equal chance of being selected. Also, the samples obtained have a high representation of the population, with the fact that the Florida hospital used for the study is a government-subsidized facility, thus catering to diverse types of patients with and without health insurance. The location of the hospital is in proximity to the poorest area of the city, with patients that only go to the hospital when they are already extremely sick (Lakoh et al., 2020). It is also the city's trauma hospital, so all accidents and criminal incidents are delivered to the hospital. In addition, it is a teaching hospital attended by highly intelligent physicians in the city and the state, with sophisticated technologies for

treatment, and as stated, it caters to every sickness and several types of patients in the city.

Results

The statistical analysis assessed the association of microbiological culture processing time with the cases of antimicrobial resistance at the Florida hospital. MLR was used for statistical analysis using five independent or predictor variables, which include the time the specimens were transported to the laboratory, the time specimens were set-up for culture, the time when organisms were identified, the time when antibiotic sensitivity testing was reported, and the time when the completed or final results were reported to the provider. The dependent variable was the cases of antibiotic resistance at the Florida hospital.

Two hundred and forty-six samples were used for the statistical analysis and analyzed using SPSS version 28.0. The study's independent variables were categorical dichotomous variables; they were coded as 1 for a time variable within the required processing time and 0 for more than the required time. The dependent variable was also dichotomous and coded for 1 for the presence of AMR and 0 for the absence of AMR in the sample. The frequency distribution of the dependent variable showed a percentage of 68% (167/246) for the presence of AMR and only 32% (79/246) for the absence of AMR.

Frequency Distributions of the Variables

Table 6 shows the gender of patients, which were 133 (54.1%) males and 113 (45.9%) females. Table 6 displays the patient's ages from 23 to 100 years old. The highest age frequency was 35, with nine patients (3.7%). Also, it displays the samples

determined to be positive for pathogenic microorganisms. Of the specimens submitted for bacterial culture, urine was the most frequent, with 85 (34.6%), followed by respiratory samples (e.g., sputum, nasopharyngeal, bronchial washing), with a count of 78 (31.7%). The third most common sample was blood, with 40 counts (16.3%). Swab samples from wounds, eyes, and inside the body for the culture of anaerobic organisms were at 39 counts (15.9%). The smallest submitted specimen for culture was body fluids, with only four (1.6%). Table 9 for the names and frequencies of antibiotic-resistant organisms identified, which includes *Klebsiella pneumoniae* (KP) and *Klebsiella oxytoca* with a count of 45 (18.3%), *Escherichia Coli* (EC) of 72 (29.3%), Methicillin Resistant *Staphylococcus aureus* (MRSA) of 76 (30.9%), *Pseudomonas aeruginosa* (PA) 29 (11.8%), Vancomycin Resistant *Enterococcus* (VRE) 15 (6.1%), and nine (3.7%) cultures were growing more than one resistant multiple antibiotic resistant organism. The hospital unit or department with the most antibiotic-resistant organisms identified were from the ICU and CCU, with a frequency value of 107 (43.5%). Followed by the general medicine department at 82 (33.3%), the emergency department at 36 (14.6%), the operating room at 15 (6.1%), and the obstetrics and gynecology departments with only six (2.4%) samples.

The frequency of the independent variables of the time from culture order to the collection of the samples collected within two hours is 165 (67.1%) and 81 (67.1%) for samples collected after two hours. Sample collection to receipt in the laboratory, 233 (94.7%) were received within two to four hours, and 13 (5.3%) received more than four hours. From receiving and logging in to the laboratory to set up for bacterial growth, 157

(63.8%) were completed within 30 mins, and 89 (36.2%) for more than 30 mins. From set up to positive culture organism identification, 238 (96.7%) were determined within 24 to 48 hours and only 8 (3.3%) after 48 hours. Antibiotic sensitivity resulted within 72 hours, 195 (79.3%) were reported on time, and 51 (20.7%) more than three days. The total hours from ordering cultures to completion of the test, 195 (79.3%) were reported on time, and 87 (35.4%) were delayed. The dependent variable on the presence and absence of antimicrobial-resistant organisms in the culture was 167 (67.9%) had antibiotic resistance present and 79 (32.1%) with absence. The data on the independent and dependent variables were presented in Table 6, which also summarizes the parameter coding and frequency distribution.

Table 6

Frequency Distribution Showing the Age, Sex, Samples, Hospital Units, and Antibiotic Resistant Organisms Isolated from November 2019 To November 2020

	Age	20 - 29	30 - 39	40 - 49	50 - 59	60 - 69	70 - 79	80 - 89	90 - 99	100 - 109	Total	Percentage
Gender	Male	5	19	13	25	30	30	10	1	0	133	54
	Female	15	13	16	19	29	14	5	1	1	113	46
	Total	20	32	29	44	59	44	15	2	1	246	
Samples submitted for culture	Urine	7	9	6	13	23	17	7	2	1	85	35
	Resp.	4	9	6	20	21	14	4	0	0	78	32
	Blood	6	5	5	5	8	10	1	0	0	40	16
	Wound	2	9	12	6	4	3	3	0	0	39	16
	Fluid	1	0	0	0	3	0	0	0	0	4	2
	Total	20	32	29	44	59	44	15	2	1	246	
Units that sent samples	ICU	4	10	7	24	34	19	8	1	0	107	43
	Med	8	11	12	14	18	14	4	0	1	82	33
	ER	3	9	7	4	3	7	2	1	0	36	15
	OR	3	0	1	2	4	4	1	0	0	15	6
	OBGyn	2	2	2	0	0	0	0	0	0	6	2
	Total	20	32	29	44	59	44	15	2	1	246	
	MRSA	7	11	16	15	13	10	4	0	0	76	31

Resistant organism identified	*E. coli*	6	12	10	9	12	19	3	1	0	72	29
	Kleb.	5	3	2	9	11	8	5	1	1	45	18
	P. aer	1	5	1	7	10	5	0	0	0	29	12
	VRE	1	1	0	0	8	2	3	0	0	15	6
	Mix	0	0	0	4	5	0	0	0	0	9	4
	Total	20	32	29	44	59	44	15	2	1	246	

Table 7

Frequency Distribution Of The Independent And The Dependent Variables With Coding Parameters

Independent Variables		Parameter coding	Number	Percentage
Time sample transported to the lab (within 2-4 hrs)	More than 2-4 hrs	0	13	5
	Within 2-4 hrs	1	233	95
Time samples were set-up for culture in the lab (within 30 mins)	More than 30 mins	0	89	36
	Within 30 mins	1	157	64
Time microorganism was identified in culture (between 24 to 48 hrs)	More than 48 hrs	0	8	3
	Within 48 hrs	1	238	97
Time when antibiotic sensitivity was reported (within 72 hrs)	More than 72 hrs	0	51	21
	Within 72 hrs	1	195	79
Time of final culture results was reported	Delay	0	87	35
	On-time	1	159	65
Dependent Variables				
Cases of Antimicrobial Resistance	Absence	0	79	32
	Presence	1	167	68

Figure 2

Percent Samples Processing Time

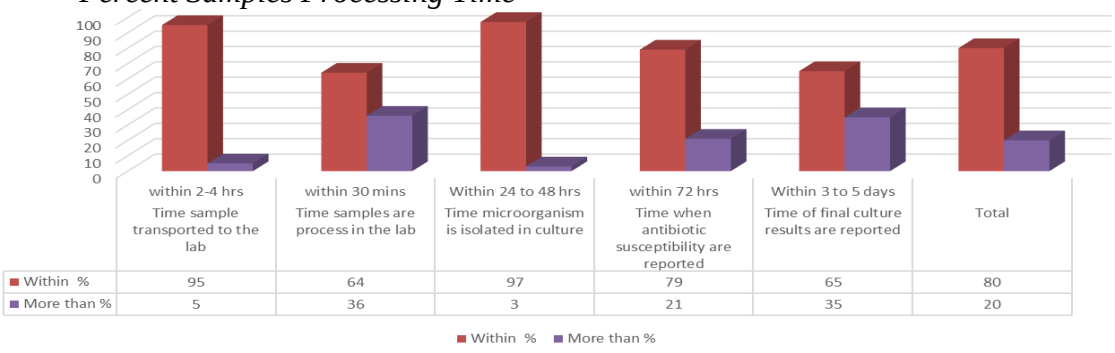
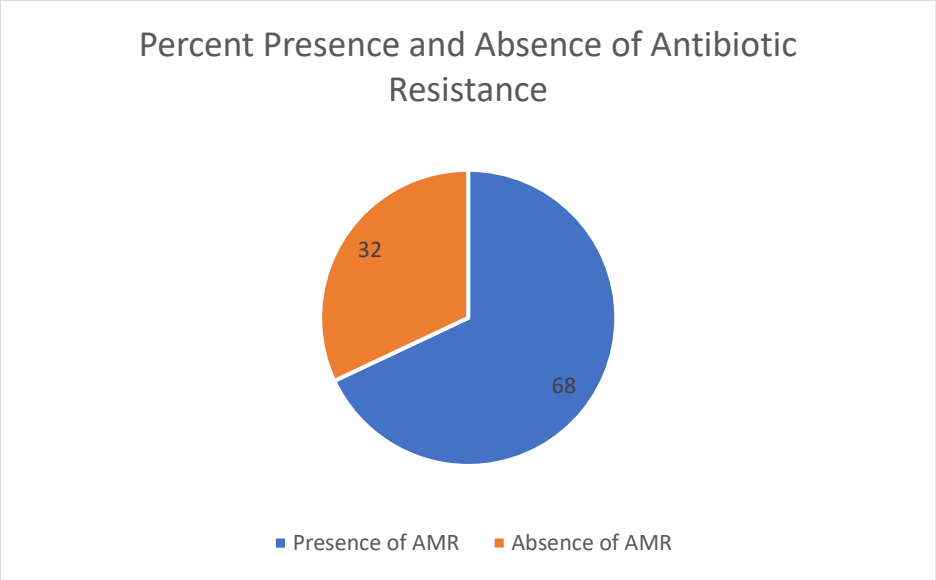


Figure 3

Percentage of Presence and Absence of Antibiotic Resistance



Binary Logistic Regression Analysis

BLR was used to analyze the independent variables of time on the transport of specimens to the laboratory, time on the setting up of specimens for culture, time for identifying microorganisms, the time when antibiotic sensitivity testing was reported, and the time when the culture results were finalized and reported in association with the dependent variable of the cases of antimicrobial resistance. Since logistic regression includes several assumptions, assumptions were tested before running the statistics on SPSS. The first assumption is that the dependent variable must be binary, shown by the study's dichotomous dependent variable, 0 for the absence and 1 for the presence. The second assumption is that observations were independent observations. The dataset is independent and not coming from repeated measures. For the third assumption, there should be independence of observations. For the fourth assumption, there was no

multicollinearity among the independent variables and evaluated using the correlation coefficient in Table 8, with no values of +/- 1.0, which indicates no collinearity of each independent variable. Also, no multicollinearity was determined by collinearity statistics with tolerance values above 0.2 and variance inflation factor (VIF) of less than 5 of all the independent variables. The study complied with the fifth assumption on the transformation of the dependent variable to logit variables, 0 for the absence of antibiotic resistance and 1 for the presence of resistance. The sixth assumption on the dataset that there should not be extreme outliers and high leverage values was achieved with the sample size of 246, which was sufficiently large for data analysis.

Table 8

Correlation Coefficient and Collinearity Statistics Evaluating No Multicollinearity

Independent variables	Correlation Coefficient	Collinearity Statistics	
		Tolerance	VIF
Time of sample transport to the lab (within 2-4 hrs)	1.00	0.993	1.007
Time of sample culture set-up (Within 30 mins)	1.00	0.97	1.031
Time of bacterial identification (Between 24 to 48 hrs)	1.00	0.955	1.047
Time of sensitivity testing (Within 72 hrs)	1.00	0.506	1.977
Total of reporting of results	1.00	0.504	1.982

RQ1

RQ1, was there an association between the time samples were transported to the laboratory and AMR cases in a Florida hospital? There was a 38% decreased odds of reporting AMR in the Florida hospital on samples transported to the laboratory within two to four hours of collection compared to those that arrived in the laboratory for more than four hours after, $OR = 0.620$, 95% CI [0.166, 2.318], p-value = 0.477. However, the

result was not statistically significant, failing to reject the null hypothesis and claiming no statistically significant association between the time samples were transported to the laboratory and AMR cases in a Florida hospital.

RQ2

RQ2, was there an association between the time samples were set-up for culture in the laboratory and AMR cases in a Florida hospital? There was a 56% decreased odds of reporting AMR in the Florida hospital on samples set-up for culture in the laboratory within 30 mins compared to those samples that were set-up more than 30 mins upon arrival in the laboratory, *OR* = 0.439, 95% CI [0.241, 0.800], *p*-value = 0.007. The result was statistically significant, the null hypothesis was rejected, and claiming a statistically significant association between the time samples were set-up for culture in the laboratory and AMR cases in a Florida hospital.

RQ3

RQ3, was there an association between the time microorganisms were isolated in culture and AMR cases in a Florida hospital? There was a 71% decreased odds of reporting AMR in the Florida hospital when microorganisms were identified in the samples cultured in the laboratory within 24 to 48 hours, compared to bacterial identification for more than 48 hours after, *OR* = 0.293, 95% CI [0.035, 2.424], *p*-value = 0.255. However, the result was not statistically significant, failing to reject the null hypothesis and claiming no statistically significant association between the time microorganisms were identified in the laboratory and the cases of AMR in a Florida hospital.

RQ4

RQ4, was there an association between the time antimicrobial sensitivity testing was reported and AMR cases in a Florida hospital? There was a 24% decreased odds of reporting AMR in the Florida hospital when antibiotic sensitivity testing of samples was completed within 72 hours, compared to testing completed more than 72 hours after, *OR* = 0.757, 95% CI [0.382, 1.499], *p*-value = 0.424. However, the result was not statistically significant, failing to reject the null hypothesis and claiming that there was no statistically significant association between the time of antibiotic sensitivity testing and AMR cases in a Florida hospital.

RQ5

RQ5, was there an association between the time the final culture results were reported and AMR cases in a Florida hospital? The odds for the time in reporting the final culture within three to five days do not affect the odds for the presence or absence of AMR when completed within three to five days as compared to results finalized three to five days after, *OR* = 1.005, 95% CI [0.574, 1.759], *p*-value = 0.986. The result was not statistically significant, failing to reject the null hypothesis and claiming that there was no statistically significant association between the time for the final reporting of results and AMR cases in a Florida hospital.

Table 9

Binary Logistic Regression Result Summary for Research Questions 1 to 5

	Research Question	*p*-value	H_o	Exp (B)	95% C.I.for EXP(B) Lower	Upper
1	Is there an association between the time samples are transported to the laboratory and AMR cases in a Florida hospital?	0.477	Not Rejected	0.62	.166	2.318
2	Is there an association between the time samples are set-up for culture in the laboratory and AMR cases in a Florida hospital?	0.007	Rejected	0.439	.241	.800
3	Is there an association between the time microorganisms are identified in culture and AMR cases in a Florida hospital?	0.255	Not Rejected	0.293	.035	2.424
4	Is there an association between the time antibiotic sensitivity testing is reported and AMR cases in a Florida hospital?	0.424	Not Rejected	0.757	.382	1.499
5	Is there an association between the time the final culture results are reported and AMR cases in a Florida hospital?	0.986	Not Rejected	1.005	.574	1.759

Multivariate Results

RQ6

RQ6, was there an association between the time of specimen transport, setting up for culture, identification of microorganisms, antibiotic sensitivity test, and the time when culture results were reported and AMR cases in a Florida Hospital? The first step of the model, as seen in Table 8, was the binary analysis summary of the five independent and dependent variables. The analysis showed only one statistically significant independent variable: the time on setting up for culture inside the microbiology laboratory. The other independent variables of the time of transport to the laboratory, identification of the

microorganism, and testing of antibiotic sensitivity were not statistically significant; the null hypotheses were not rejected and claimed no association with the AMR cases in the Florida hospital. The odds ratio results for the independent variables mostly displayed values below 1, indicating that the time for transport, culture set-up, bacterial identification, and antibiotic sensitivity testing decreases the odds of the cases of AMR in the Florida hospital. The fifth variable of the time for the final reporting of the cultures had a value of 1, indicating that the odds for the final reporting of results do not affect the odds of the presence of AMR.

The second part of the logistic regression analysis combined all the independent variables. Table 9 shows the modeling results for each variable, wherein the odds ratio results of the independent variables of the time for sample transport, time for setting up for culture, time for the identification of bacteria, and time for sensitivity testing were all below 1. The independent variables of time of transport, culture setup, organism identification, and antibiotic sensitivity test results to a decreased odds of 38%, 54%, 70%, and 26%, respectively, on reporting AMR in the Florida hospital when the processing of samples was completed within the recommended time compared to when the processing was delayed. Also, as with binary regression analysis, the independent variable of the time for the final reporting of results has an odds ratio of 1, in which the odds of reporting AMR were not affected by whether the final results were reported within or more than three to five days. The *p*-values of the time of sample transport, identification of bacteria, testing for antibiotic sensitivity testing, and reporting of final results were above the *p*-value of <0.05 and were not statistically significant, also failing

to reject the null hypotheses and claimed no statistical association with AMR cases at the Florida hospital. Only the time for setting up on culture media was statistically significant, with a *p*-value of 0.012; the null hypothesis was rejected and claimed to be associated with the cases of AMR in the Florida hospital.

Table 10

Modeling Results of all Independent Variables and Cases of AMR

			95% C.I.for EXP(B)	
	Sig.	Exp(B)	Lower	Upper
Time of sample transport to the lab (within 2-4 hrs)	.482	.618	.162	2.362
Time of sample culture set-up (Within 30 mins)	.012	.459	.249	.845
Time of bacterial identification (Between 24 to 48 hrs)	.268	.296	.034	2.548
Time of antibiotic sensitivity testing	.526	.737	.287	1.893
Total of reporting of results (Withing 72 hrs)	.500	1.304	.602	2.822

Summary

Chapter 4 presented the frequency distribution of all variables, including sex and age, the types of samples submitted for microbial culture, antibiotic-resistant organisms identified, and the hospital units where the samples were collected. Also presented was the frequency distribution of the five independent variables and a single dependent variable. The results for each research question were obtained from SPSS software version 28.0. The statistical analysis of each independent variable was run as BLR to display the association between the categorical dichotomous independent variables and categorical dichotomous dependent variable. The significance (Sig) or *p*-value was used to analyze the results whether statistically significant. A *p*-value of < .05 was considered statistically significant. The Exp(B) or odds ratio was also used to check for the association of the variables and whether the odds ratio increases or reduces the odds of

the presence of AMR in the Florida hospital. Research questions one, three, four, and five were not statistically significant and did not reject the null hypothesis. Only the second research question with the independent variable of time of setting up of the sample for culture set-up in the laboratory was statistically significant, rejecting the null hypothesis.

The purpose of the study was re-stated in Chapter 5 to review what the research was all about. Chapter 5 comprises sub-sections or headings that include the research study's summary, recommendation, and conclusion. The major findings from data collection were also mentioned to review the study's results. Moreover, Chapter 5 explains the possible reasons and factors for obtaining the results. The recommendation section stated a statement on what could have been done on handling culture samples that were finalized beyond the allotted or things beyond control. Also, in Chapter 5, an interest that would have been explored but was outside the scope of the research study was stated. Also, a recommendation statement to stakeholders and laboratory administration was included for process improvement. The conclusion mentioned the significance of laboratory processes on the cases of antibiotic resistance in the hospital and how the study results would be used to improve human conditions and for positive social change.

Chapter 5: Interpretation, Recommendation, Conclusion

Introduction

The research on laboratory practices and antimicrobial resistance in a Florida hospital was conducted to determine whether the processing time of samples for bacterial culture was associated with the cases of antimicrobial resistance in patients admitted to the hospital. The gold standard for identifying microorganisms and antibiotic sensitivity testing is by culture, which normally takes 48 to 72 hours to complete and finalize the culture. Handling samples takes at least five to six steps before completion, prompting physicians to prescribe broad-spectrum antibiotics (Alzahrani et al., 2018). With my field of work as a laboratory professional, I have assessed the gap in the knowledge of the statement of Sautter and Halstead (2018) on the clinical laboratory's role in the presence of MDRO infections in the hospital; however, the study showed no data that laboratory processing of samples for bacterial culture indeed has a direct effect on the cases of AMR.

The quantitative research study on AMR and lab sample processing uses data obtained retrospectively from admitted patients from November 2019 to November 2020 through the information system of the laboratory, the Epic Beaker. The descriptive statistics show a sample size of 246, randomly selected from all the cultures determined to be positive for resistant microorganisms. Of the 246 samples, 133 were from male patients and 113 from female patients. The inclusion for age was adults and older pediatric patients; however, only adult patients aged 23 to 100 years old were identified to have samples that were growing antibiotic-resistant organisms. Seven specimen types

were identified to have antibiotic resistant microorganisms growing, namely urine, blood, respiratory, wound, and body fluids. Urine samples were the most in number, and body fluids were the least. Six microorganisms were identified as antibiotic-resistant, and the most common in number was MRSA; significantly, nine of the samples were determined to be growing two types of resistant organisms, for example, MRSA and *E.coli* growing on the same culture plate, which indicates that the patient is unable to respond to antibiotic treatment and thus results in having a mixed infection (Morris & Cerceo, 2020). The hospital units where most of the samples were collected were also identified, and most of the samples were from the CCU and ICU, which indicates that patients who were infected with the resistant organisms were in critical condition and or needed intensive care (Pachori et al., 2019).

The binary logistic regression result showed that independent variables of time for sample transport, bacteria identification, and testing for sensitivity testing were not statistically significant, and the null hypotheses failed to be rejected. Only the time samples were set up for bacterial culture showed statistically significant results, with *p*-value of 0.007 and 0.012 on the multiple logistic regression analyses. The null hypothesis on culture set-up time was rejected and claimed association with the cases of antimicrobial resistance in the Florida hospital.

Interpretation of the Findings

Interpretation in Relation to Literature

In Table 5, the descriptive statistics showed 133 male and 113 female patients, and the age range with significant samples submitted and were positive for culture was

between 50 to 79 years old, with more men than women. The age and gender also apply to the sample submitted for culture, the hospital unit where the patients were admitted, and the antibiotic-resistant organism isolated from the cultures. Urine was the sample with the most isolated antibiotic resistant organism at 35% (85/245). Urine is normally the easiest sample to collect and is mostly submitted for culture. The ICU and CCU was the hospital unit with the most cases of antibiotic resistance identified at 43% (107/246); the result is an obvious reason that AMR organism is a deadly microorganism and could cause a high mortality rate. Methicillin-resistant *Staphylococcus aureus* is the most common resistant organism and is easily transmitted as a nosocomial or hospital-acquired infection. Although MRSA is high, medicines are available to treat MRSA infection. However, treatment is still very limited for other multidrug-resistant organisms, so patients with those types of infections are hospitalized for a while and placed in isolation and ICUs.

Moreover, the hospital units with the most growing resistant organisms have the highest number of samples from the ICU and CCU. Patients admitted to the ICU and CCU are usually very sick with weakened immune systems. As described by the WHO (2021) and the CDC (2021), AMR has been a global health threat to humans and patients in the hospital. The study results were a representation of the five resistant microorganisms isolated or identified from the samples. Nine cultures grew multiple types of resistant organisms and indicated difficulty in treating the patient's infection.

The treatment of broad-spectrum antibiotics as empiric therapy, as a prophylactic measure, and to avoid superinfections (Atif et al., 2021; Nair et al., 2019) may have

happened to the samples used in the study. Based on the culture results of the 246 antibiotic-resistant samples, 87 or 35% of cultures were reported after 72 hours or 3 days. The delay in the antimicrobial results would make a physician prescribe nonspecific broad-spectrum antibiotics to start treatment for ailing patients (Lakoh et al., 2020).

The study's overall results on sample processing time showed that 35% (87/246) were delayed in reporting the results, meaning there are still processes that need to be changed in the laboratory; moreover, as bases for limiting any delay in the final reporting of results, which may cause medical error, with physicians prescribing nonspecific antibiotics to patients because of the expected time in getting the results for bacterial culture. The CDC (2021) and Kamenshchikova et al. (2021) stated that admitted patients are at higher risk of acquiring antibiotic-resistant infections than in public, and it affects any age, but most patients with a weak immune system. Five hospital units or departments were determined to have samples positive for antibiotic-resistant organisms. The frequency distribution found from each unit was 43% (107/246) from the ICU, 33% (82/246) from the medical ward, 15% (35/246) from the emergency department, 6% (15/246) from the operating room, and 2% (6/246) from the obstetrics and gynecology department. The ICU was the highest in percentage, and according to the literature, patients admitted to the ICU were badly sick and had very weak immune systems.

Interpretations Based on the Theoretical Construct

The results on the frequency distribution of the variables in Table 6 present the number and percentage of samples handled. For the time of samples transported in the laboratory, 5% (13/246) were transported for more than two to four hours, and 95%

(233/246) transported within 2 to 4 hours. Setting up for culture, which was performed by laboratory assistance, was done within 30 mins upon arrival in the laboratory; the results were 36% (89/246) for more than 30 mins and 64% (157/246) within 30 minutes. Identification of organisms by microbiologists was completed within 24 to 48 hours, and only 3% (8/246) were reported for more than 48 hours; the rest of the cultures were reported within 24 to 48 hours, 97% (238/246). 21% (51/246) was when the antibiotic was tested for more than 72 hours, and 79% (195/246) were completed within 72 hours. The final reporting of results by the microbiologist was completed within 3 days, at 65% (159/246), and 35% (87/246) were reported beyond the required time.

Chapter 2 of the study's theoretical foundation was based on the HBM theory by recognizing an individual's behavior. Laboratory personnel’s behavior to care for the task was automatic, and they immediately worked with the specimens received in the laboratory, immediately set-up the samples for culture, identify organisms, testing for antibiotics, and report the results promptly within the defined time. Lab employees were also reinforced based on expectations of their jobs and responsibilities and used the components of thinking, reasoning, and hypothesis thinking, following Glanz et al. (2015).

Interpretations Based on the Statistical Results

In the frequency distribution of the variables in Table 6, it was seen that all of the independent variables at the time of sample processing, that includes the transport of samples, setting up for culture, identification of microorganisms, testing for antibiotic sensitivity, and completion of results, have a higher number of time and percentages

when samples are process within the required time. The results showed good processing time by all of the Florida hospital's laboratory employees. Eighty percent of the variables were processed within the time frame and 20% more than the allocated time. It indicates that the processing of the samples submitted to the laboratory for one year was mostly completed within the required time. For the dependent variable of the presence and absence of AMR, it was seen that of the 246 random samples, 167 (67.9%) had the presence of microorganisms that carry the antibiotic resistance mechanism, and 79 (32.1%) had the absence of resistance. The results could indicate the presence of AMR organisms in patients admitted to the Florida hospital.

Binary Logistic Regression Analysis

RQ1

The time of sample transport with a *p*-value of .477 was not statistically significant, the null hypothesis was not rejected, and the transport time of samples to the laboratory has no association with the cases of AMR. Also, there was a 38% decreased odds of reporting AMR when the samples were transported within two to four hours after sample collection. Normally samples from the different hospital units are sent through the pneumatic tube system, which only takes a few seconds to arrive in the laboratory and seen on the frequency distribution that 95% (233/246) were transported within the required time for transporting samples.

RQ2

The time between the receipt of the sample to the laboratory and setting up for culture within 30 mins and the presence and absence of AMR was statistically significant,

with a *p*-value of .007. The null hypothesis was rejected and was associated with the cases of AMR in the hospital. A 56% decrease in the odds of reporting AMR in the Florida hospital on samples set up for culture within 30 minutes. From the random sampling, 64% (157/246) of samples were set up for culture within 30 minutes. This variable can have a domino effect on the other processing time, such as identifying the organisms, testing for sensitivity, and the expected time for reporting results. A delay in culture set-up would mean a delay in the growth of microorganisms on the culture media for the determination of antibiotic-resistant organisms because it takes at least 18 to 24 hours for an organism to grow in the incubator and to visibly see with the naked eye the bacterial colonies growing on the surface of the culture media.

RQ3

The time for identifying the organisms from culture was not statistically significant, with a *p*-value of .255, the null hypothesis was not rejected and was not associated with AMR cases in the hospital. There was a decrease in the odds of reporting for AMR in the Florida hospital by 71% when the samples positive for microorganisms were identified within 24 to 48 hours. The frequency distribution for culture identification on time or within 24 to 48 hours at the microbiology laboratory was 97% (238/246), meaning the reading of cultures and identification of organisms was done on time. The microbiology team of the laboratory did an outstanding job in releasing the name of the organisms on time, so it is not a factor in the presence of antibiotic resistant organisms at the hospital.

RQ4

The time for antibiotic sensitivity testing has a *p*-value of .424, was not statistically significant, and the null hypothesis was not rejected and was not associated with antimicrobial resistance. Positive cultures tested for antibiotic sensitivity within 72 hours decreased the odds of reporting AMR at 24% compared to reporting after 72 hours. The number of cultures reported within 72 hours was 195/246, or 79%. The values obtained showed that the time for antibiotic sensitivity testing and reading of antibiotic reactions were not associated with the presence of AMR in the hospital. The 79% determination of sensitivity testing was not much. However, it was expected that some of the cultures needed longer incubation hours to see the full reaction of the antibiotic to the organism. Also, some antibiotic tests were unavailable in the laboratory, so the cultures were sent to a reference laboratory, delaying the reporting of results.

RQ5

The time for the final reporting of results was not statistically significant, with a *p*-value of .986. The null hypothesis was not rejected and was not associated with the cases of AMR at the hospital. The odds when reporting the final results within three to five days do not affect the odds for the cases of AMR in the Florida hospital. The interpretation was that the time of reporting results depends on the sample processing time, and measuring the time of reporting does not make sense to say that it would have a factor for the presence of antibiotic resistance.

RQ6

In the MLR analysis through modeling of the variables, the time between samples being login to the laboratory and setting up on culture media also displayed the same statistically significant results on BLR, indicating the association with the presence or cases of antibiotic-resistant infections. The other independent variables' results were identical to the binary logistic analysis. The odds ratio of the independent variables of the time of sample transport, setting up for culture, identification of the bacteria, and sensitivity testing were all below 1 and interpreted to have decreased odds for the association of processing time with the cases of AMR. Consequently, the odds ratio for the total time when the culture was finalized has an odds ratio of 1.304, or a 30% increase on the odds for the presence of AMR in the Florida hospital. The time on setting up the culture within 30 minutes was statistically significant, with a *p*-value of 0.012, rejecting the null hypothesis, and was determined statistically significant associated with cases of AMR in the Florida hospital.

Limitations of the Study

The research process on AMR and the time for processing samples for bacterial cultivation, wherein the data was obtained retrospectively from November 2019 to November 2020, have some study limitations. The limitations were initially stated in Chapter 2, wherein the study population might have rare organisms not identified two years before data analysis. Multidrug resistant organisms were not determined due to the lack of technology that could not capture the information. Although, as stated in the literature review, rare organisms would not be identified or captured through bacterial

culture identification as compared to molecular technology, there were no changes in the technology at the Florida hospital for identifying organisms for two years. Consequently, molecular technology testing was not part of this research study, so these limitations did not apply to the study. Also, the laboratory information system or Epic Beaker did not have a major upgrade that would significantly change the results. It was mentioned in Chapter 2 by LaMorte (2016) that "it might be difficult to identify a cohort group and that the documented information is not specific to a group of people," which was right, especially the huge amount of data that was received from the laboratory's information supervisor. The raw data was mixed with outpatient culture results and negative or cultures with no organisms growing. Therefore, the data had to be categorized to remove data that were not in the inclusion criteria of the research study.

Moreover, there was missing data on the time and date for other respiratory samples, and reflex to culture urine samples did not show the actual time when the urine was collected, so those data were omitted from the sampling. Another limitation was the lack of previous results to compare the phases of handling samples; consequently, the study was an initial study of the sampling process and was not considered a limitation.

Retrospective study limitations include biases and failure to repeat or correct the process since it was done in the past. There were biases on not being able to follow up on what happened, why after the provider ordered the culture, why the sample was not collected within two hours, why the samples were not received in the laboratory within two hours, and why after receiving it took more than 30 minutes to process the sample for culture or to start incubating the samples, and why it took more than 24 hours to identify

the organisms and more than 48 to 72 hours to report the antibiotic result and to finalize the culture. The incorrect process has been done and cannot be corrected; however, the study's outcome showed that most samples were processed on time; a few were delayed from the expected time, which will be easily rectified by process review and competency assessment. The study's overall limitation was that it only involved 1% of the total samples submitted for culture for a year from 2019 to 2020. Only half of the resistant group of organisms was in the study following the proposed study sample size and was chosen through random sampling.

Recommendations for Further Study

From the mentioned limitations of the study, (1) the limited cohort of only hospitalized or admitted patients were included in the study, (2) missing data on the date and time for other respiratory cultures (e.g., bronchial lavage) and urine culture samples ordered as reflexed by the computer system, (3) the limited sample size presented on the proposal, (4) a way of comparison of data, and (5) a way to recognize the individuals approached to handling samples either through the stimulus-response or cognitive response following the HBM.

The recommendations for future study are (1) to include outpatient samples to get the overall practice of handling samples, to determine when the samples from the outpatient clinics are delivered to the core laboratory, or whether the samples were received and processed on time, (2) for the missing date and time for some of the respiratory cultures and urine culture samples, a request will be sent to the laboratory’s IT to auto-populate the date and time for the types of samples, (3) for the sample size

limitations, for a laboratory that is the core or reference for all the microbiology or culture testing throughout the system hospital, a year's worth of samples was enormous. The raw data shared for the study has 32,076 culture samples, but because of the limitations and constraints of the dissertation requirement, only 1% of the samples were in the data analysis. Although the samples were collected retrospectively, there were no previous studies on laboratory practices on samples for antibiotic resistance organisms to compare the data.

Therefore, this study is beneficial for the next study as a means of comparison of individuals' ways of handling the samples. Lastly, the study's limitations were the approach of lab employees and other health personnel on the task and responsibilities since the focus was on the quantitative method for sample analysis. So, in the future, a mixed method can be used to test an individual's approach following the HBM theories to the samples for bacterial culture to identify and test for antibiotic-resistant organisms.

Implications for Positive Social Change

The association of laboratory practices or sample handling and AMR was the first study conducted at a hospital in Florida and possibly nationwide. Several studies on antibiotic resistance were not about the association between laboratory processing time. Sautter and Halstead (2018) stated that the laboratory has a role in the cases of AMR, but no studies were conducted on how the laboratory could be part of the growing number of antibiotic resistant organisms or emerging pathogens with limited treatment options. The study results through multiple logistic regression analysis with statistically significant results showed that processing time for each sample submitted to the laboratory for

identifying antibiotic-resistant bacteria was associated with the cases of AMR. The result of the study showed that the overall processing of samples within the required time limit was at 80%, and 20% of the samples were more than the required time, which continuously makes physicians treat patients with a broad-spectrum antibiotic which turns out to be unnecessary and triggers the mechanism of bacterial resistance as stated by Aslam et al. (2018) that inappropriate antibiotic treatment results to antibiotic resistance. The implication for positive social change in the study on the laboratory's processing of samples and cases of antimicrobial resistance is that the leaders in the clinical laboratory should work on improving the process for setting up samples for culture as soon as when the samples are received in the laboratory or within 30 minutes. In turn, it would allow a quicker time in the identification of the organisms as well as in the testing of the specific antibiotics and earlier time in the completion and reporting of results. The shortened time will help control the unnecessary antibiotic treatment by physicians, control longer hospitalization, and reduce the financial burden of the hospital in taking care of patients who were unnecessarily treated with antibiotics.

Moreover, the study results will be presented to the laboratory administration and the hospital patient units (e.g., ICU, OR, ED, general medicine). To allow everyone to be aware of the results and explain the importance of the timely collection, submission, and processing of samples, to achieve a 100% processing time for all samples sent to the laboratory for bacterial culture. Anyone not following the right process should be retrained or re-educated to help control antibiotic resistance.

Conclusion

The clinical laboratory plays a significant part in diagnosing and treating patients and must adhere to guidelines and policies in the timely processing and reporting of results to the patient's healthcare provider. The research study on laboratory practices and AMR showed the association between the time of handling patient samples and the cases of AMR in the hospital, which means that any delay in the processing of samples could indicate the presence of antibiotic-resistant microorganisms. The results may indicate the epidemic of unnecessary antibiotic therapies in the Florida hospital. Roger et al. (2019) stated that unnecessary antibiotic treatment results from the absence of antimicrobial testing and unspecified diagnosis. In other words, antibiotic treatments are given to patients without laboratory results, thus unnecessarily using antibiotics for viral or other diseases that are not bacterial. Because either physician would not or could not wait for the results from the laboratory and would treat the patient directly with broad-spectrum antibiotics, which are commonly given to patients and are highly associated with the prevalence of antibiotic-resistant pathogens (Rhee et al., 2020). The biggest part of the laboratory in controlling unnecessary antibiotic therapy and antibiotic resistance is to promptly work on samples for culture, to send results on time, and to communicate the results to the providers for the appropriate antibiotic treatment to the patient. Also, to reduce hospital stay and the cost of hospitalization and, most importantly, for the control, prevention, and reduction of the number of antibiotic-resistant organism infections in the Florida hospital.

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