Antimicrobial Resistance Pattern of Common Bacterial isolates in Soddo Christian Hospital

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A Thesis Submitted to

The Department of Pharmacology and Clinical Pharmacy, School of Pharmacy, College of Health Sciences, Addis Ababa University

Presented in Partial Fulfillment of the Requirements for the Degree of Master of Pharmacy in Pharmacy Practice

Addis Ababa University

Addis Ababa, Ethiopia

January, 2017

Addis Ababa University

School of Graduate Studies

This is to certify that the thesis prepared by Yalemzerf Worku entitled: *Antimicrobial Resistance Pattern of Common Bacterial isolates in Soddo Christian Hospital, Wolaita Soddo Zone, SNNPR* and submitted in partial fulfillment of the requirements of the Degree of Master of Pharmacy in Pharmacy Practice complies with the requirements of the university and meets the accepted standards with respect to originality and quality.

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Abstract

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Addis Ababa University, 2016

Infectious diseases are the leading causes of mortality and morbidity in developing countries. Management of infectious disease requires potent and effective antimicrobial drugs to which the virulent organisms are susceptible.. A retrospective cross-sectional study was done by reviewing 1500 microbiology records from September, 2009 to August, 2014. From 1500 microbiology records, 1086 bacteria were isolated. Among these (4.9%) were mixed infection . The most common isolated bacteria were S. aureus and P. aeruginosa with an isolation rate of (17.3) and (14.3%) respectively. About 47.4 % of S.aureus was oxacillin/methicillinresistant (MRSA).Ontheother hand, the resistance rate of S. aureus was lower to ceftriaxone 172 (19.8%).

S. pyogenes was resistant to tetracycline while lower resistance was observed to erythromycin,. The highest resistance rate of P. aeruginosa and E. coli were found to ampicillin and amoxicillin. From multidrug resistant bacteria, majority were gram negative among which P. aeruginosa (97.7%) was the highest followed by E. coli (95.1%). Among gram positive MDR bacteria S.aureus (89.1%) was the highest followed by S. epidermidis (87.5%). The findings of this study show that there is high resistance rate of bacterial isolates to the commonly used antimicrobials. To benefit maximum antimicrobial effect from the active antimicrobials and to reserve the threatened ones rational use of antimicrobials should be practiced.

Key Words: Antimicrobial Resistance, Antibiotic Susceptibility, Bacterial Isolates.

Acknowledgements

It is my pleasure to express my heartfelt gratitude to my advisor Teshome Nedi (PhD) for his guidance, support and appreciable advice provide me. Besides my advisor, my special thanks goes to Mr. Yisihak Abraham (microbiologist) for his insightful comments and encouragement.

I would like to thank to all of my friends, for all their support.

I would like to express my warm thanks to all the professionals of the bacteriology laboratory department of the hospital and the data collectors for their unreserved support and persistent effort during the data collection.

I would also like to thank Addis Ababa University for allowing me to join this program and for sponsoring this study.

I am very much glad to thank Wollaita Sodoo Christian Hospital for allowing me to do my project in the hospital and their full support.

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List of Abbreviations /Acronyms

AMR	Anti Microbial Resistance
DACA	Drug Administration and Control Authority
MDR	Multi Drug Resistant
SCH	Soddo Christian Hospital
SNNPR	South Nations, Nationalities and Peoples Region
TASH	Tikur Anbesa Specialized Hospital
WHO	World Health Organization
WSU	Wolaitta Soddo University

1. Introduction

1.1 Background

One of the major contributions to health care delivery in the 20th century is the discovery of potent antimicrobial agents (Mordi and Momoh, 2008). However, the emergence of resistance of bacteria to the antimicrobials raises serious concern and poses a growing threat to health-care delivery and a danger to the public globally (Godebo *et al*., 2013; Mordi and Momoh, 2009; Nkang *et al*., 2009). Though antibacterial drugs have been regarded for more than 60 years to cure infections, whether the infection was acquired in the community or in the hospital setting (WHO, 2014) resistance to antimicrobial agents has been recognized since the dawn of the antibiotic era. That is, the discovery of antimicrobial agents had a major impact on the rate of survival from infections but the changing patterns of antimicrobial resistance(AMR) caused a demand for new antibacterial agents (Nkang *et al*., 2009). Certainly, we are in a crisis of resistance with respect to antibacterial agents because of the fact that antibiotic resistance has come to be accepted as an inevitable consequence of antibiotic use (WHO, 2014).

Antibiotics are among the drugs most commonly used in health care systems where prescription is mostly made on empirical basis by prescribing broad-spectrum antibiotics (Getachew *et al*., 2013) which lead to increasingly emerging bacterial resistance to the frequently used and cheaper antibiotics in the market and in turn poses serious threat to the public and medical practitioners (Mordi and Momoh, 2009; Nkang *et al*., 2009). The widespread uses of antibiotics, together with the length of time over which they have been available have led to major problems of resistant organisms, contributing to morbidity and mortality (Azene and Beyene, 2011; Dipiro *et al*.,2011).

The development of each new antibacterial drug has been followed by the detection of resistance to it. This is because of the fact that the development of resistance is a normal evolutionary process for microorganisms and it is accelerated by the selective pressure exerted by widespread use of antibacterial drugs (WHO, 2014).

Resistant strains are able to propagate and spread where there is non-compliance with infection prevention and control measures (WHO, 2014; Dipiro *et al*.,2011). As the result, the effectiveness of currently available antibiotics is decreasing due to the increasing number of resistant strains causing infections. Once a resistant organism is introduced into a population, it is rapidly disseminated (Nkang *et al*., 2009). Therefore, it is essential to preserve the efficacy of existing drugs through measures to minimize the development and spread of resistance to them, while efforts to develop new treatment.

Available therapeutic options for antibiotic-resistant organisms are severely limited, as these organisms frequently display a multi-drug resistant (MDR) phenotype (Grant *et al*., 2014) and hospitals are the breeding ground for increasingly resistant microorganisms.

Patterns of antibiotic use and drug resistance vary from country to country and even between neighboring hospitals. Assessing the patterns of drug resistance over time can inform decision makers to implement strategies to control the development of antimicrobial resistance.

1.2 Statement of the Problem

The discovery of antimicrobials is one of the most important advances in health in human history alleviating suffering from disease and saving billions of lives over the past years. However, their life-saving power is compromised by emergence of antimicrobial resistance. Currently, antimicrobial drug resistance has become a public health concern both in developing and developed countries and is dramatically accelerated when antimicrobials are misused(Alamneh YD, 2014)..

Infectious diseases of bacterial origin are a major cause of morbidity and mortality in developing countries such as Ethiopia**.** To minimize such burdens, proper use of antibiotics plays a vital role and saves countless lives. However, the emergence of bacteria resistant to antimicrobials paused a problem (Chelkeba L (2013).

Although studies on antimicrobial resistance in different parts of Ethiopia have been conducted, pathogenic bacteria isolation and antimicrobial resistance is variable and influenced by geographic location, variations in patient population, infection control practices, level of health facility, and regional antibiotic uses (DACA , 2009).

This influences empiric antimicrobial choices which should be based on local isolation and susceptibility studies. Thus, knowledge of local pathogenic bacteria isolates and susceptibility patterns is required to detect any changes on time through periodic investigation so that modification and recommendation for empiric therapy of bacterial infections could be made (Diane etal.,2012).

There is a paucity of data regarding antimicrobial resistance of common bacteria in Wolaita Soddo Zone hence this study was initiated to provide data regarding antimicrobial resistance of common bacterial pathogens. Outcomes of this study would help in the understanding of current bacterial isolates and pattern of drug resistance in the hospital and hence serves as a guide for updating clinical guidelines and empiric antibiotic therapy.

1.3 Literature Review

1.3.1 Antimicrobial Resistance Pattern

Use of antibacterial drugs has become widespread over several decades to cure infections whether or not their use is appropriate (Kumar *et al.*, 2013). These drugs have been extensively misused in both humans and animals in ways that favor the selection and spread of resistant bacteria (Chowdhury *et al.*, 2013). Consequently, antibacterial drugs have become less effective resulting in an accelerating global health security emergency (Omulo *et al.,* 2014).

Over the past few years several studies in the world and African countries had reported the presence of anti-microbial resistant strains from clinical and environmental specimens. Recognition of resistance pattern of bacteria is necessary from time to time to give appropriate treatment and avoid adverse clinical outcomes (Kumar *et al.,* 2013).

Currently many study have shown that commonly isolated bacteria from different specimen such as *S. aureus* , *E. coli* and *P. aeruginosa* are resistance to many commonly used antimicrobials. Studies conducted on antimicrobial resistance in Ethiopia indicated increasing resistance rates of these commonly isolated pathogens to commonly prescribed antibiotics, including ampicillin, amoxicillin, penicillin, tetracycline and co- trimoxazole **(**Mulu *et al.,* 2012 ; Azene and Beyene, 2011; Mama *et al.*, 2014).

A study conducted in Nepal on isolates of wound infection , *S. aureus* showed high level of drug resistance to oxacillin and cotrimoxazole (Raza *et al.,* 2013). In addition, a study conduct in Bangladesh on isolates of different spacemen showed that *S.aureus* were resistant to amoxicillin, cotrimoxazole, ciprofloxacin and erytromycin (Chowdhury *et al.,* 2013). A retrospective study at Dessie showed that *S.aureus* was mostly resistant to amoxicillin, and tetracycline (Azene and Beyene , 2011). Similarly a study done in Felege Hiwot Referral Hospital isolated from nosocomial surgical site and blood stream infection reported that it was resistant to ampicillin, amoxicillin and ceftriaxone (Mulu *et al.*, 2012). A study conducted in Jimma University Specialized Hospital, isolates from wound infection reported that *S.aureus* was highly resistance to ampicillin , penicillin and tetracycline (Mama *et al.*, 2014). furthermore a study conducted in Gondar teaching hospital, *S.aureus* isolates from pus and/or wound discharge were resistant to tetracycline, ampicillin, cotrimoxazole and penicillin. In addition among isolates tested, 18.3% of the isolates are becoming resistant to ceftriaxone and 33.3% for vancomycin (Muluye *et al.*, 2014).

In addition to *S.aureus* isolates , *E.coli* strain also showed high resistance of commonly used antibiotics. Antimicrobial resistant global Report by World Health Organization (WHO) reported that it was resistance to fluoroquinolones and third-generation cephalosporin's in different country and for severe infections, for which *E. coli* a likely cause, may need to be initiated with broad spectrum agents like carbapenems in these populations **(** WHO 2014).

A retrospective study conducted in the Panjab University using urine samples from outdoor patients of UTI *E. coli* strain showed a high level of resistance to ciprofloxacin, norfloxacin, amoxicillin and cotrimaxozole. (Manjula *et al.*, 2013**)**.

A study conduct in Bangladesh on isolates of different spacmen showed that *E.coli* were resistant to amoxicillin, cotrimoxazole, gentamycin , tetracycline, ciprofloxacin and ceftriaxone (chowdhury et *al.*,2013). A study conducted in Jimma and Mekelle, reported that *E.coli* isolates were resistant to ampicillin, tetracycline, ceftriaxone , cotrimoxazole and gentamycin. (Mama *et al.*, 2014; Mengesha *et al.*, 2014).

P. aeruginosa also highly resistance to currently used drugs. A study conducted in Bangladesh on isolates of different spacemen showed that *P. aeruginosa were* resistant to amoxicillin, cotrimoxazole and tetracycline (chowdhury et *al.,*2013). In addition it also resistant to ofloxacin , ceftriaxone , cephalexin, ciprofloxacin and cotrimoxazole (Raza *et al.,* 2013**)**. Study conducted in Mekelle isolated from wound infection *P. aeruginosa* isolates were 100% resistant for ceftriaxone, amoxicillin, cotrimoxazole and tetracycline (Mengesha *et al.,* 2014).

A study from Felege Hiwot Referral Hospital showed that *P. aeruginosa was* 100% resistant for ceftriaxone, amoxicillin, ampicillin and nitrofurantoin. However, tetracycline and norfloxacin were drugs which relatively showed low resistant rate (Mulu *et al.,* 2012).

A study conducted in Jimma University Specialized Hospital, reported that *P. aeruginosa* have high frequency of resistant to ampicillin, penicillin and tetracycline `(Mama *et al.,* 2014).

1.3.2. Factor Affecting Antimicrobial Resistant

There are numerous potential reasons for increasing antimicrobial resistant, including drug related factors (widespread use of antibiotics, inappropriate empiric choices, use of broad-spectrum agents) and patient related factors .'(Chowdhury *et al.,* 2013; Dukes, 2012;_Leung *et al.* 2011; Tennant *et al.* 2010).

Wide spread use of antibiotics has been a major contributor to antibiotic resistant among common bacterial species. A study conducted in India reported that anti-infective agents were the most commonly used empiric therapy without sensitivity test (Venka *et al.* 2013). Additionally, a study done on antibiotic prescribing pattern in Wollo university reported that many antibiotics were still prescribed empirically in inappropriate dose and frequency of administration. In addition to selecting the incorrect antibacterial for an infection, irrational prescribing is also observed in prescribing antibacterial for conditions that do not require antibacterial at all (Getachew *et al.* 2013). Moreover, a study by Chelkeba reported that most antibiotic therapy were prescribed with incorrect dose, frequency and duration of administration (Chelkeba *et al.* 2013).

Among patient-related factors that were reported to be associated with antimicrobial resistance are believe and perception towards medication (Charani, *et al.* 2011), absence of health education on antibiotic use and resistance for patients (Alamneh, 2014), self-medication practices (Eticha and Mesfin , 2014) and non-adherence (Charani, *et al.,* 2011).

From health system related factors, health care professionals associated are one of the factor contributing to the increase of AMR. Most prescribers prescribe without a clear diagnostic result and antimicrobial susceptibility test. This indiscriminate use of antibiotics presents a major problem to the control of infectious disease (Tennant *et al.*, 2010). Baseline survey carried out by Drug Administration and Control Authority (DACA, 2009) at national level showed that almost all prescribers used clinical symptoms and signs to prescribe antibiotics, while culture and sensitivity tests were sent to only 2.2% of patients. Moreover, most of prescribers didn't know bacterial resistance patterns to commonly prescribed antibacterial in their health facilities **(**DACA, 2009). Furthermore, lack of continuing education and updated information for prescribers and dispenser might have contributed to the development of antimicrobial resistance (Getachew *et al.,* 2013).

1.3.3 Impact of Antibacterial Drug Resistance

The consequences of resistance to both individuals and the public are severe. Infections caused by resistant microbes fail to respond to standard treatment, causing treatment failures that leads to un treatable serious infections that were readily treatable until recently (WHO , 2014; Omulo *et al.,* 2014).

Patients receiving cancer treatment, organ transplants and other advanced therapies are particularly vulnerable to infection. When treatment of an infection fails in such patients, the infection is likely to become life-threatening and may be fatal (Smith *et al.,* 2013).

Antibacterial drugs used to prevent postoperative surgical site infections have become less effective or ineffective (O'Neill *et al.,* 2010). Treatment of infections with resistant strains may require the use of expensive and potentially toxic second or third line of drugs it leads to longer hospital stay due to side effects (Mulu *et al.*, 2012).

WHO study show that *E. coli* strain and *K. pneumoniae* infections were resistance to third-generation cephalosporins and fluoroquinolones. It has great impact on health and economic burden of infections caused by *E. coli* strains. In addition, there is a risk that may lead to un necessarily high usage of broad-spectrum antibacterial drugs, which will exacerbate the resistance problem (WHO, 2014; Smith *et al.,* 2013).

Antibiotics will be ineffective against these resistant microorganisms which lead to persistence and spread of these infections in the community and thus expose the general population to the risk of contracting a resistant strain of infection (John *et al.*, 2011).

There will be an increase in the cost associated with longer period of hospitalization and hospital- acquired infection occurs and infection control procedures required; greater likelihood of death due to inadequate or delayed treatment.

According to the World Health Organization (WHO), AMR is possibly the single biggest threat facing the world in the area of infectious diseases (WHO, 2014). Systematic literature review study conducted in London from 2000-2012 in the world show that the costs of AMR are a vast range of figures, from £5 to more than £20,000 million in reported additional costs per patient per episode for hospital costs (Smith *et al.*, 2012).

2. Objectives of the Study

2.1 General Objective

To assess the resistance pattern of bacterial pathogens to antimicrobials at Soddo Christian Hospital, Wolaita Soddo, SNNPR Ethiopia.

2.2 Specific Objectives

- To identify commonly isolated bacteria
- To assess antimicrobial resistance pattern of isolated bacteria
- To determine the multidrug resistance pattern of isolated bacteri
- To describe the trend of antimicrobial resistance from September, 2009 to August 2014

3. Methodology

3.1 Study Area and Period

Soddo Christian hospital is a general hospital organized as a private limited company located in Wolaita Soddo zone, SNNPR. It is founded as a non-profit making organization under the administrative board of the Saint Luke health foundation in North America. It provides medical services to all regular and referral cases from the region and across the nation. It works in collaboration with the Tikur Anbesa Specialized Hospital (TASH) where orthopedic residents attach for a month in rotation. The hospital renders services of emergency medicine, outpatient, pediatrics, internal medicine, gaynacology/obstetrics and surgery. Radiological services including CT scan are available. There is a well equipped laboratory with all chemistry, microbiology and pathology services. Currently, the hospital has 120 beds. There are 70 health professionals that have different levels and fields of specialty like medical microbiologist, internist and others. The study was conducted from 5-30 June, 2015.

3.2 Study Design

A retrospective cross-sectional study was done from 5-30 June, 2015 at Soddo Christians Hospital using bacteriology laboratory records from 2010 to 2014.

3.3 Population

3.3.1 Source Population:

- All patients who came in the hospital between September, 2009 to August, 2014.

3.3.2 Study Population

- All patients who got culture and sensitivity tests of bacteria between September, 2009 to August, 2014 which fulfill the inclusion criteria of the study.

3.3.3 Inclusion and Exclusion Criteria

Inclusion criteria

- All patients who were sent to the bacteriology laboratory from different wards of the facility for culture and sensitivity tests of bacteria September 2009 to August, 2014.

Exclusion criteria

- Incompletely filled microbiology records

3.4 Sample Size

The sample size of the study was all patients who got culture and sensitivity tests of bacteria and recorded on microbiology records between September, 2009 to August, 2014 which fulfilling the inclusion criteria of the study. As a result 1500 microbiology records were found to fulfill the inclusion criteria of the study and hence were included in the study.

3.5 Study Variables

3.5.1 Independent Variables

- age
- sex
- type of bacteria
- site of specimen

3.5.2 Dependent Variable

- Antimicrobial resistance

3.6 Data Collection

3.6.1 Data Collection Instrument

A data abstraction format was used to record data from microbiology records (annex I). The data abstraction format contains laboratory number, date of culture and sensitivity, age and sex of the patient, the name of identified bacteria, source of specimen and the susceptibility test results to antimicrobials recorded as sensitive, intermediate or resistant.

3.6.2 Data Collection Technique

Microbiology record review was performed and a data abstraction format was completed for each eligible microbiology record to obtain laboratory number, date of culture and sensitivity, age and sex of the patient, the name of identified bacteria, source of specimen and the susceptibility test results to antimicrobials recorded as sensitive, intermediate or resistant. In the microbiology laboratory identification of bacterial isolates was determined by standard microbiological techniques and antimicrobial susceptibility tests was done according to the standard operational procedures, conducted on Mueller-Hinton agar using the modified Kirby-Bauer disc diffusion method. The antimicrobial discs used were: penicillin (10 U), tetracycline (30 µg), ampicllin (10 µg), gentamycin (10 µg) , cotrimoxazole (5µg), vancomycin (30 µg), erythromycin (15 µg), ceftriaxone (30 µg), amoxicillin (10 µg), ciprofloxacin (5 µg), norfloxacin (10 µg), clindamycin (2 µg), , cefotaxime(30 µg), and oxacillin (1 µg*). S.aureus* isolates resistant to oxacillin (1 µg) were identified as MRSA.

3.6.3 Data Collectors

Two laboratory technicians and one medical microbiologist were recruited as data collectors and trained for one day on techniques of data collection.

3.7 Data Quality Control

The data collectors were trained for one day before the process of data collection. Supervision and checking was made by the principal investigator to ensure the completeness and consistency of the collected data. All collected data were examined for completeness and consistency during data management, storage and analysis.

3.8 Data Entry and Analysis

Data was entered and cleaned using EpiInfo version 2.3.1 and analyzed by statistical package for social sciences (SPSS) version 20.0. Descriptive statistics such as frequency and percentage were used to summarize demographic characteristics, status of bacteria growth, prevalence of resistance of each antimicrobial and species specific resistance rate.

3.9 Ethical Consideration

Ethical clearance was obtained from School of Pharmacy, Addis Ababa University Ethics review committee. The purpose and data collection procedure of the study was clearly communicated with the hospital and involved staff in the research process. Permission was obtained from the hospital administrator, medical director and laboratory head. Confidentiality of the data obtained was maintained by coding and using no patient identifier.

3.10 Operational Definitions

Multidrug resistance: Resistance of an organism to two or more antimicrobial drug.

Susceptible bacteria: When antibiotics are effective at killing or stopping the growth of a certain bacteria..

Antimicrobial resistance: The ability of microbes to resist the effects of drugs which is the germ are not killed, and their growth is not stopped

4. Results

4.1 Demographic Characteristics

Totally 1500 microbiology records were included in the study. Among 1500 microbiology records majority of the specimen were male 1059 (70.6%) and more than one third 557 (37.1) were in the age range of 15-29 years ranging from 1 month to 95 years as shown in Table1.

Table 1: Socio-demographic characteristics of patients attending at Soddo Christian Hospital, 2009 - 2014

Characteristics	**Number (%)**
Gender	
Male	1059 (70.6)
Female	441 (29.4)
Age (Years)	
<5	76(5.1)
5-14	246 (16.4)
15-29	557 (37.1)
30-60	524 (34.9)
>60	53 (3.5)
Not recorded	44(3.0)
Total	**1500 (100)**

4.2 Type of Specimen and Bacteria Growth Status

From the total specimens collected pus contributed the highest 1282 (85.5%) followed by urine 135 (9.0%). From 1500 specimens collected 1035 showed growth of bacteria with an isolation rate of (69.0%) from which the highest was obtained from pus 924(89.3) as shown in Table 2.

Table 2: Sources of specimen for clinical investigation in Soddo Christian Hospital, 2009 -2014

Specimen	Total Specimen (%)	Growth Bacteria (%)	Percentage from the respective specimen
pus	1282 (85.5%)	924(89.3)	72
Urine	135 (9.0%)	67(6.5)	49.6
Stool	37 (2.5%)	29(2.8)	78.4
Blood	18(1.2%)	4(0.39)	22.2
Vaginal discharge	13(0.9%)	7(0.68)	53.8
Throat swab	2 (0.1%)	1(0.1)	50.0
Others[1]	13 (0.9%)	3(0.29)	23.1
Total	1500(100)	1035(100)	69,0

[1] *Others include: Sputum, , Urethral discharge, , Pleural fluid, Peritoneal fluid, Ascites fluid, and Synovial fluid.*

source of pus : bone infection; Wound; Ear discharge and Soft tissue

4.3 Prevalence of Bacteria Isolates

From the 1035 specimens, 1086 bacteria were isolated. Among these a single infection was found in 984 (95.1%) and double infection were found in 51 (4.9%) of the specimens. From the double infection 42 were from pus and 9 from urine. *S.aureus* were the most abundant pathogens in the double infection which were found in 16 patients, followed by *S. pyogene* (11) and *P. aeruginosa* (8). *Enterobacter spp, E.coil, N. gonorrhea, α-hemolytic streptococci and Klebsiella spp.* accounted for the remaining.

The prevalence of gram negative and gram positive bacteria was 52.4% and 47.6% respectively. The top specimens from which the isolated bacteria were pus 976(89.3). Among the bacteria isolates *S. aureus* 188 (17.3%), *S. pyogene* 185 (17.0%) , *P.aeruginosa* 155 (14.3%) and *E.coli* 121 (11.4%) were the most common as presented in Table 3.

Table 3: Prevalence of bacterial isolates from different specimen in SCH, 2009 - 2014.

	Pus	urine	stool	blood	Vaginal Discharg e	Throat swab	Others[1]	Total Isolate
Gram Positive Bacteria								
S. aureus	181(35.7)	5(2.7)	0	0	0	1(0.5)	1(0.5)	188(17.3)
S. Pyogenes	182(35.9)	2(1.1)	0	0	0	0	1(0.5)	185(17.0)
α-hemolytic streptococci	113(22.3)	0	0	0	0	0	0	114(10.5)
S. epidermidis	30(5.9)	0	0	0	0	0	0	30(2.8)
Subtotal	**506**	**7**	**0**	**1**	**0**	**1**	**2**	**517(47.6)**
Gram Negative Bacteria								
P. aeruginosa	151(32.1.)	3(1.9)	1(0.6)	0	0	0	0	155(14.3)
E. coli	91(19.4)	28(23.1)	2(1.7)	0	1(0.8)	0	1(0.8)	121(11.4)
K. pneumonia	37(7.8)	4(6.4)	2(3.2)	0	0	0	0	63(5.8)
Enterobacter spp.	57(12.1)	1(1.6)	2(3.3)	2(3.3)	0	0	0	61(5.6)
Other *Pseudomonas* spp.	60(12.7)	0	1(1.8)	0	0	0	0	55(5.1)
N .gonorrhea	29 (6.7)	4(13.3)	0	0	1(3.3)	0	0	30(2.8)
Other *Klebsiella* spp.	16(3.4)	0	0	0	0	0	0	16(1.5)
P.mirabilis	15(3.1)	10(43.5)	1(4.4)	0	2(8.7)	0	0	23(2.1)
P. vulgaris	3(0.6)	10(62.5)	0	0	3(18.8)	0	0	16(1.5)
Other *Proteus* spp.	5(1.0)	0	0	0	0	0	0	3(0.3)
Shigella spp.	1(0.2)	0	12(92..3	0	0	0	0	13(1.2)
Salmonella spp.	5(1.1)	0	8(61.5)	0	0	0	0	13(1.2)
Subtotal	**470**	**60**	**29**	**2**	**7**	**0**	**1**	**569(52.4)**
Total	**976(89.8)**	**67(6.2)**	**29(2.7)**	**3(0.3)**	**7(0.7)**	**1(0.1)**	**3(0.3)**	**1086**

[1] *Others include:, Sputum, , Urethral discharge, , pleural fluid, peritoneal fluid, ascites fluid, and synovial fluid .*

4.4 Antimicrobial Resistance pattern of Isolated Organisms

Analysis of species specific resistance rates indicated that from the total of *S. aureus* (188) isolated, about 47.4 % of *S.aureus* was oxacillin/methicillin resistant (MRSA). On the other hand, the resistance rate of *S. aureus* was lower to ciprofloxacin 174 (16.1%) and ceftriaxone 172 (19.8%). *S.pyogenes* was resistant to tetracycline 105 (75.4%) while lower resistance was observed to erythromycin 161 (36.7 %), vancomycin 109(29.4%) and ciprofloxacin 176 (14.7%). as shown in table 4.

Table 4: Antibiotic resistance rate of gram positive bacteria in Soddo Christian Hospital, 2009 - 2014.

Antimicrobial	*S. aureus* N=188		*S. pyogenes* N=185		α-hemolytic streptococci N=114		*S. epidermidis* N=30	
	Ta	% Rb	Ta	% Rb	Ta	% Rb	Ta	% Rb
Clindamycin	179	36	180	32.8	110	32.7	28	28.6
Vancomycin	114	35.1	109	29.4	68	29.4	19	30.6
Erythromycin	150	36.7	161	36.7	89	*31.5*	27	33.3
Tetracycline	-	-	105	75.4	87	*41.4*	15	53.3
Ceftriaxone	172	19.8	172	16.3	107	*25.2*	26	15.4
Norfloxacin	113	31.0	-	-	-	-	21	19.1
Ciprofloxacin	174	16.1	176	14.7	108	*17.6*	26	15.4
Gentamycin	165	25.5	169	23.1	105	*35.2*	24	33.3
Penicillin	173	54.9	176	30.6	106	*52.8.*	26	50.0
Amoxicillin	175	63.4	172	32.2	105	58.1	28	60.7
Ampicllin	175	61.7	172	31.7	102	56.9	27	55.6
Doxycyclin	170	28.8	169	29.6	103	33.0	28	28.6
Oxacillin,	135	47.4	-	-	-	-	-	-
Cefotaxime	137	38.0	141	30.5	86	32.6	24	20.8

Ta = Total number of isolates tested against each antimicrobial agent,

Rb= Percent of isolates resistant to the antimicrobial agent

From the gram negative isolates *P. aeruginosa* showed high resistance rate to ampicllin 142 (72.9%) and amoxicillin 144 (68.3%) while lower resistance rate was observed to ciprofloxacin 148(31.8%) and ceftriaxone 143 (31.5%).

The highest resistance rate of *E. coli* isolates was to ampicllin 104 (76.9%) followed by amoxicillin 105 (67.6%) while lower resistance was observed to ciprofloxacilin 108 (23.2%) and ceftriaxone 102 (33.3%). The resistance rate of gram negative isolates is presented in table 5.

Table 5: Antibiotic resistance rate of gram negative bacteria. in Soddo Christian Hospital, 2009 - 2014.

Antimicrobial	*P. aeruginosa.* N=155		*E.coli* N=121		*Proteus* spp. N=42		*Klebsiella* spp. *N=179*		*Enterobact er* spp N=61		*N.gonorrhe* N=30		Others* N=26	
	Ta	%Rb	Ta	%Rb	Ta	%Rb	Ta	%Rb	Ta	%Rb	Ta	%Rb	Ta	%Rb
Amoxicillin	142	68.3	105	67.6	38	68.4	72	68.1	57	68.4	24	62.5	25	76.0
Ampicllin	144	72.9	104	76.9	38	57.9	75	69.3	55	70.9	25	60.0	25	84.0
Ciprofloxacin	148	31.8	108	23.2	38	31.6	71	32.4	57	35.1	26	26.9	25	36.0
Ceftriaxone	143	*31.5*	102	33.3	36	41.7	75	41.3	55	41.8	26	26.9	20	50.0
Cotrimoxazole	152	57.9	109	64.2	37	67.6	77	54.5	54	62.9	26	53.8	23	69.6
Tetracycline	103	*56.3*	76	63.2	27	62.9	52	65.4	49	61.2	21	47.6	20	70.0
Norfloxacin	115	*38.3*	88	39.8	26	38.5	54	44.4	49	61.2	20	15.0	21	57.1
Gentamycin	141	46.8	106	43.4	32	43.8	74	40.5	56	41.1	24	37.5	23	47.8
Doxycyclin	146	34.2	107	53.3	39	35.9	72	52.8	53	60.4	26	57.7	24	54.2
Cefotaxime	114	44.4	83	60.2	32	50.0	60	51.7	50	54.0	22	54.6	20	55.0

Ta = Total number of isolates tested against each antimicrobial agent,

Rb= Percent of isolates resistant to the antimicrobial agent

4.5. Multiple Antimicrobial Resistance Patterns of Bacterial Isolates

From the total MDR bacteria, majority were gram negative among which *P.aeruginosa* (97.7%) was the highest followed by *E. coli* (95.1%). Among gram positive bacteria *S.aureus* (89.1%) was the highest followed by *S. epidermidis* (87.5%).

Table 6: Multiple antimicrobial resistance patterns of bacterial isolates in Soddo Christian Hospital, 2009 - 2014

Bacteria	R_1	R_2	R_3	R_4	$R_{5 \text{ \& above}}$	Total	MDR* (%)
S. aureus	16 (10.9)	15(10.3)	16 (10.9)	16(10.9)	83(56.9)	146	89.1
S. epidermidis	2 (12.5)	1(6.3)	1 (6.3)	6(37.5)	6(37.5)	16	87.5
α-hemolytic	8(10.3)	9(11.5)	13 (16.7)	8(10.3)	40(51.3)	78	853
S. pyogenes	15 (10.1)	13(8.7)	17(11.4)	16(10.7)	68(45.6)	149	76.4
P.aeruginosa	3 (2.3)	7(5.3)	7(5.3)	4(3.1)	110(83.9)	131	97.7
E. coli	9 (4.9)	5(2.7)	7 (3.9)	8(4.4)	153(84.1)	182	95.1
Proteus spp.	1 (3.3)	1(3.3)	1 (3.3)	2(6.7)	25(83.3)	30	96.7
Klebsiella spp.	5 (7.1)	2(2.9)	4 (5.7)	2(2.9)	57(81.4)	70	92.9
Enterobacter spp.	5 (9.6)	3(5.8)	1(1.9)	3(5.8)	40(76.9)	52	90.4
Others*	2 (3.9)	1(1.9)	2(3.9)	2(3.9)	45 (86.5)	52	96.1

R_1-resistant to 1 antibiotic, R_2-resistant to 2 antibiotics, R_3-resistant to 3 antibiotics, R_4-resistant to 4 antibiotics, R_5 & above to 5 and above antibiotics

Others*: Shigella, and salmonella species

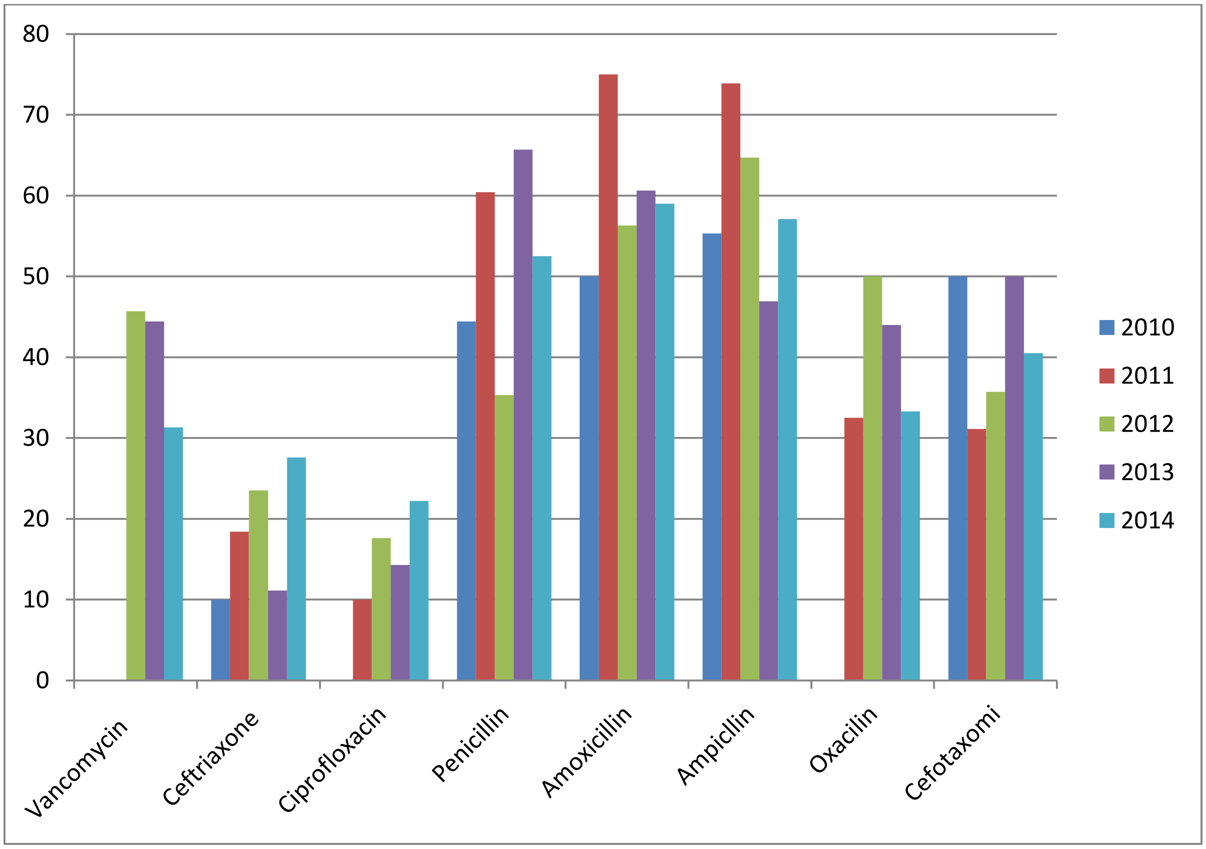
*MDR = Resistance to two or more antibiotics.

4.6 Trend of Antibiotic Resistance

4.6.1 Trend of resistance of *S. aureus*

The resistance trend of *S. aureus* to common antimicrobial had increased from 2010 to 2014 except cefotaxomi and lower resistance rate was observed to ciprofloxacin and ceftraxone in 2014.

fig 1. The resistance trend of *S. aureus* to common antimicrobials



4.6.2 Trend of resistance of *S. pyogene*

S. pyogene isolates showed the highest resistance to tetracycline and while lower resistance rate was observed to ciprofloxacin and vancomycin in 2014.

Table 7: The resistance trend of *S. pyogene* to common antimicrobials

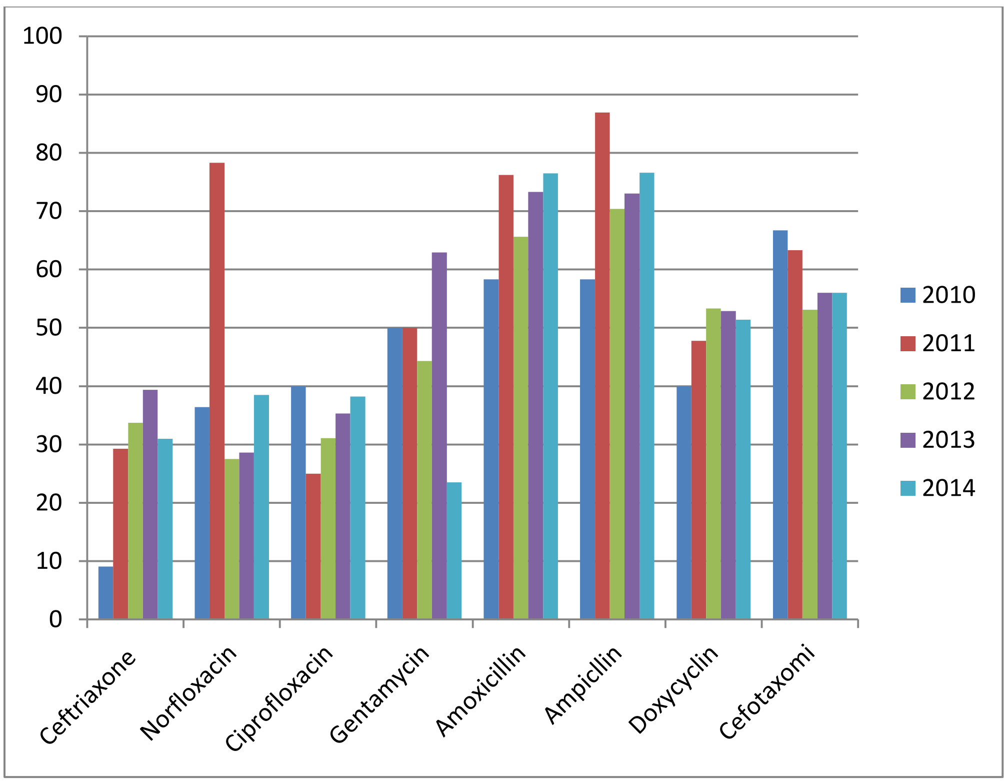
Antimicrobial	2010	2011	2012	2013	2014	χ2	P Value
Clindamycin	33.3	39.1	30.8	24.4	28.6	1.936	0.164
Vancomycin	25.0	0	27.5	36.6	28.6	0.999	0.318
Erythromycin	16.7	34.8	35.5	42.9	33.3	1.831	0.176
Tetracycline	100.0	54.3	66.5.	60.8	75.6	3.812	0.051
Ceftriaxone	0	18.6	39,6	15.0	38.5	1.914	0.167
Ciprofloxacin	25.0	17.8	13.7	17.1	14.1	2.455	0.117
Penicillin	45.2.	56.8	47.5	51.2	33.9	0.166	0.684
Amoxicillin	66.3	70.7	45.0	42.0	53.0	1.488	0.222
Cefotaxomi	47.0	36.8	27.1	35.3	31.3	2.092	0.148

χ2: Chi square for linear trend, P value<0.05 is considered statistically significant,
2010= September 2009-August 2010 ; 2011=September 2010-August 2011; 2012=September 2011-August 2012; 2013=September 2012- August 2013; 2014= September 2013- August 2014

4.6.3 .Trend of resistance of *P.aeruginosa*

P.aeruginosa was highly resistant against most of the antibiotics tested. Furthermore, the resistance rate to all antibiotics tested increased from 2010 to 2014 However, the resistance rate *P.aeruginosa* decreased from 2010 to 2014 to gentamycin and ciprofloxacin as shown in fig 2.

fig 2. The resistance trend of *P.aeruginosa* to common antimicrobials



4.6.4. Trend of resistance of *E. coli*

The highest resistance rate of *E. coli* isolates was observed to ampicllin and amoxicillin in 2014. Whereas gentamycin and cotrimoxazole resistance decreased in 2014 as presented in table 12.

Table 8: Resistance pattern of E. coli to antimicrobials in SCH

Antimicrobial	2010	2011	2012	2013	2014	$\chi 2$	P Value
Tetracycline	50.0	61.5	63.3	55.6	60.0	0.697	0.404
Ceftriaxone	25.0	23.1	35.8	27.3	34.9	1.713	0.191
Norfloxacin	27.3	43.7	38.3	42.1	53.8	0.353	0.552
Ciprofloxacin	0.0	15.4	26.0	14.3	36.7	2.762	0.097
Gentamycin	56.8	30.8	41.4	35.0	46.7	0.653	0.419
Cotrimoxazole	50.0	61.5	64.4	63.6	47.0	1.452	0.228
Chloramphenicol	33.3	50.0	50.0	47.6	37.9	0.078	0.780
Amoxicillin	66.7	80.0	50.0	57.1	72.0	0.107	0.743
Ampicllin	66.7	83.3	66.1	75.0	69.2	0.021	0.885
Doxycyclin	43.0	38.0	54.9	54.0	53.8	1.069	0.301
Cefotaxomi	0	75.0	59.3	65.0	45.8	0.772	0.380

$\chi 2$: Chi square for linear trend, P value<0.05 is considered statistically significant.

2010= September 2009-August 2010 ; 2011=September 2010-August 2011; 2012=September 2011-August 2012; 2013=September 2012- August 2013; 2014= September 2013- August 2014

5. Discussion

Successful management of patient with bacterial infection depends on the identification of bacterial pathogens and determination of their antimicrobial susceptibility pattern from clinical specimens for selection of appropriate chemotherapy. In the study period, in Wolaita Soddo Christian Hospital, from the total 1,500 specimens collected, 1035 samples were found to be positive for bacterial isolates with an isolation rate of 69.0 %. Similar studies were conducted in Gondar where the isolation rate was 70.2% (Muluye *et al*., 2014) and in Hawassa, Jimma and Dessie where the average isolation rate ranged from 68.7 to 71.1% (Kibret and Abera, 2010; Dessalegn *et al*., 2014; Mama *et al*., 2014)

In this study double infection were found in 51 (4.9%) of the patients. From the double infection *S. aureus* was the most abundant pathogen to be followed by *S. pyogene* and *P.aeruginosa* which is similar to findings of other studies (Abraham and Wamisho , 2009; Azene and Beyene, 2011). In addition *S. aureus, E. coli* and *Klebsiella* species were frequently occurred (Dessalegn *et al*., 2014). However, in another study *P.aeruginosa* and *E.coli* were the dominant isolates (Chowdhury *et al*., 2013) indicating varying distribution of bacterial etiology with varying geographical locations.

In this study, the prevalence of gram negative bacteria (52.4%) was higher than the gram positive ones (47.6%). The highest number of isolates was obtained from pus, followed by bone infection and wound. This result agrees with study results reported from other parts of Ethiopia (Abraham and Wamisho, 2009; Kibret and Abera ,2010; Azene and Beyene, 2011; Chowdhury *et al*., 2013; Dessalegn et al, 2014). Among the isolated bacteria *S. aureus*, *S. pyogene, P. aeruginosa* and *E.coli* were the most common ones as in other studies (Muluye *et al*., 2014;

Raza *et al*., 2013; Chowdhury *et al*., 2013). Still other studies reported that predominant bacteria isolated from the infected wounds were *S.aureus, E. coli, P.aeruginosa* and *K. pneumoniae* (Mama *et al.*, 2014; Mulu *et al.*, 2012; Dessalegn *et al.*, 2014).

The above mentioned bacteria are commonly found in the hospital environment which might increase wound infection rate and cross contamination among patients. In other study *K.pneumoniae* recorded the highest occurrence rate followed by *S. pneumoniae* (Egbe *et al.*,2011; Motayo *et al.*,2012). Different species prevalence rates may be related to different spacemen place or their distribution in the various environments.

In this study, antimicrobial susceptibility test was done for 991 (91.3%) of the 1086 bacteria isolated. Most of the isolates were found to be resistant to many of the antibiotics tested such as ampicllin, penicillin, amoxicillin and tetracycline. This recorded result was similar to the study report from Gonder in which most of the isolates were resistant to tetracycline, ampicillin and penicillin (Muluye *et al*., 2014). Similarly, in Jimma (mama *et al.*, 2014), all isolates showed high frequency of resistance to ampicillin, penicillin and tetracycline. In addition, high level of resistance was reported to tetracycline and penicillin from studies conducted in Bahirdar and Dessie (Mulu *et al*., 2012; Kibret and Abera, 2010). Amoxicillin and tetracycline had the highest resistance rate in studies conducted in Nigeria and Dessie (Damen , 2015; Azene and Beyene, 2014). These are the most frequently used drugs in the community and also they are cheap and easily available.

The most frequently isolated bacteria were sensitive to vancomycin, ciprofloxacin , ceftriaxone, norfloxacin and gentamycin .This finding is the same with the results documented from previous studies (Godebo et al., 2013; Azene & Beyene, 2014; Mama *et al*., 2014). This indicates the necessity of considering these active antimicrobials when empiric antibiotic therapy is thought based on the nature of the infection and indication.

The predominant isolates in the present study was found to be *S. aureus* and most of the isolates were resistant to many of the antibiotics tested. It was resistance to amoxicilin , ampicillin and penicillin . Similar results were observed in other study conducted in Ethiopia (Kibret & Abera, 2010 ; Dessalegn et al., 2014 ; Azene & Beyene, 2011; Godebo *et al.*, 2013).

The widespread uses of such antibiotics, together with the length of time over which they have been available have led to major problems of resistant organisms and it contributing to increase morbidity and mortality.

In this study among isolates tested, 47.4 % of the isolates were Oxacillin/methiciln resistant. This finding was lower than 76.7% and 100% resistant *S.aureus* to oxacillin reported by Godebo (Godebo *et al.*, 2013) and (Abraham and Wamisho 2009) in Ethiopia.

Currently the prevalence of MRSA has increased in both healthcare and community settings. MRSA is the leading cause of surgical site infection in the hospital area as result the control of wound infections has become more challenging and increase complications and costs associated with procedures and treatment due to a greater incidence of infections caused by MRSA (WHO 2014).

Moreover, 35.1% vancomycin resistance rate of *S. aureus* in this study were recorded. Similar results were documented to vancomycin resistant (Muluye *et al.*, 2014; Godebo *et al.*, 2013). However in another study found that *S.aureus* is 100% sensitive to Vancomycin (Chowdhury *et al.*, 2013; kishor *et al.*, 2015; Amare *et al.*, 2011). This difference might have resulted from the frequent use of vancomycin, the transmission of vancomycin resistant *S. aureus* from patients to patients or lack of prescription restriction. However, such incidence of vancomycin resistant *Staphylococci* in hospital as well as in community are alarming because vancomycin is currently the main antimicrobial agent available to treat life-threatening infections with MRSA.

The highest percentage of resistance of *S. pyogenes* was to tetracycline, while lower resistance was observed to erythromycin ,ciprofloxacin and vancomycin. This finding was similar to another study conducted in Germany and Senegal , tetracycline showed high resistant and all isolates was susceptible to vancomycin and erythromycin (Imohl & Linden 2015; Camara *et al.*, 2013). Erythromycin is as initial alternate choices for patient who are allergic to penicillin but many study showed that this organism was highly resistance to Erythromycin even thou lower resistance was observed in this study area.

From gram negative bacterial isolates, *P.aeruginosa* were resistant to ampicillin, amoxicillin, cotrimoxazole and tetracycline. Similar results were obtained in another study (Motayo *et al.*, 2012; Kibret & Abera , 2010; Godebo *et al*, 2013; Mulu *et al.,* 2012). In contrast lower resistance rate of the *P.aeruginosa* was recorded to ciprofloxacin, ceftriaxone and gentamycin. Similar result were reported in another study (Motayo *et al*.,2012; Kibret and Abera, 2010 ; Godebo *et al*., 2013).

This organism is frequently feared because it is highly antibiotic resistant, except amino glycosides and fluoroquinolones. The high rate of antibiotic resistant *P.aeruginosa* in burn patients complicates empiric antibiotic therapy. In this study many of the isolates were susceptible to gentamycin and can used in combination with other antibiotics for the treatment of serious infections but are generally not recommended as single drugs (Amare *et al.,* 2011).It is recommended use of combination therapy to prevent the emergence of antimicrobial resistance in patients with *P.aeruginosa* infection.

This study showed that *E. coli* isolates were highly resistant to ampicillin, amoxicillin, cotrimoxazole and tetracycline. This was similar with a report from Dessie (Aypak *et al.*, 2009; Abejew *et al.*, 2014) which is resistant to amoxicillin, ampicillin, tetracycline and cotrimoxazole. It is also relatively sensitive to ciprofloxacin, ceftriaxone and gentamycine. This is similar with another study (Kebira *et al.* 2009; Adedeji & Abdulkadir, 2009).

This study also showed that *Klebsiella s*pecies were highly resistant to ampicillin, amoxicillin, cotrimoxazole and tetracycline. Similar results were recorded in Ethiopia and elsewhere (Mulu *et al*., 2012; Kibret & Abera, 2010 ; Adedeji & Abdulkadir, 2009). Resistance to tetracycline is common because it is readily available in the country and has been widely misused. However, the isolates were less resistant to gentamycin and ciprofloxacin. Comparatively, lower resistance was found in another study (Egbe *et al.*,2011; Motayo *et al*.,2012; Kibret & Abera , 2010; Khorvash *et al*.,2009).

In this study the gram negative bacteria isolates had high MDR 499 (60.3%) than the gram positive bacterial isolates, 328 (39.7%). Also, in another study high MDR rate was seen in gram negative bacterial isolates than the gram positive isolates (Raza *et al.*, 2013). Other Ethiopian studies (Abraham and Wamisho, 2009; Kibret and Abera, 2010) reported similar findings.

However in another study the result was different from this study (Godebo *et al.,* 2013; Mulu *et al*., 2012). This might be choice of antibiotic therapy and epidemiology of causative organisms is different among different place.

Regarding the resistance profile of isolates ,among gram positive bacteria *S.aureus* and *S. epidermidis* had high MDR. This is similar to with another study (Godebo *et al*., 2013; Muluye *et al.*, 2014). In contrast this finding was difference with previous studies done elsewhere in Ethiopia (Mulu *et al.,* 2012) where less average resistance of *S.aureus* were recorded.

From the gram negative *P.aeruginosa* and *E. coli* were high MDR.. It was the same to other study in Ethiopia and other country. (Muluye et al, 2014; Godebo et al., 2013 Mekki et al., 2010)

This indicates that multi-drug resistance is increasingly becoming a major problem in the management of infection in the world including Ethiopia. This may have due to gross misuse, overuse and inappropriate use of the antibacterial agents. This raises alarms to implement a nationwide antimicrobial surveillance and in-vitro susceptibility testing with strict adherence to antibiotic policy to inhibit the spread of drug resistant microbes in the country.

Many of the studies indicated that there are increasing antibiotic resistance. In this study also the resistance rate of the most common antimicrobials was increasing from the starting study period. Thus, knowledge of the recent susceptibility pattern of each antimicrobial is important to gain maximum therapeutic benefit from the most active ones in empiric antimicrobial therapy.

6. Conclusion

High prevalence of bacterial isolates were found from pus. *S. aureus* and *P.aeruginosa* were the dominant bacteria. Most of the isolates were resistant to common antimicrobial used in clinical practices including ampicillin, penicillin, amoxicillin and tetracycline. In contrast, most bacterial isolates were susceptible to ciprofloxacin, ceftriaxone, norfloxacin and gentamycin. In this study multiple drug resistance of isolates to antimicrobials was alarmingly high . It is, therefore, necessary to do an antibiotic susceptibility test before drug prescription to decrease antibiotic resistance.

7. Recommendations

In order to decrease antimicrobial resistance and hence improve infection cure rate it is recommended to the health professional to take their local infecting organism/sensitivity pattern into account when formulating prophylaxis as well as empirical therapy guideline for the hospital. In addition it is recommended that to have strict antibiotic utilization policies within the hospital and assist clinicians in the rational choice of antibiotic therapy and thus, to prevent indiscriminate use of antibiotics.

8. Limitation of the study

As a limitation, this study may not represent general population that live in wolyita soddo area since only those who visited the Soddo Chiristian Hospital bacteriology laboratory included in the study. Only those antibiotics tested in the microbiology laboratory were included in the study. Thus, it may not include all antibiotics used in clinical practice. Being a retrospective study incomplete records and illegible hand writing eliminated some culture results and antibiotics from the study as result it impossible to do correlation analysis of age ,sex and place of the spacemen with etiology and antimicrobial susceptibility.

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Annexes

Annex-1 Data Abstraction Format

Data abstraction format for retrospective antimicrobial resistance pattern study in soddo christian hospital (2010- 2014)

S/No	Lab No.	Sex	Age	Date of culture	Bacteria isolate	Specimen	Penicillin	Tetracycline	Ampicllin	Gentamycin	Oxacillin	Chloramphenicol	Cotrimoxazole	Vancomycin	Erythromycin	Ceftriaxone	striptomycine	Amoxicillin	Ciprofloxacin	Norfloxacin	Clindamycin	Doxycyclin	Cloxacillin	Cefotaxime

Data collector Name/Signature/Date ______________________________