Baseline Assessment of the Current Practice of Antimicrobial Use and Clinical Outcome in the Management of Patients with Pneumonia Admitted to Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia: A Prospective Observational Study

By: Theodros Fenta (Bpharm)

July, 2018

Addis Ababa, Ethiopia

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Addis Ababa University

School of Graduate Studies

This is to certify that the thesis prepared by Theodros Fenta entitled "Baseline Assessment of the Current Practice of Antimicrobial Use and Clinical Outcome in the Management of Patients with Pneumonia Admitted to Tikur Anbessa Specialized Hospital" and submitted in partial fulfilment of the requirements for the degree of Master of Pharmacy in Pharmacy Practice complies with respect to originality and quality.

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Acronyms

AAU	Addis Ababa University
BID	Bis In Die (Twice a Day)
CAP	Community Acquired Pneumonia
CDC	Center for Disease Control and Prevention
CDDEP	Center for Disease Dynamics, Economics & Policy
CHS	College of Health Science
DACA	Drug Administration and Control Authority
FMHACA	Food, Medicine and Health Care Administration and Control Authority of Ethiopia
FDA	United States Food and Drug Administration
FMOH	Federal Ministry of Health
HAP	Hospital Acquired Pneumonia
HCAP	Health Care Associated Pneumonia
ICU	Intensive Care Unit
NGO	Nongovernmental Organization
PFSA	Pharmaceutical Fund and Supply Agency
QD	Quaque Die (Once Per Day)
QID	Quater In Die (Four Times a Day)
SHEA	Society for Healthcare Epidemiology of America
SOM	School of Medicine
SOP	School of Pharmacy
STG	Standard Treatment Guideline
TASH	Tikur Anbessa Specialized hospital
TID	Ter In Die (Three Times a Day)
WHO	World Health Organization

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Abstract

Baseline Assessment of the Current Practice of Antimicrobial Use and Clinical Outcome in the Management of Patients with Pneumonia Admitted to Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia: A Prospective Observational Study

Theodros Fenta,

Addis Ababa University, 2018

Increasing antimicrobial resistance presents a major threat to public health because it reduces the effectiveness of antimicrobial treatment, leading to increased morbidity, mortality, and health care expenditure. In spite of the need for new drugs to treat resistant infections, a growing number of drug companies are withdrawing from new antibiotic research and development. Therefore, the issue of how we can most effectively utilize these precious resources calls for urgent action. Hence, the objective of this study was to assess the current practice of antimicrobial utilization and clinical outcomes in the management of adult pneumonia at Tikur Anbessa Specialized Hospital (TASH), Addis Ababa, Ethiopia and design a strategy for appropriate intervention. A prospective observational study was conducted on adult patients with a diagnosis of pneumonia admitted to TASH. A data abstraction format incorporating self-administered questionnaire were used to gather information from patient charts and treating physicians. Data was analyzed using SPSS version 20. Descriptive statistics and logistic regressions were used. P-values of <0.05 were regarded as significant. Among the total of 200 patients, 52.0% were males and mean age of the patients was 39.79 (SD±17.76) years. Microbiologically and imaging/radiologically examined patients were 75 (37.5%) and 122 (61.0%), respectively. The treatment approaches in almost all patients (99.5%) were empirical. The most commonly used antimicrobial regimens were Ceftriaxone 1gm BID + Azithromycin 500mg, PO, QD, (30.0%) for community acquired pneumonia and Vancomycin 1gm BID + Piperacillin/tazobactam 4.5gm iv QID, (8.0%) for hospital acquired pneumonia and health care associated pneumonia. The duration of antimicrobial therapy was 12 (SD±5). The clinical outcomes of the patients were stable 133(66.5%), and in-hospital mortality 37 (18.5%).

In conclusion, antimicrobials were prescribed empirically without sufficient evidence of indication such as microbiological and radiologic findings.

Key words: Antimicrobials, Antimicrobial resistance, Antimicrobial Stewardship, Pneumonia, Tikur Anbessa Specialized Hospital

1. Introduction

1.1 Background

The introduction of antimicrobials has been the critical component of public health since the discovery of penicillin in the early 1940s (1), saving the lives of millions of people worldwide (2) . The rapid initiation of antimicrobials to treat infections has been proven to reduce morbidity and mortality (3), with a two years back study showing that the prompt administration of antibiotics in the management of sepsis (4).

For decades, the emergence of antimicrobial resistance in some bacterial species caused little alarm, because new and more effective agents with broader antibacterial spectra were being developed (5). However, in the past few years the successful use of any antimicrobial agent is compromised by misuse (3) and the development of resistance to that agent from the time it is first employed (6). The escalation in the diversity and prevalence of antimicrobial resistant bacteria is driven in part by increased antimicrobial use in humans and animals (7) and aided by expanded global trade and human movement (8). According to the CDC summarized report, up to 50% of all antibiotics prescribed in the U.S. acute care hospitals are either unnecessary or inappropriate (2). Similar data was obtained in Australia (5).

The inappropriate antimicrobial use increases morbidity and mortality due to avoidable drug toxicity, suboptimal treatment of the original infection, or subsequent infection with multidrug resistant bacteria, or fungi (9-12). Patients with antimicrobial resistant infections are more likely to experience ineffective treatment, recurrent infection, delayed recovery or even death (13). An all-cause mortality rate of 20.6% at 30 days in Australian and New Zealand patients diagnosed with *Staphylococcus aureus* bacteraemia has been reported, and Methicillin-resistant *Staphylococcus aureus* (MRSA) infections are associated with a higher mortality than infections due to methicillin-sensitive *Staphylococcus aureus* (MSSA) (14). A two-fold higher death rate has been reported among patients with antimicrobial-resistant infections (14).

“One thing we must do, as antimicrobial resistance increases and antimicrobial development declines, is use our current cadre of antimicrobials more wisely. Administering antimicrobials judiciously to extend their useful lifetime is but one of the things we can offer immediately to address this public health crisis. This means optimizing antimicrobial use in humans via the development of a prospective, formalized, strategy to ensure that antimicrobials are used

appropriately" (15). Therefore, the issue of how we can most effectively utilize these precious resources calls for an urgent action and international collaboration for developing effective strategies in combating antimicrobial resistance (16, 17). Among the different approaches that is used to combat antimicrobial resistance (AMR) is establishing an antimicrobial stewardship programs (ASP) in hospitals (15).

An ASP is a systematic approach to developing coordinated interventions to reduce overuse and inappropriate selection of antibiotics, and to achieve optimal outcomes for patients in cost-efficient ways. Through both monitoring and, when necessary, altering current antimicrobial prescribing practices, ASP has been shown to improve patient care, reduce antimicrobial use, reduce antimicrobial resistance, and reduce pharmacy, and overall hospital operating costs (18).

There are different strategies for implementation of ASP in a health care setting (19). Of which the Infectious Diseases Society of America and Society for Healthcare Epidemiology of America (IDSA/SHEA) guidelines identify two core proactive evidence-based strategies for promoting antimicrobial stewardship (18):

1. Formulary restriction and pre-authorization, and
2. Prospective audit with intervention and feedback

In addition, education is crucial for any program that is designed to influence prescribing behaviors. Programs are needed to disperse information in an accurate and timely fashion. Since personnel can change over time, it is also important that the message be repeated routinely. Effective implementation of ASPs will incorporate education along with active strategies, such as prospective audit and intervention (19).

Guidelines and clinical pathways can improve antimicrobial utilization by multidisciplinary development of evidence-based guidelines that incorporate local microbiology and resistance patterns. However, it is important to note that antimicrobial selection is only one component of these recommendations. Diagnosis and testing, admission criteria, nursing care, conversion to oral medication, and discharge planning can also impact quality of care and resource utilization.

A number of studies have shown that the introduction of an ASP in a hospital was associated with improved microbiologically targeted therapy, clinical outcome, expenditure (20, 21). This program effectively coordinates and promotes the hospital antimicrobial rational use (22).

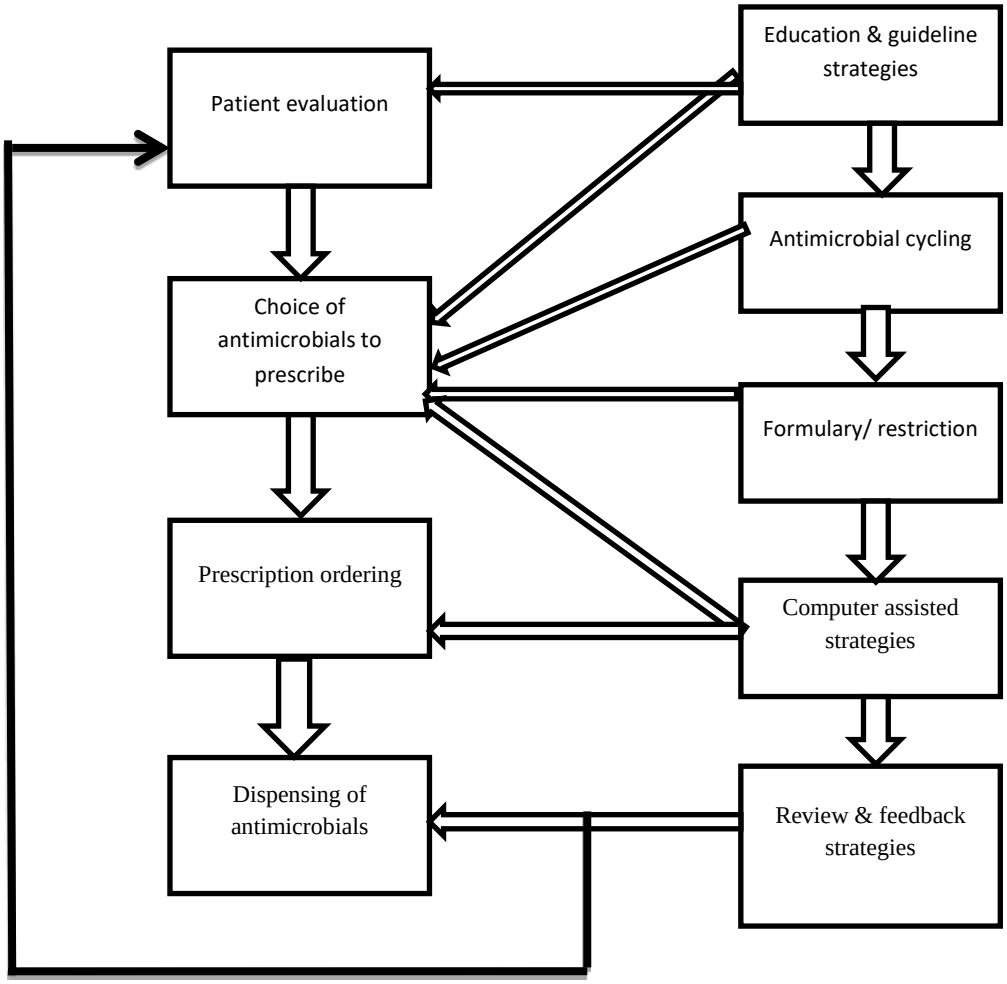

Figure 1. Antimicrobial prescribing process and antimicrobial stewardship strategies.

Across healthcare systems in different countries, there is a need for governmental regulations to mandate the implementation of ASP. In recent years, many countries have incorporated ASP as a standard to be implemented in each health facility (23-25). In 2015, this serious issue reached at the White House getting socio-political attention and a national action plan for combating antibiotic resistant bacteria was developed and the role of ASP is boldly underlined (26). However, this promising program is not yet established in Ethiopian hospitals.

1.2 Statement of the Problem

Increasing antimicrobial resistance presents a major threat to public health because it reduces the effectiveness of antimicrobial treatment, leading to increased morbidity, mortality, and health care expenditure (27). About 2 million cases of infection with resistant bacteria have been reported in the United States every year which leads to the death of 23,000 people and a direct healthcare incremental cost of 20 billion dollars (16).

Antimicrobial drug utilization is a major driver of antimicrobial resistance (28). A study in Tikur Anbessa Specialized Hospital (TASH) in Ethiopia has shown the inappropriate use of antimicrobials especially cephalosporins (29). In this study, one of the major reasons for inappropriate antimicrobial use was the management of pneumonia. Pneumonia is one of the leading causes of morbidity and mortality as far as infectious disease is concerned (30). The number of hospitalizations for pneumonia has been increasing in recent years, mainly among elderly patients and those with multiple co-morbidities (31, 32).

The possible consequences of inappropriate antimicrobial use include toxicity, the emergence of antimicrobial resistance, *Clostridium difficile* and other hospital-acquired infections (HAIs), increased morbidity and mortality, prolonged hospitalization, and increased health care expenditures (9, 11, 12).In spite of the pressing need for new drugs to treat resistant infections, the rapid emergence of antimicrobial resistance and the high cost of research and development of antimicrobials, a growing number of drug companies are withdrawing from new antimicrobial research and development (33).

Recently, AMR threatens the successful treatment of many common infections and now becoming a public health security crisis across the globe (34). The AMR review reported that about 10 million AMR related deaths will be per year by 2050, with the majority in Africa and Asia (35).

Literatures have shown that there are high burden of infectious diseases in sub-Saharan Africa and the potential health and economic consequences thereof are huge but the extent of antimicrobial resistance in the region including Ethiopia remains unknown (36, 37). Little data exists to quantify the contribution of different factors to the current levels of antimicrobial resistance.

The Ministry of health and its subordinates particularly, the Ethiopian Food, Medicine and Healthcare Administration and Control Authority (FMHACA), have been working together to combat antimicrobial resistance through developing national drug policies(38) and treatment guidelines for the different health care institutions (39). FMHACA has also developed national strategic framework for the prevention and containment of antimicrobial resistance in 2011 and the objective of this document is to tackle antimicrobial resistance through promotion of rational antimicrobial use, infection control, surveillance and to strengthen research and education in the country (40). In addition, FMHACA is the responsible government body in regulating drug related issues and has been striving to have local standard treatment guidelines, drug formularies, and good prescribing and dispensing manuals since its establishment by proclamation number 661/2009 (41). All these efforts are being done to promote the rational use of antimicrobials and ultimately to safeguard citizens. However, the effective implementation of the standards and most of the treatment guidelines are not yet studied. Besides, there is no responsible organized body that coordinates the effective use of these resources at each health facility. Though a few facilities have Drug and therapeutic committees but they were not seen working on this regard.

Therefore, this study was aiming to evaluate antimicrobial usage and clinical outcome in the current practice in the management of pneumonia. Hence, it would help provide concrete information for designing an appropriate intervention strategy to optimize better antimicrobial utilization and improve patient and economic outcomes. Ultimately, the finding will serve as an input for policy makers to have effective drug regulation in Ethiopia.

1.3 Literature Review

1.3.1 Antimicrobial Utilization and Resistance

The use of antimicrobial agents has increased in hospitalized patients across the globe over the past decades (42). Between 2000 and 2010, consumption of antimicrobial agents increased by 36% (from 54 083 964 813 standard units to 73 620 748 816 standard units). Brazil, Russia, India, China, and South Africa (BRICS countries) accounted for 76% of this increase. In most countries, antibiotic consumption varied significantly with seasons, for example in India, high transmission of dengue fever was observed in the post-monsoon season, with peak activity in September. In this country, many broad-spectrum antimicrobials (cephalosporins, fluoroquinolones, and carbapenems) were sold over the counter without presence of a documented clinical need(28).

By some estimates, half of patients hospitalized in the United States receive antibiotics, and up to half of antimicrobial use may be inappropriate (42, 43). Problems with the excessive and inappropriate use of antimicrobial agents in the United States have been widely recognized for a long time (44).

Studies from Tanzania and Mozambique indicate that resistant infections result in increased mortality in neonates and children under five (45, 46).

Two different period studies on the resistance patterns of certain microorganisms that commonly cause urinary tract infection in Gonder University Hospital have shown that the commonest isolates in their previous and recent studies were *E. coli, Klebsiella,* coagulase negative *streptococcus (CoNS), S. aureus, Proteus,* and *Citrobacter* species. Previous isolates of *Enterobacteriaceae* were 100% sensitive to ciprofloxacin, whereas 31-60% of the recent isolates had developed resistance. Previous isolates were less resistant to gentamycin than the recent ones. Multidrug resistant isolates were predominant in the recent study than previous ones (47, 48).

A study in Australia and New Zealand about the resistance episodes of *S. aureus* has shown that it is associated with considerable mortality. About 1994 episodes of *S. aureus* bacteraemia were identified, and complete 30-day follow-up data were available for 1865. Most episodes had their onset in the community (60.8%; 95% CI, 58.7%–63.0%). MRSA caused 450 episodes (24.1%; 95% CI, 22.2%–25.9%), and 123 of these (27.3%) had a susceptibility profile

consistent with community-associated MRSA. All-cause mortality at 30 days was 20.6% (95% CI, 18.8%–22.5%). Increased mortality was significantly associated with MRSA infection (14).

A retrospective cohort study in two tertiary care hospitals in the US has shown that from 172 patients who were admitted through the emergency department and intensive care unit because of community-acquired pneumonia, mortality was 19.8% at 30 days. The most common empiric antimicrobial regimen utilized in their study were ceftriaxone and azithromycin in 26%, piperacillin-tazobactam and levofloxacin in 12%, piperacillin-tazobactam and azithromycin in 8%, cefotaxime and azithromycin in 7%, ceftriaxone and levofloxacin in 7%, piperacillin-tazobactam and gatifloxacin in 5%, and ceftriaxone and gatifloxacin in 3.5%. They concluded that the use of initial empiric antimicrobial therapy with a β-lactam and a fluoroquinolone was associated with increased short-term mortality for patients with severe pneumonia in comparison with other guideline-concordant antimicrobial regimens (49).

An observational cohort study on risk factors for 30-day mortality in patients with pneumonia who receive appropriate initial antibiotics was conducted in Japan showed that mortality was 11% (61 of 579 patients) in the appropriate initial antibiotic treatment group and 17% (29 of 168) in the inappropriate initial antibiotic treatment group (50).

A study on community acquired pneumonia conducted in the United States has also shown that patients who received a β-lactam with macrolides, 30-day mortality was 17.2% (15 of 87) and for other guideline-concordant antibiotic regimes mortality was 11.4% (4 of 35)(49).

On one hand, antimicrobial resistance increases because of a number of complex factors, on the other hand pharmaceutical development pipeline is declining. So, multi-sectoral collaboration and practical interventions are obviously required and warranted so as to reduce the emergence of resistance against the magic bullets.

1.3.2 Importance of Antimicrobial Stewardship

A multicentre study in Egypt involving more than 1200 patients indicated that an ASP focusing on education supported by auditing and feedback have shown a significant impact on optimizing antibiotic use in surgical prophylaxis practices. The optimal timing of the first dose improved significantly in 3 hospitals, increasing from 6.7% to 38.7% ($p < .01$), from 2.6% to 15.2% ($p < .01$), and from 0% to 11% ($p < .01$). All hospitals showed a significant rise in the

optimal duration of surgical prophylaxis, with an overall increase of 3%-28% ($p < .01$). Days of therapy per 1000 patient-days were decreased significantly except in one hospital (51).

A study in Taiwan has shown that the average monthly length of stay of admitted patients decreased from about 7.8 ± 0.5 days in 2011 to 6.9 ± 0.3 days in 2013 ($p < 0.001$). The average monthly cost of antimicrobials decreased 46.9% from $30,146.8 in 2011 to $16,021.3 in 2013 ($p < 0.001$). Total intravenous antimicrobial defined daily doses (DDDs) per 100 bed-days of the inpatients were 66.9, 54.1 and 48.4 in 2011, 2012 and 2013, respectively. A total of 18.6 DDDs per 100 bed-days of inpatients (27.7%) decreased from 2011 to 2013. By comparing data in 2013 to those in 2011, the ASP reduced antimicrobial resistance of Gram-positive bacteria ($p<0.013$), Gram-negative bacteria ($p < 0.001$), and predominant species (all $p < 0.05$). The yearly mortality also decreased from 1.3% in 2011 to 1.1% in 2012 and 1.0% in 2013. This remarkable result is obtained through implementation of ASP which has successfully reduced length of stay, mortality, the cost of antimicrobials, DDDs, and antimicrobial resistance rate, and finally they have highly recommended expanding ASP for all local hospitals (21).

1.3.3 Switching from Intravenous to Oral Therapy

A retrospective study on practice of switch from intravenous to oral antibiotics in three Lebanese university teaching hospitals has shown that among 452 intravenous antibiotic courses from 356 patients who were eligible for conversion, only one third were switched and the others continued on intravenous antibiotics beyond day 3 ($p <0.0001$) (52).

A cross-sectional study that was conducted by Lee et al. (46) to explore clinicians' baseline knowledge, practice beliefs and acceptance of intravenous (IV)-to-oral antibiotic switching practice in Hospital Pulau Pinang had identified the most common reasons for continuing IV Therapy. These include: clinical instability of the patient (88%); uncertainty about gastrointestinal function (58%); uncertainty as to whether the oral alternatives achieve effective tissue levels (57%); reassurance that IV treatment achieves effective tissue levels (56%); uncertainty about availability of oral alternatives (41%); liability for unsuccessful treatment outcomes (31%) and others (1.4%) (53).

2. Objectives

2.1 General objective

The general objective of this study was to evaluate the current practices of antimicrobial utilization and clinical outcomes in the management of adult pneumonia patients at TASH.

2.2 Specific objectives

- To assess antimicrobial prescribing pattern (types of regimens, timing, use, duration)
- To assess the practice of use of microbiologic studies (number of tests, culture collection time, number of culture positive results, number of de-escalation therapy)
- To assess the practice of IV to PO switching
- To assess the guidelines used in the treatment of pneumonia
- To assess the clinical outcomes (stability, in hospital mortality, complications)

3. Methodology

3.1 Study Setting

This study was conducted at TASH, Addis Ababa, Ethiopia. TASH is a tertiary care teaching hospital in Ethiopia, with over 700 beds, and serves as research and training center for undergraduate and postgraduate medical students, dentists, nurses, midwives, pharmacists, medical laboratory technologists, radiology technologists, and others who shoulder the responsibilities to solve the health problems of the community and the country at large. The data was collected in the internal medicine wards which have around 95 beds. Based on the 2016 health management information system (HMIS) reported data, annual patient visits to the hospital are around 500,000 and of this about 2100 patients are admitted to the internal medicine wards.

3.2 Study Design and Period

A prospective observational study was conducted in adult patients with pneumonia admitted to the internal medicine wards of TASH. This is a pre-intervention baseline assessment and it would be followed by an intervention study conducted to assess antimicrobial utilization and the clinical outcomes in the management of pneumonia patients. Patients who were admitted at the emergency and internal medicine wards and diagnosed with pneumonia were prospectively followed without an intervention. The pre-intervention study was conducted from September 1, 2016- June 30, 2017. The intervention study will be started after the intervention tool (adult pneumonia diagnosis and management protocol) printing is completed.

3.3 Source Population

All patients who were admitted to emergency and internal medicine wards of TASH were the source population for this study.

3.4 Study Population

All pneumonia patients that were admitted in the emergency and internal medicine wards at TASH were enrolled in the study.

3.5 Inclusion and Exclusion Criteria

All adult patients with pneumonia were included. To be included in the study, patients should have a physician diagnosis of suspected or proven HAP, CAP, HCAP and AP. Exclusion criteria include:

- Patients with age less than 14 years
- Patients with multiple bacterial infectious diseases other than pneumonia

3.6 Sampling and Sample Size Determination

The annual estimated overall pneumonia patients in the internal medicine wards are around 400. Therefore, sample size is determined based on single population proportion formula using the following assumption.

$$X = (Z\alpha/2)^2 \times p\ (1-p)\ /d^2$$

Where: Proportion of pneumonia (p) = 50 %

Confidence level of 95 % chosen with z-value of 1.96

Margin of error (d) = 5%

n = 384 (sample size without adjustment and with p = 50%)

The total population of pneumonia patients who were admitted in the internal medicine wards at TASH (N) was around = 400

Corrected sample size = $\frac{nxN}{n+N}$

By using the correction formula the sample size was 195. But 200 patients were followed and complete data collected.

In the intervention study same number of patients will be included.

3.7 Data Collection and Management

3.7.1 Data Collection Instruments

Data collection instrument was developed by reviewing literature on Antimicrobial utilization, AMR and ASP guidance. The data collection format was designed to help extract information about patient sociodemographic and clinical characteristics. The data collection instrument (format) was also prepared to obtain information regarding the practice of pneumonia diagnosis and management from treating physicians particularly patient previous antimicrobial histories, medical histories, microbiological studies, radiologic studies, the type of antimicrobials, antimicrobial selection process, intravenous to per oral conversion and antimicrobial administration information from nurses' in charge.

3.7.2 Data Collectors and Training

Ten data collectors were recruited from the pharmacy, medicine and nurse departments who are working at TASH and they were trained for 1 day about data abstraction and obtaining additional information from the treating physicians. The data was then collected according to the data abstraction format. The principal investigator was always in charge for assistance and clarification when needed.

3.7.3 Data Quality Assurance

The data collection format was tested in 10 (5%) patients who were admitted to TASH. Based on the information on obtained and feedbacks from physicians, the data abstraction format and the questionnaire were modified. Information regarding change regimen, missed doses, and reasons of change and missing were included. The modified instrument was used to collect information at the specified wards based on the inclusion and exclusion criteria. Patient flows were considered random at the wards and all patients diagnosed with pneumonia were included according to the inclusion and exclusion criteria. Data consistency and adequacy were frequently checked by principal investigator and random verification was also performed.

3.7.4 Data Entry, Clean Up and Analysis

Data entry and analyses were done by data clerk and the principal investigator using IBM SPSS statistics for Windows Version 20 (IBM Corp. Released 2012, Armonk, NY: IBM corp.). Simple descriptive statistics was used to characterize the data. Univariate analysis was done and variables having p-value less than 0.25 with the outcome (either poor outcome or good outcome) were considered for further analysis. Then, independent predictors were identified by a multivariate logistic-regression analysis. All statistical tests were 2-tailed; a P value 0.05 was considered statistically significant.

3.8 Variables

- **Dependent variable**
  - Clinical outcome
- **Independent variables**
  - Socio-demographic factors
  - Host factors (risk factors and comorbidities)
  - Antimicrobial therapy related factors
  - Microbiological studies
  - Radiologic studies
  - Blood chemistry studies

3.9 Ethical Consideration

The proposal was submitted to the School of Pharmacy, Addis Ababa University ethical review committee for review and approval. The study was conducted after obtaining approval. Verbal consent from patients was obtained after provision of information regarding the purpose of the study. Patients were told the reasons of being selected to be included in the study and assured that declining participation would not have any influence on the right to get treatment. Patients were also told about their rights to withdraw from the study at any time. Participants were assured about confidentiality (privacy and anonymity) of the information obtained in the course of the study.

3.10 Operational Definitions

1. **Adult**: patients with age greater than or equal to 14 are considered an adult in TASH because they were admitted at Adult wards.
2. **Antimicrobials**: are drugs that are used for treatment of infectious diseases including pneumonia.
3. **All-cause mortality**: mortality in which the cause of death was not clear (infection and/or existing other conditions).
4. **Appropriate therapy**: the use of at least one antimicrobial to which all isolates were susceptible in vitro observed in culture and sensitivity discs.
5. **Pneumonia -related mortality**: mortality as a result of the infection (pneumonia) (death during antimicrobial therapy for the episode of pneumonia)
6. **Clinical stability**: Suspected or diagnosed pneumonia patients who had complete resolution of all signs and symptoms of pneumonia or improvement of all abnormalities on the chest radiograph. This was judged by the treating physician and monitored by vital signs and laboratory studies.
7. **Complications**: Suspected or diagnosed pneumonia patients who were not improved or admitted to the ICU after getting antimicrobial therapy which is judged by the treating physician.
8. **Immunosuppression**: comprises any immunosuppressive diseases such as congenital or acquired immunodeficiency, hematological diseases, and neutropenia (<1000 white blood cells per mL); treatment with immunosuppressive drugs within the previous 30 days; or corticosteroids doses of at least 10 mg/day of a prednisone equivalent for more than 2 weeks.
9. **Treating physicians**: These are resident and senior physicians who are practicing at TASH.
10. **Suspected pneumonia**: a patient which is given a diagnosis of pneumonia based only on clinical signs and symptoms without radiological findings
11. **Confirmed pneumonia**: a patient which is given a diagnosis of pneumonia with suggestive radiological findings.
12. **Clinical outcome**: Poor or good outcome.
13. **Poor outcome**: patients who have been treated for pneumonia but got passed away or their cases complicated.
14. **Good outcome**: patients who have been treated for pneumonia and got clinical stability/cure.

4. Result

4.1 Sociodemographic Data

A total of 227 patients who had been admitted in TASH and fulfilled the inclusion criteria were included in this study. However, data for 27 patients were not complete as a result of discharges against medical advice and some referred to other hospitals (Figure 2). The sociodemographic characteristics of the study population are described in Table 1. Among the total of 200 patients 104 (52.0%) were males and 176 (88.0%) were having age less than 65 years. The mean age of the patients was 39.8 (SD 17.8) years and most of them were referred from governmental institutions 137 (68.5%).

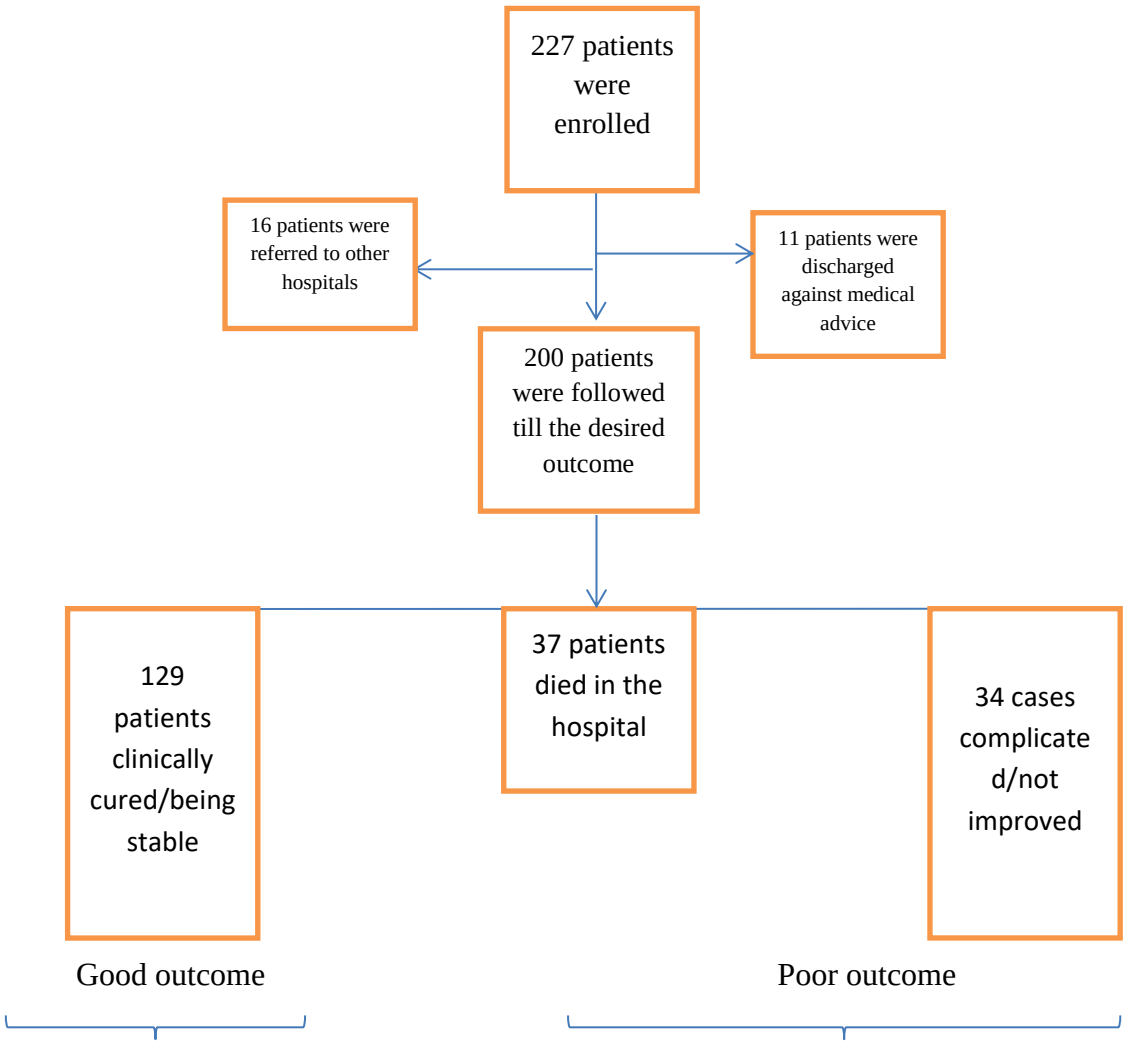

Figure 2. Enrolled and included patients' information.

Table 1. Sociodemographic characteristics of patients with pneumonia at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, September 15, 2016- June 30, 2017 (n=200).

Variable	Value	Number of patients (%)
Age category	<18Yrs	12(6)
	18-39Yrs	99(45.5)
	40-64Yrs	62(31)
	65-74Yrs	16(8)
	≥75Yrs	11(5.5)
Age (years)	Mean (SD),range	39.79(17.76),14-84
Sex of the patient	Male	104 (52.0)
	Female	96 (48.0)
Region from which the patient came from	Addis Ababa	85 (42.5)
	Oromia	50 (25.0)
	SNNP	28 (14.0)
	Amhara	27 (13.5)
	Others*	10 (5.0)
Referred from	Government institution	137 (68.5)
	Private institution	45 (22.5)
	Direct admission	18 (9.0)

***Afar, Ethiopia Somali, Tigray Regions**

4.2 Clinical Characteristics

Among the 200 patients, 140 (70.0%) of them were having recent exposure (within 90 days) to antimicrobial agents. The two most common causes of admissions were cardiovascular diseases + pneumonia and cancer + pneumonia with frequencies of 33 (16.5%) for both (Table 2). Pneumonia as a major reason of admission was observed in 3 (1.5%) patients. The most common comorbid conditions in this study population were Cancer 83 (41.5%) and heart failure 42 (21%) (Table 3 & Figure 3). Among the 200 pneumonia patients, 83 (41.5%) was diagnosed with CAP, whereas HAP and HCAP constituted 70 (35.0%) and 27 (13.5%), respectively. In addition, aspiration pneumonia (AP) alone and with HAP comprised of 20 (10%).

Table 2:Pneumonia patients admission diagnosis and their frequency at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, September 1, 2016- June 30, 2017(n=200).

Admission Diagnosis	**N (%)**
Cardiovascular Diseases + Pneumonia	33(16.5)
Cancer + Pneumonia	33(16.5)
Cancer	25(12.5)
Cardiovascular Diseases	8(4.0)
Diabetes + Cardiovascular Diseases	7(3.5)
Cardiovascular Diseases +Renal Disease + Pneumonia	7(3.5)
HIV/AIDS + Pneumonia	5(2.5)
HIV/AIDS + Cancer + Pneumonia	5(2.5)
Cancer + Renal Disease + Pneumonia	4(2.0)
Cardiovascular Diseases + Diabetes + Pneumonia	4(2.0)
Pneumonia	3(1.5)
Cancer + HIV/AIDS	2(1)
Others*	64(32)
Total	200(100)

***Different combinations of the listed diseases, systemic lupus erythematosus, Peptic ulcer disease, Visceral leishmaniosis, central nervous system disorders etc.**

Table 3:The frequency of comorbid conditions of the enrolled pneumonia patients at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, September 1, 2016- June 30, 2017(n=200).

Comorbid Conditions	**Yes (N, %)**	**No (N, %)**
Cancer	83(41.5)	117(58.5)
Heart Failure	42 (21.0)	158 (79)
Chronic Pulmonary Disease	29(14.5)	171(85.5)
Hypertension	23(11.5)	177(88.5)
Diabetes	23(11.5)	177(88.5)
Coronary Heart Disease	17(8.5)	183(91.5)
Chronic Kidney Disease	14(7.0)	186(93)
Stroke (new & old)	13(6.5)	187(93.5)
Central Nervous System disorder	9(4.5)	191(95.5)
Chronic Liver Disease	2(1)	198(99)

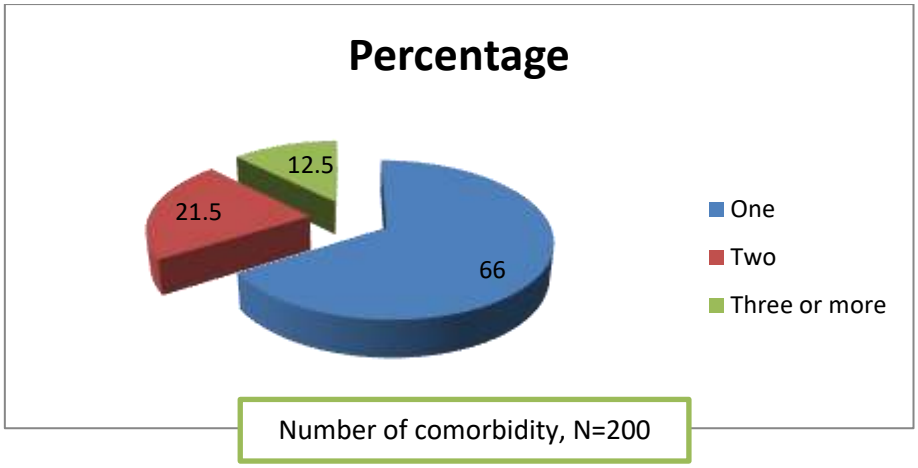

Figure 3:The number of comorbid conditions of the enrolled pneumonia patients at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, September 1, 2016- June 30, 2017.

4.2.1 Practice of Microbiologic Studies

Of the 200 patients who were admitted and diagnosed with pneumonia, only 75 (37.5%) of patients had given samples for microbiological tests. Of them, 45 (60.0%) of the samples were taken before initiation of empiric antimicrobial therapy. The most common samples taken were blood 48 (64.0%) and sputum was the least 7 (9.3%), though the patients' diagnosis was pneumonia. Out of the 75 cultured microbiologic samples, 10 (13.3%) of them only showed bacterial growth (Figure 4). The time of culture collection was observed and found to be 0 in day 1, 2(2.7%) in day 2, 15(20.0%) in day 3, 8(10.7%) in day 4, 5(6.7%) in day 5, and 45(60.0%) after day 5. One hundred twenty-five physicians who did not order microbiologic studies were asked why they did not order and nearly half of them said that the usual practice is treating based on clinical presentation (Table 4).

Table 4:Physicians reasons for not considering microbiological studies for the management of pneumonia patients at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, September 1, 2016- June 30, 2017(n=125).

Reasons given by physicians	**N (%)**
The usual practice is to treat patients based only on clinical information (Signs and symptoms)	61(48.8)
The patient has already started antimicrobials	22(17.6)
No institutional guidance that recommend testing	20(16.0)
No well-equipped microbiological lab	8(6.4)
Other reasons*	14(11.2)

*** Culture yields are very low and only radiologic information is sufficient to treat pneumonia**

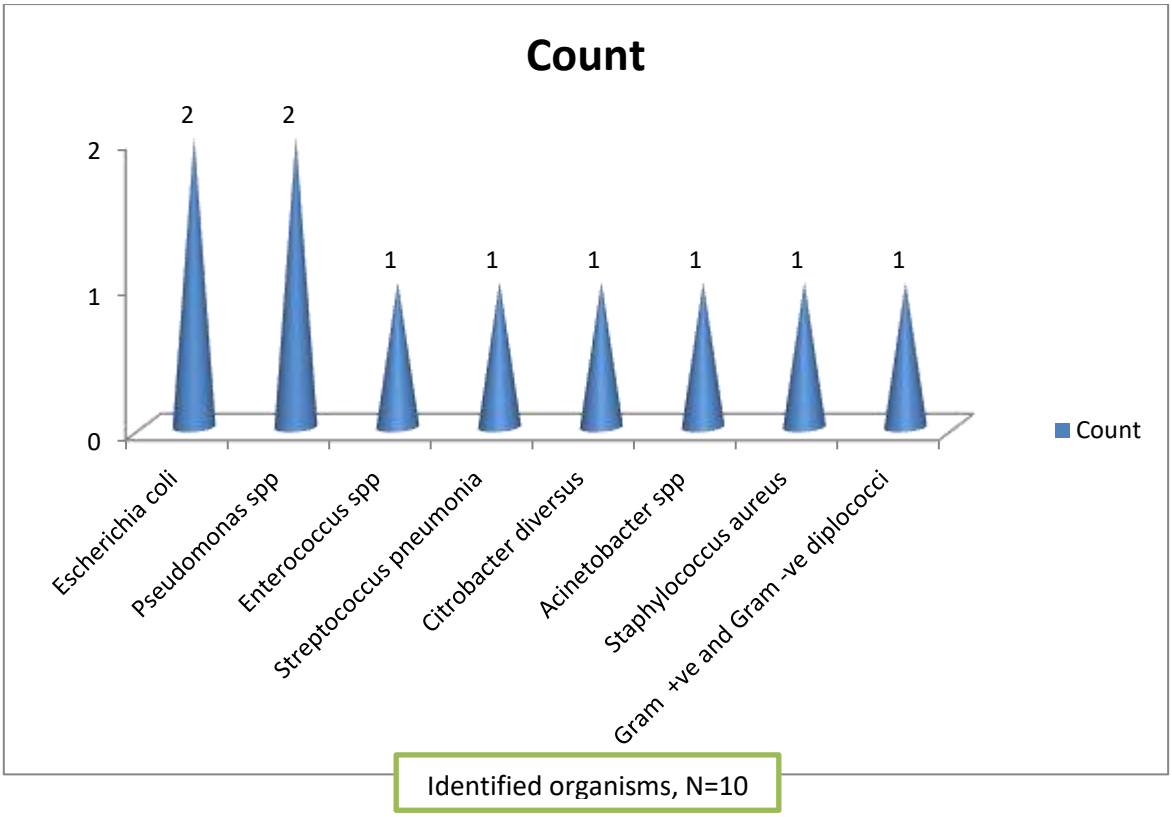

Figure 4:Identified organisms during the management of pneumonia at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, September 1- June 30, 2017.

4.2.2 Prescribing Pattern and Antimicrobial Susceptibility

According to this study, almost all the treatment approaches were found to be empirical 199(99.5%). It was also observed that there was no de-escalation of therapy even after getting the culture results. The started antimicrobials were continued in many cases for the desired duration of therapy.

The most commonly used initial Antimicrobial regimen was Ceftriaxone 1gm BID + Azithromycin 500mg, PO, QD, (58, 29.0%) for CAP) and Vancomycin 1gm BID + Piperacillin/tazobactam 4.5 gm iv QID, (15, 7.5% for HAP and HCAP) (Table 5, and 6).

Table 5:Types of regimens used in the management of pneumonia at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, September 1, 2016- June 30, 2017 (n=200).

Type of Initial antimicrobial regimen	**N (%)**
Ceftriaxone 1gm BID + Azithromycin 500mg,po,QD	60(30.0)
Vancomycin 1gm BID + Piperacillin/tazobactam 4.5 gm iv QID	16(8.0)
Ceftriaxone 1gm BID	9(4.5)
Vancomycin 1gm BID + Cefepime 1gm TID	9(4.5)
Vancomycin 1gm BID + Ceftazidime 1gm TID	8(4.0)
Vancomycin 1gm BID + Ceftazidime 1gm BID	8(4.0)
Ceftriaxone 1gm BID + Metronidazole 500 mg iv TID	8(4.0)
Vancomycin 1gm BID + Ceftazidime1g TID	7(3.5)
Vancomycin 1gm BID + Meropenem 1g TID	7(3.5)
Vancomycin 1gm BID + Cefepime 2g TID	7(3.5)
Vancomycin1gm BID + Ceftriaxone 1gm BID	6(3.0)
Vancomycin 1gm BID + Cefepime 1g BID	5(2.5)
Vancomycin 1gm BID + Ceftazidime 1gm BID + Ciprofloxacin 400 mg iv BID	4(2.0)
Vancomycin 1gm BID + Meropenem 1g BID	4(2.0)
Vancomycin 1gm BID+ Ceftriaxone 1gm,BID+ Metronidazole 500mg, iv, TID	3(1.5)
Vancomycin 1gm BID + Piperacillin/tazobactam 4.5 gm QID + Ciprofloxacin 400 mg BID	2(1.0)
Vancomycin1gm BID + Cefepime 1gm TID + Metronidazole 500 mg iv TID	2(1.0)
Vancomycin 1gm BID + Ceftazidime 1gm TID + Metronidazole 500 mg iv TID	2(1.0)
Vancomycin 1gm iv QD + Piperacillin/tazobactam 2.25g iv QID	2(1.0)
Ceftriaxone 1gm BID + Azithromycin 500mg, PO, QD + Ciprofloxacin 400mg, BID	2(1.0)
Vancomycin 1gm, BID + Ciprofloxacin 400mg, bid	2(1.0)
Vancomycin 1gm BID + Ceftazidime 2g TID	2(1.0)
Cefepime 2g TID + Piperacillin/tazobactam 4.5g QID	1(0.5)
Other regimens*	24(12.0)

*Other regimens (to list a few): Ceftriaxone 1gm, iv, BID + Azithromycin 500mg, PO, QD + Ciprofloxacin 400mg, iv, BID; Ceftriaxone 1gm, iv, BID + vancomycin 1gm, iv, Q72hrs+ Ciprofloxacin 400mg, iv, BID; Ceftriaxone 1gm, iv, BID + vancomycin 1gm, iv, QD; Meropenem 1g, iv, BID + vancomycin 1gm, iv, QD; Vancomycin 750mg, iv, BID + ceftazidime 750mg, iv, TID; Meropenem 1g, iv, BID + vancomycin 1gm, iv, QD + Ciprofloxacin 400mg, iv, BID; Cafepime 2gm, iv, TID + Vancomycin 1gm, iv, BID + Piperacillin/tazobactam 2.25mg, iv, TID; Ciprofloxacin 500mg, PO, BID + Azithromycin 500mg, PO, QD; Ceftriaxone 2gm, iv, BID + vancomycin 1gm, iv, Q72hrs + doxycycline 100mg, PO, BID; Ceftriaxone 1gm, iv, BID + clindamycin 600mg, iv, TID; Ampicillin/sulbactam 1.5gm, iv, BID+ Vancomycin, 1gm, iv, BID + Ciprofloxacin 400mg, iv, BID; cefepime 2gm, iv, TID + piperacillin/tazobactam 4.5gm, iv, QID.

It was observed that the time of initiation of antimicrobials were very difficult to trace in specified time basis. In the patient chart, it was only possible to see the date of diagnosis. However, the date and time of antimicrobial administration was available in the medication administration sheet. Since the time of diagnosis was not indicated so as to see the time within which patients received antimicrobials, the time of initiation was evaluated based on dates. Accordingly, patients who received antimicrobials with in 24h (patients who received in the date of diagnosis) were 127 (63.5%) and the rest of the patients received later than 24 h. In addition, the type of prescriptions with respect to selection of the antimicrobials, doses, frequencies and duration of therapy were varied among patients with similar diagnosis (Table 6).

Table 6:Cross tabulation showing the types of pneumonia and the initial regimens that patients received at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, September 1, 2016- June 30, 2017(n=200).

Initial antimicrobial therapy given	**Type of pneumonia**				Total
	HAP	CAP	HCAP	Others[#]	
Ceftriaxone 1gm, iv, BID	1	8	-	-	9
Ceftriaxone 1gm, iv, BID plus Azithromycin 500mg, PO, QD	1	58	1	-	60
Piperacillin/tazobactam 4.5 gm iv QID plus Vancomycin 1gm, iv, BID	11	-	4	1	16
Ceftriaxone 1gm BID plus Vancomycin1gm BID	2	1	2	1	6
Cefepime 1gm TID plus Vancomycin1gm BID	4	1	4	-	9
Ceftazidime 1gm BID plus Vancomycin 1gm BID	5	-	3	-	8
Ceftazidime 1gm TID plus Vancomycin 1gm BID	4	2	2	-	8
Pipera/tazo 4.5 gm iv QID plus Ciprofloxacin 400 mg iv BID plus Vancomycin 1gm BID	-	1	1	-	2
Ceftazidime 1gm BID plus Cipro 400 mg iv BID plus Vancomycin 1gm BID	2	1	1	-	4
Ceftriaxone 1gm BID plus Metronidazole 500 mg iv TID	-	2	-	6	8
Cefepime 1gm TID plus Vancomycin1gm BID plus Metronidazole 500 mg iv TID	-	-	-	2	2
Ceftazidime 1gm TID plus vancomycin 1gm BID plus Metronidazole 500 mg iv TID	1	-	-	1	2

Piperacillin/tazobactam 2.25g iv QID plus vancomycin 1gm iv Q24hrs	2	-	-	-	2
Ceftriaxone 1gm, iv, BID + azithromycin 500mg, Q24hrs + ciprofloxacin 400mg, iv, BID	-	1	-	1	2
Vancomycin 1gm, iv, BID + ciprofloxacin 400mg, iv, BID	2	-	-	-	2
Vancomycin 1gm iv BID plus Ceftazidime2g TID	2	-	-	-	2
Vancomycin 1gm iv BID plus Ceftazidime1g TID	3	1	3	-	7
Vancomycin 1gm iv BID plus Cefepime 1g TID	5	-	-	-	5
Vancomycin 1gm iv BID plus Cefepime 2g TID	5	-	2	-	7
Vancomycin 1gm iv BID plus Meropenem 1g BID	3	-	1	-	4
Vancomycin 1gm iv BID plus Meropenem 1g TID	5	1	1	-	7
Ceftriaxone 1gm,iv.BID + Vancomycin 1gm, iv, BID+ Metronidazole 500mg, iv, TID	-	-	-	3	3
Cefepime 2g TID + Piperacillin/Tazo 4.5g, QID	1	-	-	-	1
Others*	11	6	2	5	24
Total	70	83	27	20	200

***Other regimens as described above in Table 3.**
[#]Others includes HAP + AS, AP (HAP=Hospital Acquired Pneumonia; AP=Aspiration pneumonia)

As shown in Figure 5, it can be observed that about 13 types of antimicrobials were used for the treatment of different types of pneumonia. Out of 200 patients, 138 (69%) of the patients received vancomycin and it was the most commonly prescribed empiric antimicrobial agent for pneumonia. Regarding polypharmacy, the average number of antimicrobial prescriptions per patient was 2.76≈ 3, which means that almost many of the patients were exposed at least for 3 antimicrobial agents regardless of the type of pneumonia.

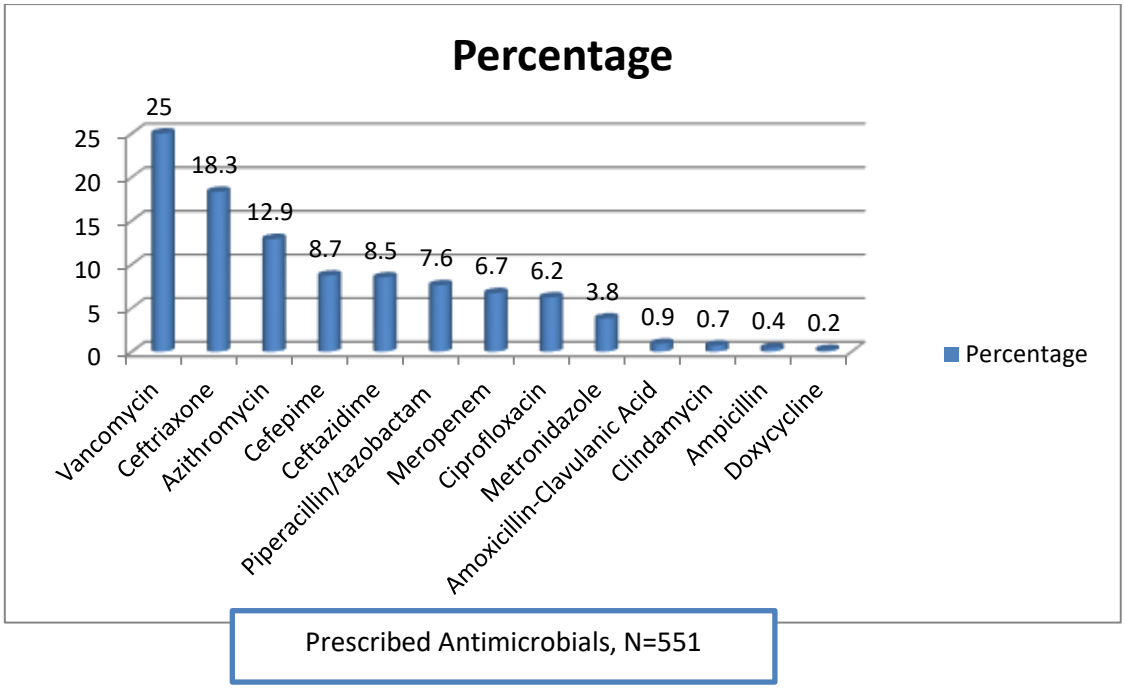

Figure 5: The most commonly used empiric antimicrobials (frequency and percent) for the management of pneumonia at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, September 1- June 30, 2017.

Based on the susceptibility data obtained from the 10 culture positive results, most of the identified organisms were seen to be resistant to the frequently prescribed Bata-lactams (penicillins and cephalosporins) (Table 7). According to the identified organisms, the appropriateness/adequacy of the initial antimicrobial regimens are described in Table 8.

Table 7:List of identified organisms and their resistance pattern to selected antimicrobials in the management of pneumonia at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, September 1, 2016- June 30, 2017(n=10).

Identified Organisms	**Susceptible to**	**Resistant to**
Streptococcus pneumonia	Piperacillin/Tazobactam, Clindamycin	Not reported
Escherichia coli	Meropenem, Amikacin	Ceftriaxone; Ceftazidime; Cefepime; Amoxicillin-Clavulanic acid; Ciprofloxacin
Escherichia coli	Chloramphenicol, Meropenem, Amikacin	Ampicillin, Cefotaxime, Ceftriaxone, Ciprofloxacin, Amoxicillin-Clavulanic Acid, Sulphamethoxazole
Pseudomonas spp	Ciprofloxacin, Amikacin, Meropenem, and Ceftazidime	Ampicillin, Amoxicillin-Clavulanic Acid, Sulphamethoxazole
Pseudomonas spp	Ciprofloxacin, Piperacillin/tazobactam, Meropenem, Cefepime, Amikacin	Not reported
Enterococcus spp	Vancomycin	Ampicillin
Citrobacter diversus	Meropenem, Amikacin	Ampicillin; Ceftriaxone; Cefotaxime; Gentamycin; Sulphamethoxazole; Amoxicillin-Clavulanic Acid
Acinetobacter spp	Not susceptible to any of tested drugs	Ceftriaxone; Ceftazidime; Cefepime; Amoxicillin-Clavulanic Acid; Piperacillin/Tazobactam; Ciprofloxacin; Gentamycin; Imipinem; Cotrimoxazole
Staphylococcus aureus	Tobramycin, Meropenem, Ceftriaxone, Ciprofloxacin	Penicillin
Gram negative and gram positive diplococci	Clindamycin, Erythromycin, Oxacillin	Gentamycin

Table 8:Cross tabulation showing identified organisms, susceptibility data and initial antimicrobial therapy to demonstrate adequacy and appropriateness at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, September1- June 30, 2017 (n=10).

Identified Organism	Susceptible to	**Initial Antimicrobial Therapy Given**							Adequate /appropriate (Yes/No)
		Ceftri 1gm BID + Azithro 500mg, QD	Cefta 1gm TID + Vanco 1gm BID	Pipera/tazo 4.5 gm iv QID + Vanco 1gm BID	Pipera/tazo 2.25g iv QID + Vanco 1gm iv Q24hrs	Vanco 1gm iv bid + Cefta 2g tid	Vanco 1gm iv bid + Mero 1g tid	Others	
Strep pneumonia	Pipera/Tazo, Clindamycin	-	-	1	-	-	-	-	Yes
E coli	Chloramphenicol, Mero, Amikacin	1	-	-	-	-	-	1*	No, No*
Pseudomonas Auerugenosa	Cipro, cefta, Cefe, Mero, Amika, Pipera/Tazo	-	1	-	-	-	-	1[#]	Yes , Yes[#]
Enterococcus spp	Vancomycin	1	-	-	-	-	-	-	No
Citrobacter diversus	Meropenem, Amikacin	-	-	-	-	1	-	-	No

Acinetobacter spp.	Not susceptible to any of the tested drugs	-	-	-	-	-	1	-	No
Gram -ve and Gram +ve diplococci	Tobramycin, Mero, Ceftri, Cipro	1	-	-	-	-	-	-	Yes
Staph. aureus	Clindamycin, Erythro, Oxacillin	-	-	-	1	-	-	-	No
Total		3	1	1	1	1	1	2	

***Cefepime 1gm, IV, Q24hr; #Ciprofloxacin 400mg, IV, BID**

Amika=amikacin; Azithro=Azithromycin; Cipro=Ciprofloxacin; Ceftri=Ceftriaxone; Cefe=cefepime; Erythro= Erythromycin;

Mero=Meropenem; Vanco=Vancomycin, Pipera/tazo=Piperacillin/tazobactam,

Out of 200 patients who received antimicrobial agents, many patients didn't receive them properly on their prescribed time. About 60 (30.0%) of the patients were missed their antimicrobial doses due to different reasons during the course of treatment (Table 9).

Table 9:Reasons for missing antimicrobial doses during the management of pneumonia at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, September 1, 2016- June 30, 2017(n=60).

Reasons of missing doses	N (%)
Stock outs of antimicrobials in the hospital	22(36.7%)
Missing the drug administration on the prescribed time	20(33.3%)
Patients and/or their care givers didn't avail the antimicrobials in the wards for timely administration	10 (16.7%)
Unknown reasons were 8(13.3%)	8(13.3%)

The study also assessed whether there was change in the initial antimicrobial regimen or not during the course of treatment and it was found that there were 83(41.5%) first time changes and the most common reason associated with the changes were poor response to the initial antimicrobials. The detailed reasons are given in Table 10.

Table 10:Reasons for change in initial antimicrobial regimen for the management of pneumonia at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, September 1, 2016- June 30, 2017(n=73).

Reasons for change in regimen for the first time	N (%)
Poor response	25(30.1)
Drug shortage (stock outs)	18(21.7)
Change in diagnosis	13(15.7)
Inadequate selection (broader coverage)	11(13.3)
Side effect of antimicrobials	6(9.6)
Due to discharge after being stable	2 (2.4)
Others*	8(9.6)

*** Conversion to oral medications; ID physician decision;**

It was also observed that antimicrobial regimen changes were also seen for the second time and third time. Regimens of 26 patients were changed for the second time and 6 for the third time. Poor response was the main reason for second and third time changes.

The mean and standard deviation of the total duration of antimicrobial therapy was 12.05(±5.09). Almost 70% of the patients received for more than 10 days and about 35% for more than 14 days.

The most common prescribing physicians were internal medicine residents 169 (84.5%), emergency medicine residents 24(12.0%), and others which included medical interns 7(3.5%).

The guidelines/protocol used for prescribing antimicrobials for the management of pneumonia patients were also asked and the most common guide to prescribe antimicrobials was reference eBooks (Harrison and Uptodate) (113, 65.5%). In addition, others which included their own personal experiences constituted about 2.5% (Figure 6).

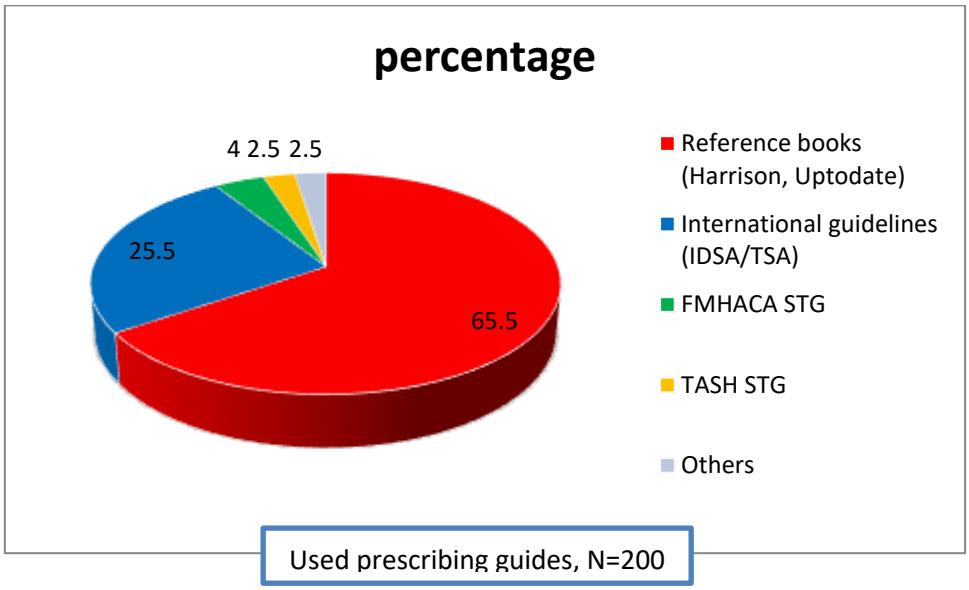

Figure 6:Antimicrobial prescribing guides used by physicians for the management of pneumonia at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, September1- June 30, 2017.

The prescribing physicians were asked whether they consulted a clinical pharmacist in the selection of appropriate antimicrobials and other pharmaceutical care activities and their response was no. The reasons for not consulting were also asked and the most common reason was absence of assigned clinical pharmacist in the wards (191, 95.5%). The rest of the reasons were “The given treatment was sure to cure the disease and no need to consult a clinical pharmacist”, “I don’t have information whether to consult a clinical pharmacist in patient

management", "clinical pharmacists are not interested in patient management and do not avail themselves in the wards" .

4.2.3 Switching from Intravenous to Oral Therapy

Eligibility of patient for IV to PO conversion (based on SHEA criteria) was assessed and it was found that 67 (33.5%) patients were eligible for conversion excluding the converted ones. About 166 (83.0%) of patients were taking other oral medications during the course of treatment of pneumonia. However, only in 4 (2%) patients conversion was made. Even these conversions were done lately. All of the physicians who were treating the 200 patients were asked about the practice of IV to PO conversion at TASH. Almost all of them wrote down their reasons for not practicing IV to PO conversion in the data collection sheet and the commonest reasons were summarized as follows: The usual clinical practice is administration of IV antimicrobials for hospitalized patients and conversion only made at the time of discharge (82, 41.8%); patients are critical and need IV (52, 26.5%); no comparable oral alternative agent to convert (37, 18.9%); IV is more effective than PO antimicrobials (10, 5.1%), and other reasons (15, 7.7%). The reasons included in the other category just to quote some were: "We don't follow IV to PO conversion criteria as a rule; the patient diagnosis is not yet confirmed and it is good to continue IV antimicrobial therapy; the patient is unable to swallow oral medications; the patient has developed sepsis and IV meropenem is the only option; only two days dosing are left and better to complete with IV therapy; the patient was misdiagnosed and now he stopped the antimicrobials and started treatment for PTE; she is stage iv RVI patient having anemia and better to give IV antimicrobials; the patient is getting free treatment and can't afford to buy PO medication; I suspect that resistant bacteria is the cause of his illness and IV antimicrobial needs to be given for full course of treatment; treatment discontinued before seven days etc".

4.2.4 Vital Signs, Imaging and Laboratory Values

Vital signs such as body temperature, blood pressure, pulse rate, respiratory rate, and oxygen saturation were also followed and recorded starting from day of diagnosis till the final clinical outcome status was obtained. Hence, it was seen that 91(45.5%) were found febrile (≥37.8^{o}C), 89(44.5%) were afebrile and 20 (10.0%) were unknown.

Renal function tests were done for 189(94.5%) of the patients. The level of serum BUN before the start of antimicrobials was found to be normal (3-20mg/dl) in 66(33%) of patients and 99 (49.5%) patients were having >30mg/dl. The level of serum creatinine before initiation of therapy was less than or equal to 1.4mg/dl in 158 (83.6%) and greater than 1.4mg/dl in 31(16.4%), and the proportion came down to 74.1% and up to 25.9%, respectively, after initiation of treatment.

The use of radiologic imaging as a supplement to clinical history and physical examination was also assessed and it was found that only 122(61.0%) of the patients were examined. The types of radiologic examinations used were CXR 92(75.4), Chest CT 24(19.7), others (e.g. ultrasound, CT + CXR) 6(4.9%). Eleven (9.0%) patients had normal radiologic findings, 65(53.3%) had suggestive of pneumonia, and 46(37.7%) showed different findings which were related to the comorbid conditions such as "pulmonary edema; bilateral pleural effusion + congestion + enlarged liver+ mitral stenosis; pleural effusion; cardiomegaly +? cystic bronchiectasis; cardiomegaly with bilateral pleural effusion etc.".

4.2.5 Clinical Outcome

All the patients were followed starting from the initiation of antimicrobial therapy till a clinical outcome was achieved and antimicrobial therapy was discontinued. The clinical outcomes of the patients were observed immediately after completion of treatment and physicians who were following the patients were asked about their clinical status after antimicrobial therapy. Accordingly, the observed findings were stable/improved (129, 64.5%), mortality due to pneumonia (13, 6.5%), all-cause mortality (24, 12.0%), and no improvement (34, 17.0%). The total in hospital mortality was 37 (18.5%). The findings particularly stability was not confirmed by an independent physician and might have interviewee bias.

Table 11:Cross tabulation showing the type of pneumonia and clinical outcomes at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, September 1- June 30, 2017(n=200).

Type of pneumonia	Outcome status		Total
	Good outcome	Poor outcome	
HAP	45	25	70
CAP	58	25	83
HCAP	11	16	27

Others*	15	5	20
Total	129	71	200

***HAP + AS, HAP=Hospital Acquired Pneumonia; CAP=Community Acquired Pneumonia; HCAP=Health Care Associated Pneumonia; AP (AP=Aspiration Pneumonia)**

4.2.6 Predictors of Poor Outcome in Pneumonia Patients

Initially, since a logistic regression model requires the dependent variable to be expressed dichotomously, the clinical outcome was coded into a good outcome (stable and improved patients) and poor outcome (died and complicated cases). Univariate binary logistic regression was used to identify independent determinants for poor outcome with a p-value of less than 0.25 and these were selected as potential predictors for further analyses. But variables like age, which happen to be clinically important, were taken as predictors of mortality even if the univariate analysis results were greater than 0.25. Multivariate logistic regression analysis was performed to assess independent predictors of poor outcome (hospital mortality and complications). Accordingly, it was found that patients with the following 5 characteristics demonstrated higher probability for poor outcomes: recent antimicrobial use history (p=0.023, AOR 2.50(1.13-5.52)), patients with cancer (p=0.022, AOR 3.49(1.19-10.23)), Recent recurrent URTI (p=0.048, AOR 3.63(1.01-13.08)), patient with respiratory rate >24breaths/min or <12breaths/min (p=0.014, AOR 2.44(1.20-4.96)) and High level of BUN >20mg/dl (p=0.042, AOR 2.27(1.03-5.02)) (Table 11).

Table 12:Multivariate logistic regression analysis of factors associated with poor outcome among pneumonia patients who received antimicrobial therapy at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, September1- June 30, 2017.

Variables		Clinical Outcome (N, %)		COR (95%C.I.)	AOR (95% C.I.)	P-value
		GOC	POC			
Sociodemographic characteristics	<18Yrs	10(7.8)	2(2.8)	1	1	
	18-39Yrs	60(46.5)	39(54.9)	3.25(0.67-15.63)	0.27(0.03-2.38)	0.240
	40-64Yrs	40(31.0)	22(31.0)	2.75(0.55-13.69)	1.17(0.26-5.11)	0.834
	65-74Yrs	12(9.3)	4(5.6)	1.67(0.25-11.07)	0.85(0.18-3.9)	0.833
	≥75Yrs	7(5.4)	4(5.6)	2.86(.41-20.14)	0.38(0.05-2.98)	0.354
Patient medical history	Recent AME					
	No	59(45.7)	21(29.6)	1	1	
	Yes	70(54.3)	50(70.4)	2.00(1.08-3.72)	2.50(1.13-5.52)	0.023
	Recent recurrent URTI					
	No	124(96.1)	62(87.3)	1	1	
	Yes	5(3.9)	9(12.7)	3.6(1.16-11.19)	3.63(1.01-13.08)	0.048
Type of Pneumonia	HAP	45(34.9)	25(35.2)	1	1	
	CAP	58(45.0)	25(35.2)	0.78(0.39-1.53)	1.05(0.47-2.38)	0.900
	HCAP	11(8.5)	16(22.5)	2.62(1.05-6.51)	2.26(0.81-6.34)	0.122
	Others*	15(11.6)	5(7.0)	0.60(0.19-1.85)	1.37(0.35-5.33)	0.646

Type of Comorbidity	Patients with HF	30(23.3)	10(14.1)	1	1	
	Patients with Ca	44(34.1)	38(53.5)	2.59(1.12-5.98)	3.49(1.19-10.23)	0.022
	Patients with OC	55(42.6)	23(32.4)	1.25(0.53-2.98)	1.48(0.49-4.46)	0.485
Vital Signs	Respiratory rate >24 or <12 breaths/min					
	No	73(58.9)	28(40.0)	1	1	
	Yes	51(41.1)	42(60.0)	2.15(1.18-3.90)	2.44(1.20-4.96)	0.014
Laboratory findings	Serum Level of BUN					
	≤20mg/dl	50(40.7)	16(24.2)	1	1	
	>20mg/dl	73(59.3)	50(75.8)	2.14(1.09-4.18)	2.27(1.03-5.02)	0.042

***HAP + AS, AP=Aspiration pneumonia; BUN= Blood Urea Nitrogen; Ca=Cancer; OC= Other Comorbidities; URTI=Upper Respiratory Tract Infection**

AME= Antimicrobial exposure

5. Discussion

An appropriate antimicrobial utilization is a cornerstone for the containment of antimicrobial resistance and good clinical and economic outcomes. However, inappropriate uses of antimicrobials have devastating effect on patients as well as the general population. This study was therefore designed to assess the practice of antimicrobial utilization and clinical outcomes in the management of adult patients with pneumonia who were admitted to TASH. Pneumonia was selected because it is one of the commonest infectious diseases in TASH.

Out of the 200 patients, samples for microbiological testing were done only for 75 (37.5%) patients and most culture results were reported after 5 days. Studies done elsewhere, however, indicated that blood cultures were obtained within 24 h and before the initial dose of antimicrobials in 81% of the patients (49). Another study showed that 98% had microbiologic culture specimens obtained during their hospitalization (54). The huge gap seen in the current study setting might be as a result of poor attention towards the use of microbiological data, and the laboratory might not be equipped with rapid diagnostic kits. It is obvious that the identification and detection of a pathogen susceptible or resistant to the chosen empiric antimicrobial therapy is an important outcome of microbiological studies and this determines definitive therapy and infection prognosis. It is of note that samples collected for investigation in these study patients was possible as a result of project supported study carried out on hospital acquired infections, which provided culture media and sensitivity discs.

The study finding showed that most patients were treated without evidence of microbiological data. Meanwhile, this result is in agreement with the treating physicians' response regarding the use of microbiological studies (Table 4). Recommendations from published guidelines for the treatment of pneumonia advises to initiate treatment with broad-spectrum antimicrobials, but it has to be accompanied by appropriate de-escalation based on culture results (55). A study (54) indicated that from 240 patients included in the study and treated with the simultaneous combination of piperacillin/tazobactam and vancomycin, antibiotic regimens were de-escalated in 151 (63%) and 175 (73%) patients by 72 and 96 h, respectively. However, in this study no de-escalation therapy was observed even after obtaining culture results. The delay in culture collection might be a reason for absence of de-escalation therapy besides the reasons described in the above paragraph.

Many of the clinically stable and unstable patients (complicated cases) who were on a combination of broad spectrum antimicrobials had completed the started treatments for the entire course. And about 30% of the patients received additional broader antimicrobial agents because of poor response to the initial ones. There may be different reasons for these to happen. On one hand, as some treating physicians expressed, there was a loss of trust of the culture results of microbiology laboratory. On the other hand, most physicians may not worry about resistance issues than the situations of the patient at the time of antimicrobial therapy. Because they did not usually want to 'take risks' and/or 'to be on the safe side' they usually prescribe broad spectrum antimicrobials without proper considerations (56, 57). But this practice may increase patients' exposure to unnecessary antimicrobials, emergence of resistance and increases health care costs (58, 59). In general, the data suggests that the use of microbiological data is very limited not only in the management of pneumonia, but also in the management of other infectious diseases. Such kind of practice at tertiary care level hospital is not acceptable.

In the current study, almost all treatment approaches were empirical (199, 99.5%). Empiric antimicrobial therapy is generally categorized as appropriate (adequate) or inappropriate (inadequate) based on microbiological culture and susceptibility findings. Empiric therapeutic regimens are considered appropriate if the identified microorganism is susceptible to at least one of the antimicrobial agent (60, 61). However, in this study only four out of ten patients who received empiric antimicrobial regimens were seen having culture results with appropriate coverage (Table 8). Other studies have shown that appropriate empiric antimicrobial therapy has been associated with decreased mortality in patients with many different types of infection; however, absence of culture and susceptibility data are also having devastating outcomes both on the patient and economic perspectives (9, 11, 12).

Among the 200 patients, 140 (70.0%) of them were having recent exposure to antimicrobial agents. Many studies have revealed that prior antimicrobial drug exposure is associated with colonization and infection by resistant pathogens (58, 59, 62). Hence, consideration of the previous exposure before initiation of empiric antimicrobial treatment is not generally observed in this study. This might be due to lack of awareness on antimicrobial resistance and/or limited training on this global alarming issue. A study on inadequate antimicrobial treatment has shown that in-appropriateness of the empirical antimicrobial regimen was significantly associated with a higher mortality rate (10). Unfortunately, it was very difficult to evaluate the appropriateness of the rest of the patients' antimicrobial therapy in this regard.

In the current study, more than 30 types of antimicrobial regimens were used. Particularly, empiric use of the very costly and lifesaving antimicrobial agents like vancomycin, Meropenem and third and fourth generation cephalosporins (Ceftriaxone, Ceftazidime and Cefepime) were common in this hospital (Table 5). It was seen that there were a number of factors that influence antimicrobial selection. This was happening in one hand due to the absence of a standardized hospital specific protocol which led the prescribing physicians to choose whatever antimicrobial agent they intend to use, on the other hand it is due to the frequent stock outs of most of the antimicrobials in the hospital and this led the treating physician to prescribe the available antimicrobial agents in the inpatient pharmacies. Hence, an appropriate strategy and rational balance should be maintained in the selection of empiric antimicrobial agents so as to minimize their overuse and/or unnecessary use provided that continuous supply of the antimicrobial agents is not an issue.

In this study, out of 551 prescriptions, 138 (25%) of the prescriptions were vancomycin which was the most common empiric antimicrobial agent for pneumonia at TASH. Accordingly, about 70% of the patients received this drug empirically. A study on empiric use of vancomycin revealed that the empiric use of vancomycin was discontinued within 96 h in 39.0% of prescriptions (187/480 prescriptions), but the drug was used continuously for ≥96 h in 61.0% (293/480 prescriptions). The most frequent clinical reason for initiation of vancomycin treatment was pneumonia (63). Third and fourth generation cephalosporins were also prescribed next to vancomycin in the current study (Figure 5). Antimicrobial de-escalation is a strategy of proper antimicrobial utilization so as to balance empiric use and reduce emergence of resistance. However, this is not seen in this study. In addition, in the current study, missed doses were observed in 60 (30.0%) of the patients. This may result from the absence of a clinical pharmacist assigned to work in the wards that may at least provide consultation on antimicrobial utilization and pharmaceutical care services to the patients. All these factors may contribute to the rapid development of antimicrobial resistance. Currently, vancomycin is the only available antimicrobial agent for methicillin resistant *Staphylococcus aureus* (MRSA) infection in Ethiopia. Global reports showed that infections caused by MRSA, and vancomycin-resistant *enterococci* (VRE), are associated significantly with increased mortality (64-66). As a result, control of hospital acquired infections is becoming a global health priority (17, 67). To that effect, the practice of antimicrobial utilization at TASH is alarmingly increasing and needs a coordinated immediate intervention.

This study was also assessed the guidelines that the treating physicians were using to prescribe the antimicrobials for the management of pneumonia patients (Figure 6). The use of local guidelines was seen minimal in this study. The reason behind this might be the local standard treatment guidelines were not prepared considering tertiary care services. It is also known that the guidelines were prepared without actual local antibiogram data. This suggests that the hospital physicians were mainly dependent on eBooks and international guidelines. Different guidelines and books are published at different times and in many cases their recommendation are not the same (19). This concept is also demonstrated in the guide to good prescribing which is prepared by WHO (68). This in turn led to the diversified use of antimicrobial agents in the management of patients with even similar pneumonia diagnosis. The indicated eBooks and international guidelines are basically prepared based on their own country antimicrobial resistance patterns and most are for education purposes. In addition, these eBooks and guidelines recommend having institution specific guideline developed based on their own institutional antibiogram (55). Several literatures and published guidelines described that the use of different strategies have been found helpful for more appropriate and cost-effective use of antimicrobial in hospitals. Such strategies focused on restriction (automatic stop orders, restricted antimicrobial list, and mandatory approval by infectious diseases specialists). Others also focus on education (face-to-face discussion, conferences, distribution of printed material, audit with feed-back), or are based on tools to help physicians in their decision making (practice guidelines, computer programs) (19, 69).

The current study also assessed the practice of IV to PO conversions using defined criteria which is adopted from the SHEA guideline. Accordingly, it was found that 67 (33.5%) patients were eligible for possible IV to PO conversions. Another study done at Lebanese hospital in which out of the total 452 antibiotic courses from 356 patients who were eligible for conversion, only one third were converted (70). However, in this study conversions were seen only in 4 out of 551 antimicrobial courses. This might be as a result of the treating physicians' limited awareness on advantages of IV to PO conversion and their attitudes towards effectiveness of PO antimicrobials. This was reflected in their response to the question regarding the very limited practice of IV to PO conversion. About 82 (41.8%) of the treating physicians said that administration of IV antimicrobials for hospitalized patients is a usual practice in this hospital and conversion only made at the time of discharge and about 10 (5.1%) of the treating physicians also said IV is more effective than PO antimicrobials. This was also

demonstrated in a study in which about 47% out of 221 of physicians responded that patients should receive a standard duration of IV antibiotics (53).

Another study done in a 450 bedded general department of a tertiary care hospital of India documented that the average expense for antimicrobials and the length of stay of patients could be reduced from early IV to PO conversion (71). Antimicrobial agents cost are about 25 to 40% of the total medication budget in hospitals in the United States (72, 73). However, this is much higher in the Ethiopia context where the prevalence of infectious diseases is very high (74). So, considerations of possible conversions are crucial in a resource limited country like Ethiopia.

In the current study, good or poor clinical outcome was the primary end points. Based on this study finding, the overall in hospital mortality was 37 (18.5%). In addition, about 34 (17%) of the patients were not improved though two or more combinations of antimicrobials were administered for more than 10 days. This may be due to either misdiagnosis or patients may have been infected with one or more resistant pathogens. This in turn may be on one hand as a result of absence of microbiological and radiologic studies (X-ray) for many of the patients and on the other hand many of the patients had received antimicrobials as they had visited other health care institutions before admission to TASH. An observational cohort study on risk factors for 30-day mortality in patients with pneumonia who receive appropriate initial antibiotics was conducted in Japan showed that mortality was 11% (61 of 579 patients) in the appropriate initial antibiotic treatment group and 17% (29 of 168) in the inappropriate initial antibiotic treatment group (50). Another study on community acquired pneumonia conducted in the United States has shown that patients who received a β-lactam with macrolides, 30-day mortality was 17.2% (15 of 87) and for other guideline-concordant antibiotic regimes mortality was 11.4% (4 of 35) (49). However, the in hospital mortality rate in this study was very high (18.5%) unlike above two studies (49, 50) that followed patients' status till 30 days. This result suggests that the quality of care of patients with infectious diseases was minimal at TASH as compared to the previous study settings. Absence of sufficient number of infectious diseases specialists, hospital specific antimicrobial treatment protocols, continuous supply of antimicrobials and better microbiological laboratory services may justify the poor quality of care.

High level of serum creatinine after the start of antimicrobial therapy was observed in these study patients. This was because many of the patients in the current study as observed from their admission diagnosis are associated with different types of comorbidities and also most of

them were taking nephrotoxic drugs such as vancomycin, ceftazidime, piperacillin-tazobactam and their combinations which can cause acute kidney injury. However, a study done by Palacios et al also found that the infection by itself may damage the kidney cells and cause to increase serum creatinine (75). In one or another way, the univariate analysis has shown that the damage of the kidney due to existing comorbidities, antimicrobial utilization and the infection thereof increased risk of mortality in these study patients.

In this study, extended duration of therapy was observed in 73 (36.5%) of the patients as compared to the recommended duration of therapy in the references that the treating physicians were claiming to use to prescribe the antimicrobials. Though the optimum duration of treatment of pneumonia varies from guideline to guideline, most guidelines indicate treatment durations ranging from 5 days to 10 days for CAP, HAP/VAP (55). In this study, it was observed that unless the treating physician documented the discontinuation of therapy in the medication order sheet, nurses continue administering antimicrobials for prolonged durations. It is well known that extended duration of therapy is associated with emergence of antimicrobial resistant organisms, an unacceptable adverse effects, increase length of hospital stays and hospital associated costs (76). This is reflected in a study that showed the emergence of resistant pathogens especially *Enterobacteriaceae* and *P.aeruginosa* and colonization in patients treated for prolonged therapy for ≥14 days (77). This finding suggests for urgent close monitoring of antimicrobial utilization and a clear guidance are required to curb misuses.

Identification of risk factors for poor outcome was an important strategy during infectious disease management so as to provide a specialized care according to the number of risk factors associated with the patients. Hence, this study tried to assess the possible predictors of poor outcome in patients with pneumonia. Accordingly, around five risk factors were identified and these risk factors are in line with different studies done across the globe.

In this study, recent antimicrobial use history (p=0.023) was one of the predictors of poor clinical outcome. Patients who had previous exposure to antimicrobial agents encountered 2.5 times poor outcome than patients who did not have. Another study which was conducted in Barnes-Jewish Hospital, a 1200-bed urban teaching hospital has also shown that recent antibiotic exposure is associated with increased hospital mortality (adjusted odds ratio, 1.70; 95% confidence interval, 1.41–2.06; p = 0.005) in Gram-negative bacteremia complicated by severe sepsis or septic shock (78). This is due to the fact that those patients coming to TASH are referred from different lower health care institutions and other hospitals according to the

countries referral system or structure. So, these patients usually received different antimicrobial agents prior to admission at TASH. In this study, about 140 (70.0%) of the patients were having recent antimicrobial agent exposure. This may resulted in colonization and subsequent infection with resistant bacteria (10). Therefore, clinicians caring for such kind of patients should consider their recent antimicrobial experience and balance the empiric antimicrobial regimens for the suspected infection till the microbiological studies are obtained.

In the current study, patients with cancer are statistically associated with poor outcome (p=0.022) in patients with pneumonia. This is also consistent with a study on the role of neutropenia on outcomes of cancer patients with community-acquired pneumonia (79). In their study, the mortality rate was significantly higher in patients with cancer when compared with patients without cancer (43 out of 310 patients, 14% versus 213 out of 2,650, 8.0%, respectively; p=0.001). However, the mortality is higher in the present study (23 out of 83, 27.7% with cancer Vs 13 out of 117 without cancer, p=0.005) and this might be associated with the poor quality of antimicrobial therapy in the hospital. Several other studies also demonstrate that the mortality of cancer patients with lower respiratory tract infections is very high (80, 81). Therefore, pneumonia patients with malignancies require careful workup and frequent evaluation of the antimicrobial therapy.

In this study, history of prior recurrent upper respiratory tract infections (URTIs) are also found predictors of poor outcome (p=0.048). Another study has showed that URTI is a risk factor for pneumonia especially in immunocompromised patients (82). Many of the patients included in this study were immunocompromised (44%) and they may experience recurrent bacterial infections. One of the most common recurrent bacterial infections in these kinds of patients is URTIs (82). Hence, consideration of their past medical history in antimicrobial therapy is undoubtedly crucial to decrease their risk of morbidity as well as mortality.

In the current study, patients with high level of blood urea nitrogen (BUN) (>20g/dl) have shown increased mortality (p=0.047) in this study patients. Similar studies also demonstrated that high levels of BUN (>30g/dl) and (>20mg/dl) are associated with increased in 90-day and 30-day mortality respectively (50, 83). High level of BUN (>20g/dl) is one of the severity assessment criterion for CAP (CURB-65). Another study on CAP also noted that patients who on admission experience elevated blood urea were strongly associated with increased mortality (84). However, patients included in this study were also diagnosed with HAP, HCAP, AS. Therefore, high level of BUN may also indicate the severity for HAP and HCAP pneumonia.

Patients with respiratory rate (RR) >24breaths/minute or <12breaths/minute are associated with increased mortality (p=0.014). In this study, patients with abnormal RR were with an odds ratio of 2.5 times greater for poor outcome than the normal ones. Respiratory rate is also the other criterion for severity assessment in patients with CAP having RR greater than or equal to 30 breaths/minute. However, in this study lower RRs (<12 breath/min) was considered as abnormal and included in the study. This is also documented in a retrospective study on CAP in Germany where the risk of dying significantly increases in patients having respiratory rates above 20/min and below 12/min patients with a respiratory rate of 27–33/min had an odds ratio (OR) of 1.72 for in-hospital death, and those with a respiratory rate above 33/min had an OR of 2.55 (85).

6. Limitation of the Study

- Poor documentation
    - Treating physicians did not document all the necessary information like time of admission and time of initiation of antimicrobial therapy.
    - Nurses who were administering antimicrobials to the patients did not properly document the administered antimicrobials in the medication administration sheets.
    - Vital signs were not timely and properly recorded.
- Important laboratory tests such as blood glucose level and serum albumin were not done in most of the patients.

7. Conclusion

The practices of antimicrobial utilization in Tikur Anbessa Specialized Hospital are complicated by different service related factors and physician attitudes. The empirically initiated antimicrobials were seen completed without sufficient evidence of indication and microbiological and radiological findings. Besides, the practices are not supported with relevant local guidelines and no multidisciplinary approach was apparent in the management of infectious diseases. In general, to improve proper antimicrobial utilization and patient clinical outcomes, the hospital requires a coordinated intervention from all concerned bodies and need to establish a functional antimicrobial stewardship program as soon as possible.

8. Recommendations

- The hospital should have an appropriate antimicrobial utilization strategy and specific infectious disease management guidance and establish ASP.
- The hospital should assign clinical pharmacist in the wards.
- The hospital need to have sufficient infectious disease physician and infectious disease trained clinical pharmacists
- The hospital microbiology laboratory need to be furnished with appropriate diagnostic materials and devices
- The hospital need to have uninterrupted supply of antimicrobial agents
- The hospital should develop antibiogram
- The hospital should have list of antimicrobial which are prescribed based on infectious disease specialist consultation
- There should be team based approach of infectious disease management
- Patients' characteristics which are predictors of mortality like previous antimicrobial exposure, recurrent URTI, cancer, high level of BUN and abnormal RR need to be considered while treating pneumonia patients.

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10.Annex I. Data collection format

በአዲስ አበባ ዩኒቨርሲቲ

ጤና ሳይንስ ኮሌጅ

የፋርማሲ ትምህርት ቤት

ጥቁር አንበሳ ስፔሻላይዝድ ሆስፒታል ውስጥ በመታከም ላይ በሚገኙ የሳንባ ምች (ኒሞኒያ) ህሙማን ስለህክምና አሰጣጥ ሁኔታ መረጃ ለመሰብሰብ የተዘጋጀ መጠይቅ ነው።።

መለያ ቁጥር/card no.:_____

ተሳታፊዎች በጥናቱ ለመሳተፍ ፈቃደኝነታቸዉን የሚገልፁበት ቅጽ

ጤና ይስጥልኝ እኔ __ቴዎድሮስ ፈንታ__ እባላለሁ በአሁኑ ወቅት በአዲስ አበባ ዩኒቨርሲቲ፣ ፋርማሲ ትምህርት ቤት በፋርማኮሎጅና ክሊኒካል ፋርማሲ ትምህርት ክፍል የሁለተኛ ድግሪ ተማሪ ነኝ። በመሰራት ላይ ያለው ጥናት የሳንባ ምች (ኒሞኒያ) ህሙማን ህክምና አሰጣጥ ሁኔታን ለመገምገም እና የሕክምና አሰጣጡን ለማሻሻል ኢላማ አድርጎ የተነሳ ጥናትና ምርምር ነው። መረጃ መሰብሰቢያ ቅጹም ይህንኑ አላማ አድርጎ የተዘጋጀ ነው። በመሆኑም ከእርስዎ ፡ ከእርስዎ ካርድ ላይ እና ከሐኪምዎ መረጃ ለመውሰድ እንፈልጋለን። በዚህ ጥናት ውስጥ የርስዎ ተሳታፊነት ሙሉ በሙሉ በርስዎ ፈቃደኝነት ላይ የተመሰረተ ነዉ፤ በዚህ ጥናት ውስጥ መሳተፍዎም ሆነ ላለመሳተፍ መወሰንዎ በሆስፒታሉ ውስጥ በሚያገኙት አገልግሎት ላይ ምንም አይነት ተጽእኖ የማይኖረው ሲሆን ተሳትፎውን በማንኛውም ሰአት ማቋረጥ ወይም ጥያቄዎችን አለመመለስ ይችላሉ። ለጥናቱ የሚስፈልጉት መረጃዎችና ለለተነሱት ጥያቄዎች የሚሰጧቸው መልሶች ሙሉ በሙሉ በምስጢር የሚጠበቁ ሲሆን የርስዎም ስም በማንኛዉም መልኩ በጥናቱ ውስጥ አይገለጽም፤ እንዲሁም የሚሰጡት ምላሽ ከርስዎ ማንነት ጋር በማንኛውም መልኩ አይያያዝም።

በጥናቱ ለመሳተፍ ፈቃደኛ ነዎት?

አዎ ☐ አይደለሁም ☐

ፈቃደኛ መሆናቸውን ካረጋገጡ መረጃ መሰብሰብ ይጀምሩ

ፈቃደኛ ካልሆኑ ወደሚቀጥለው ተገልጋይ ይሸጋገሩ

Data collection format

1. Demographic characteristics:
   - 1.1. Age:_____
   - 1.2. Sex:_____
   - 1.3. Region: _____
   - 1.4. Card No:_____
   - 1.5. Referred from: _____
   - 1.6. Date of admission:_____
   - 1.7. Phone no:_____
2. Past medical history:_____
3. Past surgical history:_____
4. Does the patient have recent antimicrobial medication use history? Yes ☐ No ☐
5. Admission diagnosis :_____
6. Date of pneumonia diagnosis_____
7. Type of pneumonia:-
   - 7.1.1. Hospital acquired pneumonia (HAP) ☐
   - 7.1.2. Community acquired pneumonia (CAP) ☐
   - 7.1.3. Health care associated pneumonia (HCAP) ☐
   - 7.1.4. Aspiration Pneumonia (AP) ☐
   - 7.1.5. Other specify:_____
8. Factors that predispose pneumonia (You can mark "√" one or more risk factors)
   - 8.1. Cigarette smoking ☐
   - 8.2. Upper respiratory tract infections ☐
   - 8.3. Alcohol ☐
   - 8.4. Corticosteroid therapy ☐
   - 8.5. Old age (age >65) ☐
   - 8.6. Recent influenza infection ☐
   - 8.7. Pre-existing lung disease ☐
   - 8.8. Others ,Specify_____
9. Change in diagnosis (if any):_____
   - 9.1. Date of change: _____
   - 9.2. Reason of change (Ask the physician in charge):
     - 9.2.1. Additional Investigation data obtained ☐
     - 9.2.2. New clinical sign and symptom observed ☐
     - 9.2.3. Senior consultation (specify) _____
     - 9.2.4. Other (specify)_____
10. Is there microbiologic test (gram stain and/or culture and sensitivity)?
    - 10.1. Yes ☐
    - 10.2. No ☐
11. Date of sampling for the microbiologic test_____
12. If yes to question 10, microbiologic study results:
    - 12.1. Source:_____ gram stain:_____
    - 12.2. Causative pathogen:_____
    - 12.3. Susceptibility data:_____
    - 12.4. Time of culture collection:_____
13. If no to question number 10, what was the reason (Ask the physician in charge)?
    - 13.1. No institutional guidance that recommend testing ☐

13.2. No well-equipped microbiology lab ☐
13.3. This is the usual practice ☐
13.4. Other reasons, specify_____

14. Initial antimicrobial therapy? Empiric ☐ definitive ☐
15. Initial Empiric/definitive Antibiotic therapy:
    15.1. Name of antimicrobial (s), dose, route, frequency:_____
    _____
    _____
    15.2. Time and date of initiation:_____
    15.3. Duration:_____
    ___
    15.4. Any missed doses and reason_____
16. Prescribing physician (empiric or definitive):
    16.1. infectious disease physician ☐
    16.2. infectious disease fellow ☐
    16.3. internal medicine resident ☐
    16.4. internist ☐
    16.5. emergency medicine resident ☐
    16.6. emergency medicine specialist ☐
    16.7. other specify ☐
17. Is there any medication use consultation with a clinical pharmacist?
    17.1. Yes ☐ 17.2. No ☐
18. If the response is No? What was the reason?
    18.1. Not consider their role
    18.2. Absence of assigned clinical pharmacist in the ward
    18.3. The clinical pharmacist is not interested in patient management
    18.4. Other specify ……..
19. Which guideline is used to prescribe the above (q. 15) medication (s) to the patient?
    19.1. FMHACA ‘s STG
    19.2. Institutional guideline (TASH)
    19.3. Other international guideline (s) (specify):_____
    19.4. Reference Book (s) (specify)_____
    19.5. Other (specify)_____
20. Is there a change in antimicrobial agent (s) or regimen?
    20.1. Yes ☐ 20.2. No ☐
21. If yes to the above question, mention the following information
    21.1. **1st time change**: Name of antimicrobial (s), dose, route, frequency:_____
    21.2. Time and date of change: _____
    21.3. Duration:_____
    21.4. Any missed doses and reason:_____

21.5. **2nd time change**: Name of antimicrobial (s), dose, route, frequency:_____

21.6. Time and date of change: _____

21.7. Duration:_____

21.8. Any missed doses and reason:_____

21.9. **3rd time change**: Name of antimicrobial (s), dose, route, frequency:_____

21.10. Time and date of change: _____

21.11. Duration:_____

21.12. Any missed doses and reason:_____

22. Reason for change:

22.1.	Poor response	☐	22.4.	Drug shortage	☐
22.2.	Inadequate selection	☐	22.5.	Not defined	☐
22.3.	Side effect of antimicrobials	☐	22.6.	Change in diagnosis	☐

22.7. Other specify:_____

23. Prescribing physician (the physician that changes the regimen):

23.1.	Infectious disease physician	☐	23.4.	Internal medicine resident	☐
23.2.	Infectious disease resident	☐	23.5.	other (specify)_____	
23.3.	Internist	☐			

24. Route of drug administration changes:

✓ **Patient Eligibility Criteria and incidence of conversion**

- Criteria for patient eligibility

i. Inclusion criteria for IV to PO therapy conversion

- Intravenous antimicrobial for > 24 hrs
- Clinical improvement (Temp. < 37.8^0C, O_2 saturation >92%, stable blood pressure, Pulse rate <100 beats.min^{-1}, respiratory rate, <25 breaths.min^{-1})
- Afebrile for >24 hours (core temperature <38^{o}C)
- Oral administration of fluids is feasible
- Oral administration of tablets is feasible

ii. Exclusion criteria for IV to PO therapy conversion

- Oral routes compromised (vomiting ,nil by mouth, severe diarrhea , swallowing disorder, unconscious)
- Quinolone Exclusion for those receiving continuous enteral feeds
- An appropriate oral medication is not available
- Patients develop sepsis after pneumonia diagnosis (ie.2 or more the following: temp > 38 or <36^{o}C,heart rate > 90bpm,respiratory rate >20 breath/minute, WCC > 12 x 10^3/micL or < 4 x 10^3/micL) / deteriorating clinical condition (86) .
- Patients develop febrile neutropenia after pneumonia diagnosis (ANC less than 1 x 10^9 /L)
- Patients develop Serious deep seated infection after pneumonia diagnosis that requires IV therapy as a co-morbid (e.g. meningitis, endocarditis, infection of a prosthetic device.

24.1. Is there IV-to-PO route conversion?

Yes ☐ No ☐

24.2. Instead of IV drugs, is oral medication started without fulfilling of eligibility criteria?

Yes ☐ No ☐

24.3. If the answer is "Yes", Reasons…….

i. Absence of first line IV medication ☐
ii. Patient doesn't tolerated IV routes ☐

iii. Others , specify _____

24.4. Which oral medication is used because of absence of first line IV medication

_____

24.5. Are there any other oral drug prescriptions prescribed for and received by patients while on IV antibiotic therapy. Yes ☐ No ☐

24.6. If your answer yes, list the drugs and its indication_____

_____

24.7. Additional IV antibiotics for admitted patients without changing/revision of the first established diagnosis. Yes ☐ No ☐

24.7.1. 1st time:-Start date & time _____End date & time _____

Name of antimicrobials, Dose, Frequency:

_____

Duration._____

24.7.2. 2nd time:- Start date & time _____End date & time _____

Name of antimicrobials, Dose, Frequency:

_____

Duration._____

24.8. Is there any revision/change of diagnosis and order of medications after the first established diagnosis? Yes ☐ No ☐

24.8.1. Revised/changed diagnosis (2nd time),

Specify._____

Start date & time,_____ End date & time _____

Name of antimicrobials, Dose,

Frequency._____

Duration._____

24.8.2. Revised/changed diagnosis (3rd time),

Specify._____

Start date & time _____End date & time _____

Name of antimicrobials, Dose,

Frequency._____

Duration._____

24.9. Was conversion made after fulfilling of eligibility criteria?

24.9.1. Yes ☐

24.9.2. No conversion ☐

24.10. If the answer to query no. 24.9 is "Yes". Which to which?

Intravenous (IV)	Oral (PO)
Start date _____	Conversion date _____
Start time _____	Conversion time_____
Name1._____	Name1._____
2._____	2._____
Dose_____	Dose _____
Frequency_____	Frequency _____
Duration_____	Duration _____

24.11. At what time was conversion made?

- Converted at early with eligibility criteria (conversion was made within 2 to 4 days after admission) ☐
- Converted with in 24 hr after fulfilling eligibility criteria ☐
- Converted in between 24-48 hr after fulfilling eligibility criteria ☐
- Converted in between 48-72 hr after fulfilling eligibility criteria ☐
- Converted after 72 hr of fulfilling eligibility criteria ☐ Number of Day, Date & Time, specified;_____
- IV stopped lately after fulfilling eligibility criteria ☐ Number of Day after clinical stability , Date &Time specified;_____
- Converted in upon discharge or', ☐ No. of Day, Date &Time specified_____
- IV stopped at point that switching becomes possible' ☐ No. of days_____
- IV to PO converted without fulfilling eligibility criteria ☐

Note. If IV therapy was stopped on the day clinical stability is achieved and no oral therapy was initiated, the patients are categorizing as 'IV stopped at point that switching become possible'.

24.12. Follow-up patient status after IV to PO conversion (at least 72 hours).

24.12.1. Continued PO until discharged/clinical stability. Yes ☐ No ☐

24.12.2. Converted to other PO agents :- After omission of the first PO medication ☐

Additional PO medication ☐
For additional PO medication: - Name, dose, frequency _____
Reason/Indication _____Duration _____Cost_____
Start Date & Time_____ End Date & Time_____

24.12.3. Converted back to IV agents to previous one ☐ OR other agent ☐

Name, dose, frequency _____
Reason/Indication_____
Duration_____ Cost_____

24.13. If the answer is **"No"** for question number **24.9** (No conversion made after fulfilling of eligibility criteria) and continuation of IV therapy on day 3 or more than 3 days of treatment.

Why?_____

_____

25. Which guideline is used after revision/change of the diagnosis?

25.1. FMHACA 's STG ☐

25.2. Institutional guideline ☐

25.3. Other international guideline (s) (specify):_____

25.4. Reference Book (s) (specify)_____

- **Duration of antimicrobial therapy and hospital stay**

i. Total duration of antibiotic therapy while hospital stay : -
Start date & time_____ End date & time _____

ii. Duration on IV antibiotic therapy: - Start date & time _____
End date & time _____

iii. Duration on PO antibiotic therapy while hospital stay and continued after discharge: -
Start date & time _____End date & time _____

iv. Total duration of antibiotic therapy while hospital stays and continued after discharge.
Start date & time_____ End date & time _____

v. Time to clinical stability as per clinical improvement parameter (Temp. < 37.8^{0}C, O_2 saturation >92%, stable blood pressure, Pulse rate <100 beats.min^{-1}, respiratory rate, <25 breaths.min^{-1}): Admission, Date & Time _____Clinical improvement observed, No. of Day. Date & Time _____

vi. Number of IV antibiotic prescriptions for which duration will be specified (total number of drugs)_____

26. Clinical Outcome:

26.1. Clinical cure/stability ☐

26.2. Mortality Due To Pneumonia ☐

26.3. All- cause mortality ☐

26.4. Other (specify)_____

27. Total Length of hospital stay due to pneumonia _____

28. Date of admission_____

29. Date of discharge_____

30. Vital signs:

V/s start from pneumo dx	Date/Time													
	Normal range													
T(C)^o	36.5-37.2													
BP(mmHg)	<120/80													
PR (per min)	60-100bts/min													
RR (per min)	12-16bre/min													
SaO_2 on atm.	>92%													
SaO_2 on oxy.	>95%													

30.1. Laboratory findings: start from pneumonia dx

Tests			Data / Result													
	parameters	Ranges														
CBC/FBC	WBC/TLC															
	Neutrophils%															
	Lymphocytes%															
	RBC															
	Hb test															
	PCV/Hct															
	MCV															
	MCH															
	MCHC															
	Retic.count															
	Monocytes															
	Eosinophils															
	Basophils															
	PLT															
	RDS															
	ESR															
	CRP															
	PT															
	aPTT															
	INR															
LF Ts	Bilirubin total															
	Direct/conj.															

	ALT/SGPT														
	AST/SGOT														
	ALP														
	LDH														
	Albumin														
	Globulin														
	Total Serum Prot.														
RFRs	BUN														
	Cr_s														
	UA														
ELECTROLYTES	Na														
	Cl														
	K														
	HCO_3/CO_2														
	Ca														
	Mg														
	PO_4														
BG & HbAIc & OTHER TESTS	RBS														
	FBS														
	HbAIc														
		Date													
Radiology	**CXR**														
	Chest CT														
Other tests															