Intravenous-to-oral antimicrobial therapy conversion: clinicians' knowledge, beliefs, acceptance and current practice at Jimma University Specialized Hospital, Southwest, Ethiopia

ALEMSEGED BEYENE, B.Pharm

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Alemseged Beyene,B.Pharm

Advisors

1. Wubeante Yenet : B.Pharm, MSc, Ph.D
2. Sintayehu Fekadu : MD, DTMH
3. Gizat Molla : B.Pharm, MSc, MBA

Abstract

Background: *The practice of early intravenous to oral antimicrobial therapy conversion has not received much emphasis, but if practiced to its full extent presents a unique and exciting opportunity to reduce costs significantly while improving the quality of patient care. Many studies had convincingly demonstrated the efficacy, safety and the economic impact of timely intravenous (IV) to oral (PO) route therapy conversion. This study was conducted to explore clinician's baseline knowledge, beliefs, acceptance and current practice of IV to PO antimicrobial therapy conversion among hospitalized patients at medical and surgical wards of Jimma University Specialized Hospital, Southwest Ethiopia.*

Methods: *A self-administered questionnaire was distributed among practicing physicians to assess their baseline knowledge, beliefs, acceptance and current practice on IV to PO antimicrobial conversion. Hospital based observational study was conducted to assess the practice and factors that influence IV to PO antimicrobial therapy conversion from March to June 2013 at medical and surgical wards of Jimma University Specialized Hospital. Patient cards, charts and medication records were also reviewed for appropriateness of IV to PO therapy conversion program at least every 24hrs using a pretested data collection format. The non-parametric tests, Kruskal-Wallis and Mann-Whitney tests were used to determine the clinicians on the differences of ratings for clinical factors and agreement to a set of practice statement. Independent-samples t-test* was used to compare converted and non-converted patients. *Two-tailed P values of <0.05 were regarded as significant.*

Results: *A total of one hundred nine practicing clinicians were included in this study. The factors most highly rated for antimicrobial conversion were the ability to maintain oral intake (81.1%), normalized temperature (81.1%) and stabilization of co-morbid conditions (83.5%). Majority of the clinicians (85.3%) agreed with the traditional clinical rule that "patient should be afebrile for 24 hours before IV to oral conversion". Senior physicians had the highest knowledge score among the clinicians. However, there was no considerable difference on opinion about a guideline being integrated into practice. 71 patients were included in the study, of this two third 48(67.6%) of the patient were eligible for IV to oral antimicrobial conversion. However, 20.9% were timely converted, while 45.8% of them were*

not converted and the IV therapy was stopped among the remaining 27.1% patients at point that conversion was possible. Significant minority, 6.3% of patients were converted from IV to PO therapy without fulfilling eligibility criteria. A shorter duration of IV therapy was recorded for converted (2.80±1.87) versus non-converted patients (8.50±6.32), (P=0.009).Clinicians' barriers to an early conversion in clinically stable patients included presence of co-morbidity 28.6% (8/ 28), should receive a standard duration of intravenous antibiotics 25 %(7/25), forgetting to convert to oral agents 21.4 %(6/28).

Conclusion: *Clinicians believed that patients with moderate to severe infection could be converted from IV to oral antimicrobials once they are able to tolerate oral intake, the temperature had normalized and after stabilized co-morbid conditions. However, there was considerable variation in several antimicrobials practice belief. Hence, guidelines that are carefully developed are necessary to address the heterogeneity in the practice beliefs we observed. The converted patients had shortened IV duration than the non-converted one. Besides, the conversion from IV to oral antimicrobials is often unnecessarily delayed in patients hospitalized with moderate to severe infection due to different types of barriers.*

Keywords*: antimicrobial therapy, clinicians, Jimma University Specialized Hospital, Ethiopia, Intravenous to oral conversion.*

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ACRONYMS AND ABBREVIATIONS

CAP: Community acquired pneumonia

COPD: Chronic obstructive pulmonary disease

IV to PO: Intravenous to Oral

IV: Intravenous

JUSH: Jimma University Specialized Hospital

PO: Oral

UTI: Urinary tract infections

CHAPTER ONE:

INTRODUCTION

1.1. BACKGROUND

Antibiotics are widely being prescribed to treat infections, both in the community and hospital setting. The rational use of medicines has been defined by the WHO as requiring that patients receive medications appropriate to their clinical needs, in doses that meet their own requirements, for an adequate time, and at the lowest cost to them and their community.

The overuse and misuse of antibiotics in hospitals have an impact on therapeutic efficacy, bacterial resistance and costs that warrant the implementation of programs to improve the use of antibiotics in hospitals especially in countries with limited resources (1).

One of the methods to improve rational use of antibiotics is by implementing IV to PO therapy Conversion. 'Intravenous (IV) to Oral (PO) Therapy Conversion' comprises three types, such terms include "switch therapy", "sequential therapy" and "step-down therapy" to describe the conversion of IV to PO therapy, using the same or a different compound, as soon as patients are judged clinically stable, according to specified criteria, without the loss of antimicrobial potency (2).

The term "anti-microbial conversion" describes the practice of converting intravenous anti-microbial therapy to an alternative oral formulation; IV-to-oral antibiotic switching programs have been adopted in many countries way back in the 1990s. Ever since then, many studies have been carried out and had convincingly demonstrated the efficacy, safety and its economic impact in the clinical institution (3).

The escalating costs associated with antimicrobial chemotherapy have become of increasing concern to physicians, pharmacists and patients alike. A number of strategies have been developed to address this problem. This study focuses specifically on the strategy of converting patients from intravenous to oral medication regardless of whether the same or a different class of drug is used (4). An intravenous (IV) to oral conversion program can lower drug costs for an institution and its patients. Numerous studies have documented clinical

efficacy, fewer complications, shorter hospital stays, and cost savings by converting patients from IV to PO therapy (5-6).

The ideal medication to include in an IV to PO therapy conversion program has several characteristics. The oral dosage form should have excellent bioavailability (ideally greater than 80%), be well tolerated upon administration, and its use should be supported by clinical data. Other optimal properties include the availability of multiple oral dosage forms (e.g. tablets and liquids) and dosing at a frequency equivalent to or less than the IV formulation (2).

The most common medications targeted for a program of this type are antimicrobials, because these agents often account for 20%–40% of an institution's drug budget (7). However, several other drugs can be converted also, such as IV histamine (H2) receptor antagonists, enalaprilat, dexamethasone, methylprednisolone, and diuretics (8). Numerous anti-infectives, such as ciprofloxacin, ofloxacin, rifampin, cefuroxime, amoxicillin-clavulanate, clindamycin, fluconazole and metronidazole, have high oral bioavailability(8).The most effective programs include automatic interchange, discussions with prescribers, and the placing of notes in patients' medical charts (9).

Proper identification of patients, diagnosis , medications, and contraindications to oral therapy are all essential aspects for a successful IV to PO therapy conversion program (2). Conventional inclusion criteria for conversion from IV to PO antimicrobial therapy are signs of clinical improvement; functioning GI tract as evidenced by consuming and tolerating scheduled PO medications; and/or PO diet without signs of nausea, vomiting, or diarrhea (10-11). Patients may be excluded from IV to PO antimicrobial conversion if the following are determined to be present: malabsorption disorders, high aspiration risk, and/or intensive care unit (ICU) admission. Patients on antimicrobials with a more severe infection or immunocompromised status maybe excluded from IV to PO conversion programs (10-12).

1.2. STATEMENT OF THE PROBLEM

Over-prescribing and misusing empiric, therapeutic, and prophylactic antibiotics appears to be a national health problem especially in resource limited countries. Inappropriate use of antimicrobial agents results in serious and dangerous consequences to patient care and adds cost unnecessarily to the institutional antimicrobial budget (13-14).

Though most of the PO antimicrobial agents have excellent bioavailability with similar antimicrobial activity to those parenteral agents, the patients were not timely converted to PO antimicrobial therapy after admission in hospital ward, although they are candidates for IV to PO therapy conversion.

Majority of antimicrobial resistance (AMR) was initially observed in hospital acquired infection but soon also becomes wide spread in community acquired infection (15). For this case among hospitalized patients, IV catheter provides a major role as a portal for bacterial and fungal growth results from prolonged time use of intravenous medication.

Currently the cost expenditure of IV antimicrobials is highly increasing, there has been mounting pressure to reduce the use of IV antimicrobials. The practice of early conversion program from intravenous to oral therapy in the hospital patient has never received much emphasis ,but if utilized to its full extent represents a unique and exciting opportunity to reduce costs significantly while improving the quality of patient care (16).

In addition to the fact that, antimicrobial prescribing pattern is uncontrolled fashion since ever the earliest year of anti-infective era, so institutional policymaking and implementation are very important for rational use of antimicrobial including timely switch of parentral to oral antimicrobials (3).

While many studies have been carried out to measure the impact of IV to PO conversion therapy on hospital's finance, patient's comfort and satisfaction, very few studies have been conducted to provide a detailed description of the implementation process as well as to identify the barriers to implementation .

Antimicrobials represent approximately 25% of the hospital drug budget and 1.5- 4.5% of total health care costs. So, the development and implementation of protocol/guidelines are important to provide a cost-effective conversion from IV to PO antimicrobial administration and to reduce the length of hospitalization without compromising patient care (17).

In developing countries, including Ethiopia the health professionals don't play major role in the proper utilization of IV to PO antimicrobial converting practice. Only a limited number of researches described, though not in Ethiopia, how to implement therapeutic interchange program in which patients are converted from IV to PO medication based on eligible criteria in a general population of medical patients with assessing barriers (18), and explored clinicians' baseline knowledge, practice beliefs and acceptance (19).

Before the implementation of a formalized early IV to PO conversion program for hospitalized patients, what patient and physician characteristics influence the timing of the conversion to oral treatment and whether physicians perceive barrier to an early –conversion strategy (18). There are no studies that have examined the factors contributing to unintended IV to PO conversion, despite fulfillment of clinical parameter for patients admitted at Jimma University Specialized Hospital (JUSH). Poor healthcare infrastructure, lack of education and training, minimal regulatory control on the supply and quality of antimicrobials, inappropriate hygiene, overcrowding, lack of resources for infection control, and a lack of appropriately trained infection control personnel are some of the barriers to the effective implementation and audit of interventions by health personnel in developing countries (20).

There is no established document, guidelines and/or protocols regarding intravenous to oral antimicrobial therapy conversion practice in Ethiopia. This has been resulted in an increased cost of medication, hospital acquired infections, work load of clinicians, pharmacists and nurses' duties, hospital stay and overall health care system expenditure. Therefore, the aim of this study to evaluate the physicians' knowledge, perception and the current practice of conversion from IV to PO antimicrobial therapy early in the treatment phase for appropriate patients and the determinants.

CHAPTER TWO:

2.1 LITERATURE REVIEW

In previous time, patients with severe infections first treated by intravenous antibiotics followed by oral therapy. Unfortunately this approach results in unnecessary prolongation of intravenous treatment, with all its inherent disadvantages. Intravenous to oral therapy conversion, however, ensures an early convert to the oral route when the patient is clinically stable (21).

Dosage formulation and bioavailability play an important role in conversion therapy. For the reason that not all IV antibiotics are available as an oral formulation, clinicians need to be familiar with which oral antibiotics are equivalent to intravenous antimicrobials. High bioavailability, i.e.>90%, is preferred for oral agents in IV to PO antimicrobial therapy conversion. Also, oral antimicrobials should be well tolerated with a less potential side-effects profile and have a 'low resistance potential' (22).

Appropriate oral medication use produces equivalent clinical outcomes, causes fewer complications, less patient inconvenience, and is generally less costly. There are many medications that can be included in IV to PO conversion program. Patients eligible for IV to PO therapy conversion should tolerate oral medications, be converted to an oral agent that acts similarly or equivalent to the IV counterpart, meet inclusion criteria, not have any contraindications to PO therapy, and be improving clinically (2).

The advantage of timely and appropriate IV to PO conversion are well recognized and represents a cost-effective strategy by decreased drug acquisition, hospitalization and non-drug costs (23-24); decreased duration of IV therapy (25-26); decreased workload and nursing time (23);that also minimized side effects associated with intravenous lines (11, 27) and facilitates earlier hospital discharge (24) .

Patients are more comfortable if they do not have an IV catheter in place. Attachment to an IV pole can restrict movement, which can hinder early and/or frequent ambulation. Patients who continue to receive parenteral therapy are at an increased risk for infusion-related adverse events. In addition, the presence of an IV catheter provides a portal for bacterial and fungal growth. These secondary infections can lead to additional antibiotic therapy, prosthesis failures, sepsis, and in a small number of cases, death. Using PO therapy also reduces hidden expenses such as the cost of IV sets and pumps, laboratory monitoring, and nursing and pharmacy personnel time. Most significantly, early use of PO therapy may allow for earlier discharge from the hospital (2).

The presence of tube feedings should be taken into considerations in the conversion of IV to PO therapy. For certain medications specifically the fluoroquinolones, warfarin, and phenytoin absorption and effectiveness are reduced in the presence of enteral feedings. This is not an absolute contraindication unless the tube feeding cannot be interrupted. The conversion from IV to PO therapy in the presence of continuous tube feeding will be managed with the help of the provided guidelines reported on studies of Lourenco R, 2001. and Gilbar PJ. ,1999 (28-29). Patients receiving continuous enteral nutrition are excluded from therapeutic interchange to oral fluoroquinolones (because concomitant use may significantly decrease fluoroquinolone bioavailability) (30).

Patients who are converted from IV to PO therapy need to be monitored by the pharmacist to make sure they are progressing satisfactorily on oral therapy. Data concerning length of stay and total days of therapy can be collected to help justify the conversion program and to document economic savings. Monitoring parameters include temperature, WBC count, culture and sensitivity results, patient assessment, clinical outcome, adverse effects, x-rays, presence and characteristics of a cough, and wound appearance (5, 7).

In 2004, Vogtlander N et al, at the Department of General Internal Medicine, University Medical Center Nijmegen, in the Netherlands, involved the departments of internal medicine, surgery, and neurology and the emergency department at a tertiary referral university medical center in a study of all consecutive patients receiving therapeutic antibiotics reported that the antimicrobial treatment costs account for 25% of the drug budget in the hospitals, with

broad-spectrum intravenous (IV) agents usually accounting for a significant proportion of this expenditure. The choice, timing of the initial dose, IV to PO conversion, and streamlining of antibiotics mean that adjustment of initial empirical treatment to narrow-spectrum therapy, guided by culture, microscopy susceptibility tests are important components of rational use of antimicrobial (31).

Study carried out by Lee S L *et al* 2012 in the University Sains Malaysia at Pulau Pinang Hospital, of the 422 eligible clinicians, the clinician's questionnaire response rate accounts 52.4%(19) ; in other prospective cohort study by Engel MF *et al* 2013 reported at two teaching hospital in the Netherlands , 97(91%) were interview from 107 involved physicians(18); while clinician's characteristics of the respondents are mean age is 30.5 ± 6.3 and the mean years of clinical practice is 5.05 ± 5.51. One fifth (18%) clinicians practiced as general internal medicine and other medical subspecialties, meanwhile over 86.0% claimed that their department practiced IV-to-oral antibiotic switching. The mean time of switching in the past week was reported to be 4.29 ± 5.43(19);Of the 148 patients , the mean ± SD age is 67 ± 17 years and 71(48%) were female (18).

In 2012, Lee S L *et al* reported that, from a clinical perspective, the Physicians response rated as "very important" determinants in deciding when to converted patients from IV to oral antibiotics, most highly rated were the ability to maintain oral intake (85.6%) and microbiology etiology (85.0%), where as the least pertinent while deciding the converted were the returning of blood pressure (44.3%) and oxygenation (48.9%) to baseline. Majority (76%) of the Physicians agreed the traditional clinical rule that should be afebrile the patients for 24 hours before IV-to-oral conversion. In addition to that "patient should receive a standard duration of IV antibiotic" account 47% agreed and 36% disagreed, while almost equal proportion of physicians agreed (27%), disagreed (36%) and (37%) are neutral about the belief that "The WBC count is returning to within the reference range before IV-to-oral conversion". Sixty nine percent of the physicians agreed that "patients should not be converted if more than one of the following is present – heart rate (HR) ≥ 100 beat per minute , respiratory rate (RR) ≥ 20 breath per minute, blood pressure (BP) ≤ 100 mmHg, white blood cell $<4 \times 10^9$/L or $>12 \times 10^9$/L. At last 84% physicians agreed that "oral route

should not be compromised while considering the conversion". Beside this, the acceptance of IV to oral antibiotic conversion guideline in practice, 92.7% of physicians agreed with such introductory step (19).

Similarly, in a written survey study by Halm et al, 2001in seven teaching and non-teaching hospitals in Pittsburgh,Pa, antibiotic conversion decision in pneumonia ,the following factors were rated as very important : absence of suppurative infection (93%),ability to maintain oral intake (79%), respiratory rate at baseline (64%),no positive blood culture findings (63%),normal temperature (62%), oxygenation at baseline (55%),mental status at baseline (50%).Fifty-eight percent of physicians believed that "patients should be afebrile for 24 hours before conversion to oral antibiotics," and 19% said "patients should receive a standard duration of intravenous antibiotics." (32).

Van Niekerk et al. 2011 study in the general medical wards of a tertiary-level hospital in South Africa ,the five most common admission diagnoses were lower respiratory tract infections (26.7%–40%), HIV (13.3%–27.3%), tuberculosis (19.3%–29.3%), cardiovascular diseases (12%–19.3%) and chronic obstructive pulmonary disease (11.3%–12.7%) (26). Nighty five (64%) patients had one or more co-morbidities ; the prevalent co-morbidities were lung disease (n=49;33%) and malignancy (n=18;12%)(18); the three most common chronic diseases present before admissions were CV disease (28%–33.3%), HIV (20%–26.7%) and TB (11.3%–17.3%)(26).

The percentage of patients in which converted from IV to Oral while pre-implementation audit using (n=150) of study population result in 13% converted, 67% could have been converted but not converted, 21% IV stopped at point that converting (26).

The five most common IV antibiotics used at van Niekerk et al. study site were ampicillin (21.5%; 134/622), amoxicillin/clavulanic acid (14%; 87/622), cefuroxime (11.9%; 74/622), cefazolin (11.9%; 74/622) and ceftriaxone (9%; 56/622). The most common oral antibiotic prescribed for conversion therapy was amoxicillin with or without clavulanic acid (26) .

Van Niekerk et al. (2011) reported that, the time it took for patients to reach clinical stability during pre-implementation audit (4.7± 2.5 days).IV to Oral converted patients generally had

a shorter time to clinical stability (3.2–4.1 days) than non-converted patients (3.9–4.5 days). Converted patients were observed in hospital after the initiation of oral therapy for a mean of 3.6 days (pre-implementation audit), moreover this group spent less time in hospital than non- converted patients. Duration of IV therapy after clinical stability for non-converted patients (days) mean ± SD 3.8±2.4 (n=100). Number of IV antibiotic prescriptions for which duration was specified (n=total number of prescriptions) 40 (n=204), and the length of hospital stay (days) converted patients mean± SD 8±5.0 (n=19), whereas the non-converted patients mean ± SD 11.5±5.6 (n=100). The number of oral drug prescriptions prescribed for and received by patients on IV antibiotic therapy accounts (90.7%–97.3%); its result was showing few patients had gastrointestinal absorption problems (26).

In 2012, S L Lee et al reported on a substantial differences were noted between medical and pediatric physicians for ratings of the agreement that "patient should not be switched to oral antibiotics if HR ≥ 100 min, or RR ≥ 20 BPM, or BP ≤ 100 mmHg or white cell count < 4 x 109/L or >12 x 109/L is present(19).

In 2001, case study on Huntington Memorial Hospital, which is a 525 bed, full-service , community hospital affiliated with two major university, Wong-Beringer A, et al reported on reasons for continuing patients on IV therapy include: clinical instability of the patient (71%); uncertainty about gastrointestinal function (39%); about which oral alternative would be appropriate (39%) ; uncertainty about availability of oral alternatives (37%); and simply no thinking it at the time (35%) (33). Similar study by S L Lee et al (2012), reported on the reasons for continuing IV therapy: 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%) (19).

2.2 CONCEPTUAL FRAME WORK

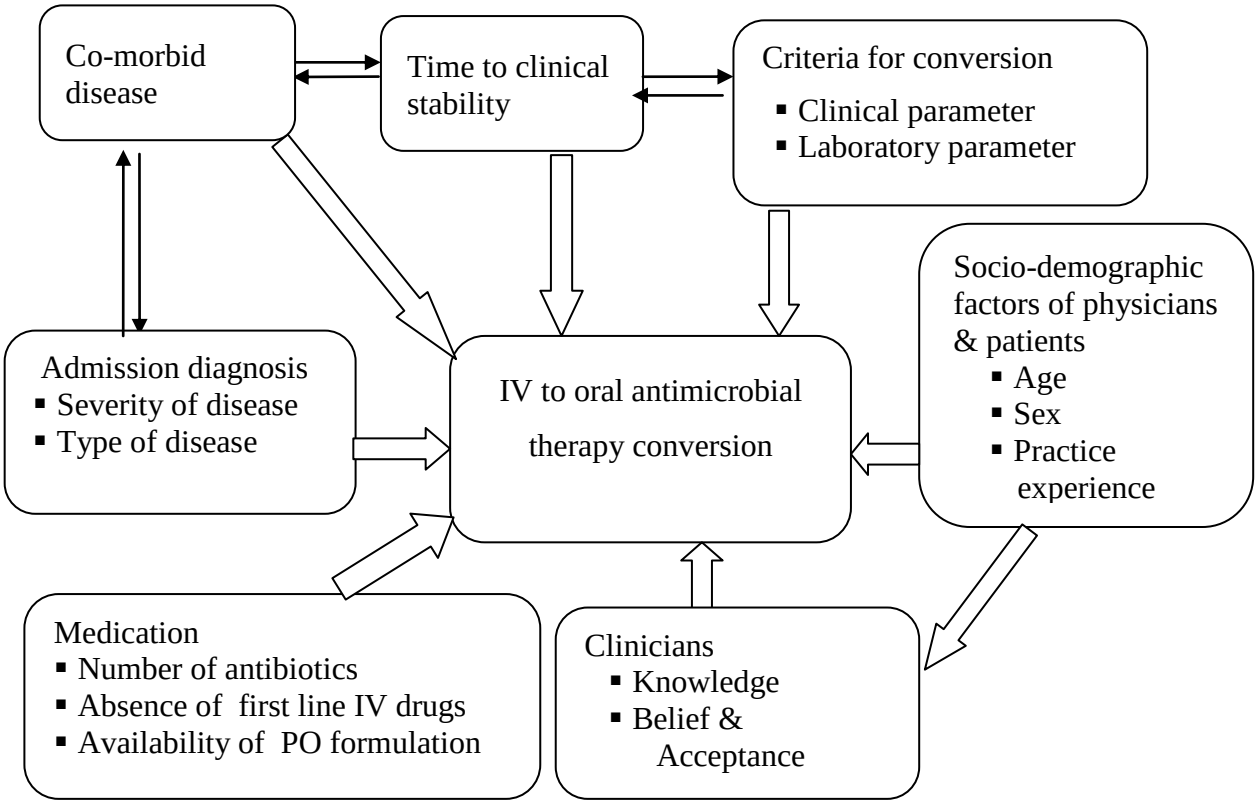


Figure 1:- A conceptual frame work to depicting an interaction between the determinant factors and its outcomes (intravenous to oral antimicrobial therapy conversion).

2.3. SIGNIFICANCE OF THE STUDY

This study has explored clinician's baseline knowledge, belief, acceptance and current practice of IV to PO antimicrobial therapy conversion. It identified the reasons for delayed or non-converting of IV to PO antimicrobial therapy conversion. The findings of the present study is crucial to come up with specific recommendations for practice of timely conversion of IV to PO antimicrobial therapy, which will have a paramount importance on cost and safer use of antimicrobials. The findings will also be used as primary and important sources of reference prior to the implementation of IV to PO antimicrobial conversion guidelines at institutional level.

The finding of this research as a baseline, forwards practical recommendations for policy makers and service providers to create confidence and gives clue for health policy maker for designing appropriate use of antimicrobials suitable to IV to PO antimicrobial therapy conversion. In effect, the preliminary finding of this research is open a road map for further exploration of practice and perceived barriers for effective implementation of IV to PO conversion at hospitals.

CHAPTER THREE:

OBJECTIVES

4.1. GENERAL OBJECTIVE

To explore clinicians' knowledge, belief, acceptance and current practice of IV to Oral antimicrobial therapy conversion among hospitalized patients in Jimma University Specialized Hospital, Southwest Ethiopia.

4.2. SPECIFIC OBJECTIVES

- To assess the knowledge of the prescribing physicians regarding intravenous to oral therapy Conversion
- To assess the perception of prescribing physicians towards intravenous to oral antimicrobial therapy conversion
- To determine the proportion of patients who are converted from intravenous to oral antimicrobial therapy based on the eligibility criteria at medical and surgical ward
- To determine the duration of IV antimicrobial therapy of inpatients at medical and surgical ward
- To identify the reasons for delayed conversion or non-conversion from intravenous to oral antimicrobial therapy among eligible inpatients.

CHAPTER FOUR:

PARTICIPANTS AND METHODS

4.1. STUDY AREA AND PERIOD

The study was conducted at Jimma University Specialized Hospital (JUSH) medical and surgical wards between March and June, 2013. JUSH is a teaching hospital located in Jimma Town of Oromia National Regional State, 350 Km Southwest of the capital city, Addis Ababa. It is the only referral hospital in Southwest Ethiopia with 450 beds and 750 health professionals and supportive staff where a multidisciplinary team of diverse professionals provide a range of health care services for approximately 9000 inpatients and 80,000 outpatients each year. The overall catchment population for this hospital is nearly 15 million.

The medical wards (A, B &C) have a total bed capacity of 89 and run by 12 specialists, 28 resident physicians, 18 BSc and 26 diploma level nurses. Similarly, the surgical wards (A&B) also having 78 beds and practicing by 6 specialists, 24 resident physicians, 18 BSc and 23 diploma level nurses. There are various groups of students attaching both wards.

5.2. STUDY DESIGN

Hospital based cross-sectional survey was conducted through self-administered questionnaire to explore clinicians' general baseline knowledge, beliefs and acceptance of IV to PO antimicrobial conversion practices at Jimma University Specialized Hospital. The questionnaire filled by the clinicians' was not case specific, rather general. Data regarding the current practice of IV to PO antimicrobial therapy conversion in the hospital and patient eligibility was collected through a structured checklist and observation.

5.3. POPULATION

5.3.1. Source Population

All clinicians practicing at and patients admitted to medical and surgical wards of Jimma University Specialized Hospital.

5.3.2. Study Population

For the study of knowledge and perception of IV to PO antimicrobial conversion therapy 154 of residents and senior physicians practicing at the hospital were included. For the evaluation of the current practice of IV to PO antimicrobial therapy conversion, 71 of patients admitted to medical wards for pneumonia and urinary tract infections; and to surgical wards for skin and soft tissue infection (e.g. Cellulitis, Soft tissue laceration, Pyomyositis etc), and bone and joint infection (e.g. Osteomyelitis) at JUSH during the time of data collection were included for the study.

5.4. INCLUSION AND EXCLUSION CRITERIA

5.4.1. Inclusion criteria

- All specialist and resident physicians practicing at Jimma University Specialized Hospital
- All adult patients admitted to medical and surgical wards during the study period in which the prescription should have at least one IV antimicrobial for conditions of community-acquired pneumonia (CAP), urinary tract infection (UTI), skin and soft tissue infection, and/or bone and joint infection.

5.4.2. Exclusion criteria

- Serious deep seated infection that requires IV therapy as a co-morbid (e.g. meningitis, endocarditis, deep abscess, cystic fibrosis, infection of a prosthetic device) because prolonged IV treatment is often necessary in these patients.
- Recognized surgical prophylactic schemes lasting < 24 hr.
- Neutropenia (leukocyte count $<0.5 \times 10^9/L$)
- Hospital acquired pneumonia
- Long duration treatment (> two months) with unsettled working diagnosis.

5.5. SAMPLE SIZE AND SAMPLING METHOD

All full time senior physicians and residents practicing general medicine, critical care, surgery, obstetrics & gynaecology, paediatrics, psychiatry, opthalmology, dermatology, and acute care during the study period was included in cross sectional survey.

All adult patients admitted to medical and surgical wards for community-acquired pneumonia, urinary tract infection, skin and soft tissue infection and /or, bone and joint infection during the study period in which the prescription should have at least one IV antimicrobial were included in the study.

5.6. DATA COLLECTION AND MEASUREMENT

Two data collection formats were prepared by principal investigator after thoroughly reviewing different literatures. Data was collected using pre-tested and self-administered structured questionnaires for clinicians and checklists were used to extract information from patients.

5.6.1. Data collection form for clinicians

The survey questionnaire (in English) had seven sections. The first section comprises of demographic data of the respondents, including age, gender, current position, specialty and length of service in clinical practice.

The second section asked respondents to rate the importance of the given 13 clinical factors involved in deciding IV-to-oral antimicrobial conversion. They were identified in a previous study (32), which shares similar objectives with the current study, as important factors to the hospital discharge decision. Respondents rated each factor using a 5-point Likert scale, as very unimportant, unimportant, neutral, important and very important.

To better understand clinician practice beliefs, the third section asked the respondents to state the level of agreement to the given five clinical statements about the converting practice adapted from the similar study(19), using another 5-point Likert scale (1, strongly disagree to 5, strongly agree).

The fourth section comprised a checklist by which respondents were allowed to select the possible reason(s) identified in a previous study (33) as the main reasons clinicians continue

patients on IV therapy. Respondents were also allowed to state their reasons if they were not already provided on the list.

The fifth section consisted of five questions to assess the clinicians' baseline knowledge about the conversion practice. Respondents were requested to answer the five questions based on a clinical scenario adapted from the literature (2), which is also commonly encountered in the local population.

The sixth section consisted of a yes/no question, to examine whether the respondent would agree with the introduction of IV to oral antimicrobial converting guideline in the clinical practice.

The seventh section consisted of multiple like questions (none, low, average, high or not applicable), to recognize the existing level of practice, awareness and knowledge of clinicians in their practicing area about IV to oral antimicrobial therapy conversion.

The 7-section questionnaire made up the four main domains that measure the clinicians' practice beliefs (section 2-4), baseline knowledge (section 5), their acceptance of the converting practice (section 6) and their opinion on the existing level of practice (section 7) on conversion.

A total of 136 questionnaires were distributed to morning and ward room attending clinicians by study investigator. A second replacement questionnaire booklet was disseminated to those who did not respond to the first questionnaire .At the six weeks, a total of 115 filled questionnaire were assembled. However, only 109 questionnaires were completed.

For clinicians' knowledge, beliefs and practice of intravenous-to-oral antimicrobial therapy conversion was measured using 5-point Likert scale.

5.6.2. Data collection form for patients

For patients, the data was collected by trained five ward BSc nurses with the aid of attending residents and close supervision by the principal investigator.

Patients' data abstraction tool (in English) had six distinct parts. The first part collected demographic data, age, sex, educational level, residence, monthly income and type of patient ward.

The second section consisted of diagnosis disease and prescribed drugs, the third section comprised patient inclusion and exclusion criteria for converting to oral antimicrobials, adapted from Laing et al.(34)and Senn et al.(35).

The forth section asked clinicians to respond to the barriers of an early antimicrobial conversion for clinically stable patients from list of possible reasons or open ended question.

The fifth section comprised the duration of antimicrobial therapy, clinical stability and hospital stay.

The sixth section also consisted of vital sign sheet together with route of antimicrobial administration

A total of 89 patients who were admitted to Jimma University Specialized Hospital with a disease of community acquired pneumonia (CAP), urinary tract infection (UTI) and, skin and soft tissue infections were included in the study. Fourteen patients were excluded, 2 were excluded because of long duration treatment (> two months) due to difficulty of diagnosis conformation , 3 had missing data and 4 were excluded for other reasons. Of the 80 included patients, 9 patients died before intravenous to oral conversion; this left 71 patients for analysis.

Every 24 hrs after admission, the patient data and the route of antimicrobial administration (IV/orally) were recorded. Clinical stability was assessed and defined as temperature < 37.8^0C, oxygen saturation >92% without additional administration of oxygen, stable blood pressure without the need for saline infusion or vasopressive medication, heart rate <100 beats.min^{-1}, respiratory rate ,<25 breaths.min^{-1} and absence of mental confusion that arose after the onset of infection(36-37). If patients were able to swallow and were free of nausea or vomiting they were marked as ‘‘able to take oral medication’’. The vital sign not documented in the medical chart were recorded by the data collector nurses. Recording of clinical data continued after a patient was converted to oral antibiotics for at least 72 hrs.

5.7. STUDY VARIABLES

5.7.1. Dependent Variable

- Intravenous to oral antimicrobial therapy conversion.
- Knowledge, beliefs and acceptance of clinicians towards IV to oral conversion.

5.7.2. Independent Variable

- Socio-demographics characteristics of both Physicians and patients

  (e.g age, sex, qualification level of Physicians, year of clinical practice)
- Admission diagnosis
- Co-morbid disease
- Criteria for conversion
- Time to clinical stability
- Availability and number of antibiotics
- Severity of admission diagnosis
- Type of the disease

5.8. DATA QUALITY ASSURANCE

To maintain the quality of the data, a data collection self administered questionnaires and checklist was prepared and pre –tested for its completeness for coverage of critical domains and wording clarity crosscheck by physicians and on randomly selected patients' card, respectively. The questionnaire designed for clinicians, an overall Cronbach's α coefficient of 0.808 was obtained, indicating good inter-item reliability.

5.9. PILOT STUDY

The pilot study was conducted among 7 (3 senior and 4 resident physicians) to maintain the quality of data to be collected and identify the potential problems in the proposed study tools. In addition to this the pre-test was conducted on 5 patients before one week at medical ward. So that appropriate corrective measure could be taken on time.

5.10. DATA PROCESSING AND ANALYSIS

The collected data was cleaned, categorized and coded and was entered in Epi info version 7. Then the data were entered and analyzed using SPSS for windows version 21.0.

The differences of ratings for clinical factors and agreement to a set of practice statements among clinicians of various demographic characteristics were examined using Kruskal-Wallis and Mann-Whitney tests. Two-tailed P values of <0.05 were considered statistically significant. If statistical significance was noted with Kruskal-Wallis test findings, post hoc analysis with Mann-Whitney test was conducted with Bonferroni correction. The same non-parametric tests were used to examine associations between categorical clinician variables and baseline knowledge scores, as the scores were skewed (i.e. Kolmogorov-Smirnov test, $P<0.05$).

Chi-square test was used to evaluate the association between the grade of clinicians and the proportion of acceptance of a guideline in practice.

Independent-samples t-test was used to compare the proportion of converted and non-converted patients, as well as the duration IV therapy with the converted and non converted patients.

5.11. ETHICAL CONSIDERATION

Ethical clearance to carry out this study was obtained from the institutional review board, Jimma University (Ref. No .RPGC/103/2013). Information on the purpose and procedures of the study was given verbally to all clinician respondents, and verbal consent was obtained before distributing self-administered questionnaire . Despite that, for patients all religion and ethnicity was respected and also assure of complete confidentiality of information be kept, while the patient written informed consent was obtained.

5.12. DESSEMINATION PLAN

The principal finding of the study will be submitted to department of pharmacy at Jimma University and other concerned institution including Jimma University Specialized Hospital, Food, Medicine and Healthcare Administration and Control Authority (FMHACA), and Federal Ministry of Health (FMoH) to design interventional strategy at their side. It will be also presented to annual scientific conference of Ethiopia Pharmaceutical Association (EPA) and published in peer reviewed journal.

5.13. STRENGTH AND LIMITATION OF THE STUDY

- It was the first study in Ethiopia; the survey was done with clinicians across a broad spectrum of specialties.
- Besides this, the IV-to-oral antimicrobial conversion practice has been studied at this point of time and the same set - up.
-Time constraint and incomplete patient data.

5.14. OPERATIONAL DEFINITIONS AND DEFINITION OF TERMS

1. **Adequate Knowledge:-**The physicians report > 80% rated as " very sure " is obtained from " very sure " and "extremely sure " responses grouped together to represent an overall assessment of knowledge.
2. **Attitude** –an opinion or general feeling about intravenous to oral antimicrobial therapy conversion.
3. **Clinical parameter-**referring to the clinical data that comprise temperature (^{0}C), oxygen saturation (%), respiratory rate (per minute), blood pressure diastolic, systolic (mmHg), and heart rate to evaluate patient response(18).
4. **Clinical stability** defined as: temperature < 37.8^{0}C, oxygen saturation >92% without additional administration of oxygen, stable blood pressure without the need for saline infusion or vasopressive medication, heart rate <100 beats/min, respiratory rate, <25 breaths/min and absence of mental confusion that arose after the onset of infection (36-37).

5. **Delayed conversion–**referring to the patient who was not converted from intravenous to oral therapy after being clinically stable for 48 hrs.
6. **Early conversion: -** referring to the conversion of intravenous treatment to oral therapy in clinical stable patients on day 2 to 4 of hospital admission(27).
7. **Favorable attitude:-**The response rate of physicians report >50% for acceptance of IV to PO antimicrobial therapy conversion protocol/guidelines.
8. **Hospital acquired pneumonia** defined as patients who have been hospitalized for at least 2 days.
9. **Inadequate knowledge:-** The physicians report >20**%** rated as "very unsure " is obtained from "somewhat sure", "very unsure " and "not sure at all " responses grouped together to represent an overall assessment of knowledge**.**
10. **Intravenous to oral antimicrobial therapy conversion**- describes the practice of converting intravenous antimicrobial therapy to an alternative oral formulation.
11. **Knowledge: -** the ability to give response on questions in relation to IV-to-PO antimicrobial therapy conversion practice.
12. **Practice**- health professionals doing conversion from intravenous to oral antimicrobial therapy based on eligibility criteria for inpatients.
13. **Sequential therapy** refers to the act of replacing a parenteral version of a medication with its oral counterpart(2).
14. **Step-down therapy** refers to converting from an injectable medication to an oral agent in another class or to a different medication within the same class where the frequency, dose, and the spectrum of activity (in the case of antibiotics) may not be exactly the same(2).
15. **Switch therapy** -is used to describe a conversion from an IV medication to the PO equivalent that may be within the same class and have the level of potency, but is a different compound(2).
16. **Timely conversion –**referring to the patient is converted from intravenous to oral therapy in clinical stable patients with in 48 hrs.
17. **Unfavorable attitude: -** The response rate of physicians report < 50% for acceptance of IV to PO antimicrobial therapy conversion protocol/guideline.

CHAPTER FIVE:

RESULTS

5.1. Socio-demographic characteristics of the study participants

5.1.1 Socio-demographic characteristics of clinician participants

A total of one hundred nine practicing clinicians were included in this study. The mean age of the clinicians was 31.32±5.15 and the mean year of clinical practice was 5.93± 4.32. Nearly one-third of (29.4%) of the physicians were practicing general internal medicine, and those who practice in gynecology and obstetrics accounte for 23.9%, pediatrics for 19.3%, surgery for 18.3%, and other medical subspecialties (9.2%). Nearly one fourth of the respondent clinicians (26.6%) were senior physicians (specialists), and the remaining 73.4% were practicing as residents at Jimma University Specialized Hospital. The general characteristics of the respondent physicians are summarized in Table 1.

Table 1:- Demographic and practice characteristics of physicians, Jimma University Specialized Hospital, South West Ethiopia, March – June 2013,(n=109).

Characteristics			Respondents
			N (%)
Physician Characteristics	Gender	Male	103(94.5)
		Female	6(5.5)
Practice Characteristics	Current Position	Resident 1	24(22)
		Resident 2	31(28.4)
		Resident 3 or 4	25(22.9)
		Specialist/ Consultant	29(26.6)
	Specialty	Internal medicine	32(29.4)
		Obstetrics & Gynecology	26(23.9)
		Pediatrics	21(19.3)
		Surgery	20(18.3)
		Ophthalmology	5(4.6)
		Psychiatry	2(1.8)
		Anesthesiology	2(1.8)
		Dermatology	1(0.9)

5.1.2 Socio-demographic characteristics of participating patients

Of the 80 included patients , 9 patients died before intravenous to oral conversion ;this left 71 patients for analysis (Table.2).Over all , the mean ± SD age was 39.45± 16.44 and 36(50.7%) were female.

Table 2:- Socio-demographic characteristics of patients at Jimma University Specialized Hospital, South West Ethiopia, March – June, 2013. (n=71).

Characteristics	Respondents N (%)
Demographic data	
Subjects	71(100)
Age in years	39.45 ± 16.44
Gender	
Male	35(49.3)
Females	36(50.7)
Educational level	
Illiterate	39(54.9)
Primary school	18(25.4)
Secondary school	9(12.7)
College and above	5(7.0)
Residence	
Urban	33(46.5)
Rural	38(53.5)
Monthly income	
<501	18(25.4)
501-1000	42(59.2)
1001-2000	9(12.7)
Above 2000	2(2.8)

The four most common admission diagnoses were community acquired Pneumonia (67.6%), Skin and soft tissue infection (9.9%); Community acquired pneumonia plus UTI (9.9%) and, Urinary tract infection (8.5%). Fifty one (71.8%) patients had one or more co-morbid disease; the three most common chronic diseases present before admission were cardiovascular disease (54.9%), Tuberculosis (25.5%) and Diabetes mellitus (11.8%).(Table.3)

Table 3:- Pattern of diseases and prescribed drugs for intravenous to oral converting practice at Jimma University Specialized Hospital, South West Ethiopia, March – June, 2013, (n=71).

Characteristics	Respondents N (%)
Diagnosis for antimicrobial therapy	
Community acquired Pneumonia(CAP)	48(67.6)
Skin and soft tissue infection	7(9.9)
Community acquired pneumonia + UTI	7(9.9)
Urinary tract infection (UTI)	6(8.5)
Bone and joint infection	2(2.8)
Urinary tract infection + bone and joint infection	1(1.4)
Co-morbidity	
Subjects	51(100)
Cardio vascular disease (CVD)	28(54.9)
Tuberculosis	13(25.5)
Diabetes mellitus	6(11.8)
Human immunodeficiency virus (HIV)	1(2.0)
>1 Co-morbidity	3(6.0)
Patients were receiving intravenous antimicrobial	
Ceftriaxone	55(77.5)
Chloramphenicol + Cloxacillin	8(11.3)
Ceftazidime	2(2.8)
Ampicillin + Ceftriaxone	2(2.8)
Ceftriaxone + Cloxacillin + Metronidazole	2(2.8)
Cloxacillin + Ceftriaxone	1(1.4)
Gentamicin +Ceftriaxone	1(1.4)

5.2 Antimicrobial converting Decision

The majority of the clinicians (84.4%) claimed that their departmental practice, awareness and knowledge of IV-to-oral antimicrobial conversion (% rated as "departmental practice" is obtained from "Average practice" and "High practice" responses grouped together to represent an overall clinicians opinion reported on departmental practice , awareness and knowledge of IV-to-oral antimicrobial conversion).The mean duration of conversion IV to oral therapy was reported to be 6.43$\pm$ 3.33 days in the past four months.

Table 4 shows the factors that clinicians rated as "very important" determinants in deciding when to convert patients from IV to oral antimicrobial therapy. The factors most highly rated were the ability to maintain oral intake (88.1%), temperature returned to normal and stable over 24 hr period (88.1%) and co-morbid conditions stabilized (83.5%). The clinical features judged the least pertinent while deciding the conversion were the general appearance of the patient (45.0%) and no positive blood culture (51.4%).

Table 4:- Clinical factors rated as "very important" in deciding intravenous to oral dosing conversion, Jimma University Specialized Hospital, South West Ethiopia, March -June 2013.

Clinical factor	**Percentage (%) rated as "very important" ¥ (n= 109)**
Able to maintain oral intake	88.1
Afebrile or Temperature returned to normal and stable over 24 hr period	88.1
Co-morbid conditions stabilized	83.5
Mental status returned to baseline and no loss of consciousness	81.7
Respiratory rate returned to baseline	78.0
Oxygenation returned to baseline	78.0
White cell count returned to baseline	75.2
Heart rate returned to baseline	71.6
Microbiology etiology	70.6
No evidence of suppurative (i.e. pus-producing) infection	67.0
Blood pressure returned to baseline	67.0
No positive blood cultures	51.4
General appearance	45.0

¥ % rated as "very important" is obtained from "important" and "very important" responses grouped together to represent an overall agreement to each of the clinical factor.

Majority (85.3%) of the clinicians agreed with the traditional clinical rule that "Patients should be afebrile for 24 hrs before conversion to oral antimicrobials". In disparity, only 14.7% of clinicians felt that "patient should receive a standard duration of IV antimicrobial". Fifty four percent of clinicians disagreed, and 23.9% agreed that "white cell count should return to the reference range before IV-to-oral conversion". Over half of the clinicians (58.7%) agreed that "patients should not be converted if more than one of the following is present – heart rate (HR) ≥ 100 beats per min, respiratory rate (RR) ≥ 20 breath per min, blood pressure (BP) ≤ 100 mmHg, white blood cell <4 x 10^9/L or >12 x 10^9/L. Finally, over three quarters of the clinicians (79.8%) agreed that "oral route should not be compromised while considering the conversion". The comparisons of IV-to-oral antimicrobial converting practice beliefs among clinicians on five clinical statements are summarized on Table 5.

Table 5:- Clinicians practice beliefs on IV to oral antimicrobial conversion at Jimma University Specialized Hospital, South West Ethiopia, March – June 2013, (n=109).

Clinical Practice Statement	Strongly disagree and disagree	Neutral	Agree and strongly agree
	N (%)	N (%)	N (%)
Patients should be afebrile for 24 hours before IV-to-oral conversion (Temperature >36°C and <38°C)	**8(7.3)**	**8(7.3)**	**93(85.3)**
Patients should always have a complete IV course of antibiotics as standard practice	**82(75.2)**	**11(10.1)**	**16(14.7)**
Patients should not be converted if more than one of the following is present- I. Heart rate ≥ 100 min II. Respiratory rate ≥ 20BPM III. Blood pressure ≤ 100mmHg IV. White cell count < 4 x 10^9/L or >12 x 10^9/L	**32(29.4)**	**13(11.9)**	**64(58.7)**
The white cell count should always return to the reference range before IV-to-oral conversion	**59(54.1)**	**24(22.0)**	**26(23.9)**
The oral route should not be compromised when considering IV-to-oral conversion	**12(11.0)**	**10(9.2)**	**87(79.8)**

5.3 Differences in Clinical Factor and Practice Belief Ratings among Clinicians

When clinical factor ratings were compared between specialist/consultant clinicians and resident clinicians, there were no significant differences for most of the items except for ratings of the normalized white cell count (P=0.006), blood pressure returned to baseline (P=0.009) and absence of positive blood cultures (P=0.049), by means of which those residents had higher ratings on these items for antimicrobial converting decision.

Differences in practice beliefs among clinicians of various specialties are displayed in Table 6. There were significant differences among clinicians aimed at four of the five clinical practice statement ratings. Post hoc analysis revealed that significant differences for the agreement that "Patients should be afebrile for 24 hours before IV-to-oral conversion" were between clinicians of internal medicine versus obstetrics and gynecology specialties (P=0.000), surgery specialty versus obstetrics and gynecology (P=0.000), obstetrics and gynecology versus pediatrics specialties (P=0.000) as well as other specialties versus obstetrics and gynecology (P=0.000, critical level of significance P=0.005). There were also significant differences on the statement that "Patients should not be converted if more than one of the following is present - Heart rate $\geq$ 100 beats per min or Respiratory rate $\geq$ 20 BPM or Blood pressure $\leq$ 100 mmHg or White cell count $< 4 \times 10^9$/L or $>12 \times 10^9$/L " between internal medicine and pediatrics (P=0.000),surgery and pediatrics(P=0.000),surgery and other specialties (P=0.003) as well as pediatrics versus obstetrics and gynecology (P=0.000,critical level of significance P=0.005). Also, significant differences were noted on the statement that "The white cell count (WBC) should always return to the reference range before IV-to-oral conversion" between surgery and pediatrics (p=0.000) as well as surgery and other specialties (P=0.001,critical level of significance P=0.005).Finally, the significance differences were also revealed between surgery versus obstetrics and gynecology for ratings of the agreement that "patients should always complete IV course of antimicrobial as a standard practice" (P=0.002,critical level of significance P=0.005).(See Table 6).In addition , the significance differences among various specialties on practice beliefs explained by the mean rank on Table 7.

Table 6: Comparisons of IV-to-oral antimicrobial convertion practice beliefs among clinicians of various specialties at Jimma University Specialized Hospital, South West Ethiopia, March- June 2013,(n=109).

Clinical Practice Statement	Mean∞ ± SD					
	Internal medicine (N=32)	Gynecology & Obstetrics (N= 26)	Pediatrics (N=21)	Surgery (N=20)	Others ‡ (N=10)	Overall Mean+ SD P value ∂
Patients should be afebrile for 24 hours before IV-to-oral conversion (Temperature >36°C and <38°C)	4.22± 0.79	4.92± 0.39	3.86±1.06	4.10±0.91	3.80±0.79	4.26±0.89 P=0.000 [a]
Patients should always have a complete IV course of antibiotics as standard practice	2.16±1.14	1.69± 0.88	2.05±1.20	2.65±1.14	2.40±0.84	2.14±1.10 P=0.019 [b]
Patients should not be converted if more than one of the following is present- I. Heart rate ≥ 100 BPM II. Respiratory rate ≥ 20BPM III. Blood pressure ≤ 100mmHg IV. White cell count < 4 x 10^9/L or >12 x 10^9/L	3.72±1.19	3.38±1.29	2.19±1.12	4.05±0.94	2.90±0.88	3.33±1.29 P=0.000 [c]
The white cell count should always return to the reference range before IV-to-oral conversion	2.81±1.26	2.58±1.03	2.10±0.77	3.20±0.77	2.10±0.57	2.62±1.04 P=0.003 [d]
The oral route should not be compromised when considering IV-to-oral conversion	4.03±1.15	4.08±0.84	3.90±1.14	4.10±0.85	4.00±0.94	4.03±0.99 P=0.978

∞ Clinicians were asked to rate the extent of agreement and disagreement to the 5 clinical statement above as- 1-Strongly disagree; 2-Disagree; 3-Neutral; 4-Agree; 5-Strongly Agree.
The mean presented is an average measure based on responses from the clinicians according to specialties.
‡ Others include specialties such as ophthalmology, psychiatry, anesthesiology and dermatology.
∂ Data were analyzed using Kruskal-Wallis test. P values presented are for overall comparisons between clinicians of various specialties.
a Internal medicine versus obstetrics and gynecology specialties P=0.000,surgery specialty versus obstetrics and gynecology P=0.000 (Critical level of significance P=0.005)
b Surgery versus obstetrics and gynecology P=0.002(critical level of significance P=0.005)
c Internal medicine versus pediatrics P=0.000,surgery versus pediatrics P=0.000 (Critical level of significance P=0.005)
d Surgery and pediatrics (P=0.000) as well as surgery and other clinicians P=0.001 (Critical level of significance P=0.005)

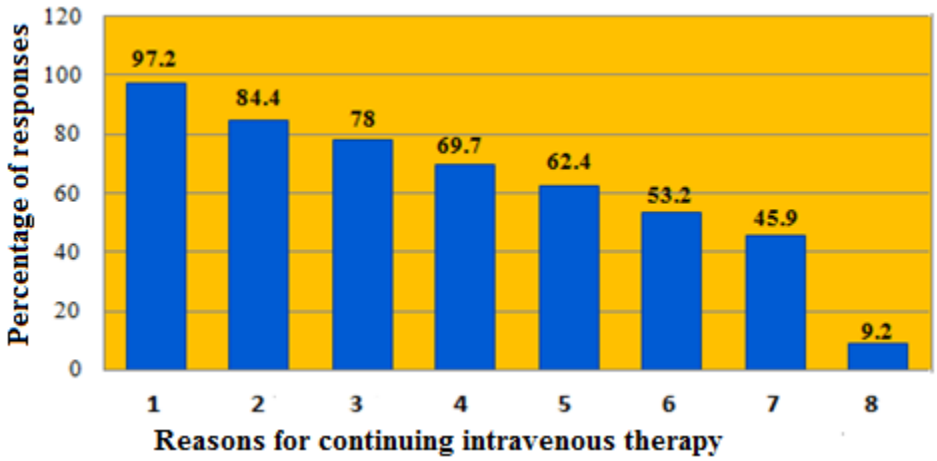
Table 7:-Practice beliefs rating by Mann-Whitney test among clinicians of various specialties at Jimma University Specialized Hospital, South West Ethiopia, March-June 2013(n=109).

Ranks				
Clinical Practice Statement	Specialty of the physician	N	Mean Rank	Sum of Ranks
Patient should be afebrile for 24 hrs before IV-to-PO conversion	Internal medicine	32	22.48	719.50
	Obstetrics & Gynecology	26	38.13	991.50
	Total	58		
Patient should be afebrile for 24 hrs before IV-to-PO conversion	Obstetrics & Gynecology	26	30.98	805.50
	Pediatrics	21	15.36	322.50
	Total	47		
Patient should be afebrile for 24 hrs before IV-to-PO conversion	Surgery	20	15.75	315.00
	Obstetrics & Gynecology	26	29.46	766.00
	Total	46		
The WBC should always return to the reference range before IV -to-PO conversion	Surgery	20	27.90	558.00
	Pediatrics	21	14.43	303.00
	Total	41		
Patient should always have a complete IV course antibiotics	Surgery	20	30.08	601.50
	Obstetrics & Gynecology	26	18.44	479.50
	Total	46		
Patients shouldn't converted if more than one of the following :-HR,RR,BP & WBC	Internal medicine	32	33.59	1075.00
	Pediatrics	21	16.95	356.00
	Total	53		
Patients shouldn't converted if more than one of the following :-HR,RR,BP & WBC	Surgery	20	28.98	579.50
	Pediatrics	21	13.40	281.50
	Total	41		
Patients shouldn't converted if more than one of the following :-HR,RR,BP & WBC	Obstetrics & Gynecology	26	29.25	760.50
	Pediatrics	21	17.50	367.50
	Total	47		
The WBC should always return to the reference range before IV -to-PO conversion	Surgery	20	19.00	380.00
	Others (Ophthalmology, Psychiatry, Anesthesiology and Dermatology)	10	8.50	85.00
	Total	30		

5.4 Reasons for continuing IV therapy by participating clinicians

Regarding reasons for continuing IV antimicrobial therapy, clinical instability of the patient (97.2%), uncertainty about gastrointestinal function (84.4%), whereas, among 9.2% of clinicians five of them replied as diagnosis is not confirmed, three of them responded they need senior physicians consult and finally the two of them listed "simply not think about it at a time"(See Figure 2).

Figure 2: - Clinicians response for reasons of continuing intravenous therapy in theory (physicians- specific questionnaire) at Jimma University Specialized Hospital, March - June2013 (n=109).



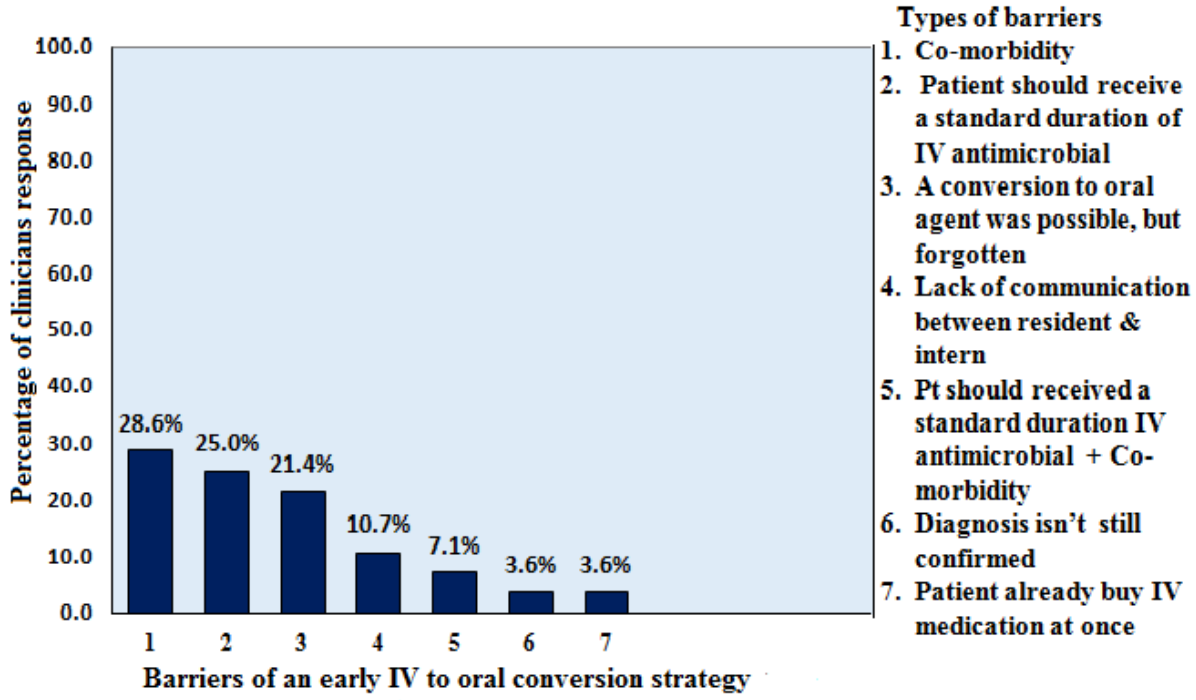
Key:-

1. Clinical instability of the patient
2. Uncertainty about gastrointestinal function
3. Uncertainty as to whether the oral alternatives achieve effective tissue levels
4. Reassurance that IV treatment achieves effective tissue levels
5. Presence of co-morbidity
6. Liability for unsuccessful treatment outcomes
7. Uncertainty about availability of oral alternatives(in stock)
8. Others including, simple not think about it at a time; diagnosis is not confirmed; and need senior physicians consult (only for residents).

5.5 Barriers of an early IV to oral conversion strategy in ward patients

By means of the case-specific interviews, we evaluated the barriers to oral antimicrobials conversion after clinical stability. We evaluated the barriers reported by clinicians treating the 28.6% (8/28) patients in whom presence of co-morbidity. As well as, one resident responded patient already bought IV medication at once (See Figure 3).

Figure 3:-Clinicians' response, barriers to an early conversion strategy by patient specific checklist at Jimma University Specialized Hospital, South West Ethiopia, March - June 2013,(n=28).



5.6 Comparisons of Baseline Knowledge Scores among Clinicians of Various Characteristics

The median total knowledge score was 4.0. Significant differences in the knowledge scores were observed between resident clinicians and specialists/consultants (P=0.009). Also, there were significant differences in the scores among groups of clinicians' claimed on their departmental practice, awareness and knowledge of IV-to-oral antimicrobial conversion by which post hoc analysis showed that the differences were noted between response rating of low and average practice (P=0.006,critical level of significance P=0.008). However, there were no significant differences among clinicians of different genders and specialties (P>0.05).Beside this, the clinicians were also noted their differences baseline knowledge score responses from a total of five questions. Over half of the clinicians 65(59.6%) got a knowledge score of greater than four in at least four of the five questions designed to assess their knowledge. The differences of baseline knowledge scores among clinicians are displayed in Table 8.

Table 8:- Differences in baseline knowledge scores ∞ among clinicians of various characteristics at Jimma University Specialized Hospital, South West Ethiopia, March – June 2013, (n=109).

Categorical Clinician Variables	N	Total Knowledge Score Mean (SD)	Range	Total Knowledge Score Median	Inter-quartile Range	P Value
Gender	109	3.43(1.24)	0-5	4.00	1.00	P=0.417♥
Male	103	3.41(1.25)	0-5	4.00	1.00	
Female	6	3.83(1.17)	2-5	4.00	2.00	
Current Position	109	3.43(1.24)	0-5	4.00	1.00	P=0.014♀,a
Resident 1	24	3.08(0.97)	1-4	3.00	2.00	
Resident 2	31	3.26(1.21)	0-5	3.00	1.00	
Resident 3 and 4	25	3.52(1.36)	0-5	4.00	1.00	
Specialist/Consultant	29	3.83(1.31)	0-5	4.00	2.00	
Current position	109	3.43(1.24)	0-5	4.00	1.0	P=0.009♥
All residents	80	3.29(1.19)	0-5	4.00	1.0	
Specialist/Consultant	29	3.83(1.31)	0-5	4.00	2.0	
Specialty	109	3.43(1.24)	0-5	4.00	1.00	P=0.104♀
Internal Medicine	32	3.69(0.93)	1-5	4.00	1.00	
Gynecology and Obstetrics	26	3.31(1.19)	0-5	3.50	1.00	
Pediatrics	21	3.71(1.27)	0-5	4.00	2.00	
Surgery	20	3.35(1.42)	0-5	4.00	2.00	
Others €	10	2.50(1.51)	0-5	2.00	2.00	
Clinicians opinion told on departmental practice, awareness and knowledge of IV-to-oral antimicrobial conversion	109	3.43(1.24)	0-5	4.00	1.00	P=0.003♀,b
Low	14	2.50(1.56)	0-5	2.00	2.00	
Average	62	3.66(1.13)	0-5	4.00	1.00	
High	30	3.60(0.89)	2-5	4.00	1.00	
Not applicable	3	1.33(1.53)	0-3	1.00	-	

∞ Baseline knowledge score is an aggregate measure based on responses to the 5 questions in relation to IV-to-oral antimicrobial conversion practice. The total score is 5. Scores range from 0-5.

€ Others include specialties such as ophthalmology, psychiatry, anesthesiology and dermatology.

♥ Mann-Whitney U test. Kolmogorov-Smirnov test output showed that the data were significantly different from normal distribution. P < 0.05. Thus, nonparametric test was used.

♀ Kruskal-Wallis test. Kolmogorov-Smirnov test output showed that the data were significantly different from normal distribution. P<0.05. Thus, nonparametric test was used.

- **a- Resident 1 versus specialists/consultants P=0.004 (Critical level of significance, 0.008)**
- **b- Departmental practice clinicians response rating of low versus average practice were significant differences (P=0.006,critical levels of significance P=0.008)**

5.7 Clinicians' Acceptance of IV-to-oral Antimicrobial Converting Guidelines or Protocols

Of clinicians' acceptance of an IV-to-oral antimicrobial converting guideline/protocol in practice, 78.0% agreed with such initiative. However, 22.0 % of them disagreed with it. Reasons of objection include absence of culture and sensitivity test and displeasure of abiding by a rigid guideline/protocol when treatment should be individualized according to patient's needs and concerns. There were no significant differences between grades of clinicians for acceptance of guideline/protocol. (See Table 9).

Table 9:- Association between the grade of the clinicians and the acceptance of the implementation of an IV-to-oral antimicrobial conversion guideline/protocol at Jimma University Specialized Hospital, South West Ethiopia, March - June2013,(n=109).

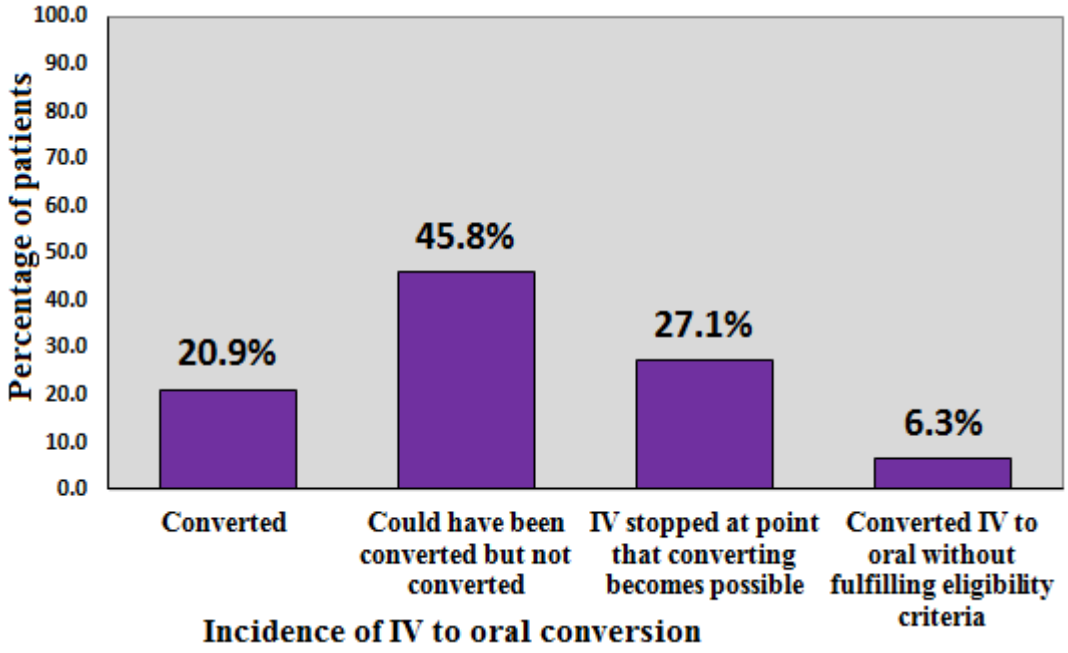
Grade of clinicians	Acceptance of an IV-to-oral antimicrobial converting protocol/guideline (Percentage of Clinicians ¥, %)		
	Yes	No	P value [a]
Resident 1	18.3	3.7	P=0.483
Resident 2	23.9	4.6	
Resident 3	17.4	5.5	
Specialist/Consultant	18.3	8.3	
Total	78.0	22.0	

¥ Respondents were asked to answer a yes/no question to examine whether they would agree with the introduction of an IV- to-oral antimicrobial conversion protocol/guideline in the clinical setting.
a Data were analyzed using Chi-square test.

5.8 Incidence of conversion therapy

From a total of 71 patients, 48(67.6%) of them who started IV antimicrobials were eligible for intravenous to oral antimicrobial conversion. However, from eligible subjects only 10(20.9%) patients were timely converted, 22(45.8%) patients could have been converted but not converted,13(27.1%) patients were IV stopped at point that converting become possible and 3(6.3%) of patients were converted without fulfilling eligibility criteria (See Figure 4).

Figure 4:-The percentage of patients in the incidence of IV to oral conversion at Jimma University Specialized Hospital, South West Ethiopia, March- June 2013, (n=48).



5.9 Antimicrobials prescribed, time to clinical stability, observation period after conversion and length of hospital stay

Ceftriaxone was prescribed in the overwhelming majority of patients 77.5 %(55/71), two patients received with ampicillin, and two patients with cloxacillin and mertonidazole. As well as, cloxacillin plus chloamphenicol were prescribed to 11.3 %(8/71) of patients and ceftazidime was received two patients. The most common oral antimicrobial prescribed for conversion therapy was amoxicillin with or without clavulanic acid 51.9% (14/27) and chloramphenicol plus cloxacillin 29.6%(8/27). The time it took for patients to reach clinical stability was (n=68, 6.04±3.25). Converted patients generally had a shorter time to clinical stability (1.03–5.77 days) than non-converted patients (3.37–7.45 days) (P=0.020).

Converted patients were observed in hospital after the initiation of oral therapy for a mean of 5.18 days, as result converted patients (9.0±5.23) spent less time in hospital than non-converted patients(13.45±5.48) , (P=0.039).

5.10 Duration of IV antimicrobial therapy

A shorter duration of IV therapy was recorded for converted (3.30 ± 2.26) versus non-converted patients (8.64 ± 2.70), (P=0.009). As well as, the duration of IV therapy received by non-converted patients after clinical stability was 1.14 – 5.32 days (3.23± 2.09). The number of IV antimicrobial prescriptions for which duration of treatment specified by physicians was 87. (See Table 10)

Table 10:-Intravenous to oral antimicrobial therapy conversion outcomes at Jimma University Specialized Hospital, South West Ethiopia, March – June 2013.

Variable	Implementation
Duration of IV therapy	
all patients	
mean± SD	7.66 ± 3.25 (n=71)
median; range	7;0 – 15
converted patients	
mean± SD	3.30 ± 2.26 (n=10)
non-converted patients	
mean± SD	8.64 ± 2.70 (n=22)

Time to clinical stability (days)	
all patients	
mean± SD	6.04± 3.25 (n=68)
median; range	5;0 – 16
converted patients	
mean± SD	3.40± 2.37 (n=10)
non-converted patients	
mean± SD	8.69± 3.73(n=22)
Observation period after conversion (days)	
mean± SD	5.18± 4.60 (n=28)
median; range	4.5;0 – 15
Duration of IV therapy after clinical stability for non-converted patients (days)	
mean ±SD	3.23± 2.09 (n=22)
median; range	3; 0 – 8
Number of IV antimicrobial prescriptions for which duration was specified (n=total number of prescriptions)	7(n=87)
Length of hospital stay (days)	
all patients	
mean± SD	13.42 ± 7.89(n=71)
median; range	11; 1 – 44
converted patients	
mean± SD	9.0 ± 5.23 (n=10)
non-converted patients	
mean± SD	13.45 ± 5.48 (n=22)
Total antibiotic acquisition costs (birr)	12247.52
Cost saving analysis	
Total amount saved	
Converted groups	1537.42 (n=10)
Non-converted groups	2040.03 (n= 22)

Cost implications

A total amount of birr 1537.42(n=10) was saved for converted patients and a further birr 2040.03 (n= 22) could have been saved if non-converted patients had also been converted.

Combined use of IV antibiotics and oral medications

For all community acquired pneumonia patients while they were admitted in ward, immediately took IV ceftriaxone or ceftazidime with oral doxycycline even if the patient was not candidate to oral medication due to the absence of IV first line drug that could be substituted oral doxycycline. The ability to tolerate oral medication was used as eligible criteria for converting patients, it was worthwhile to record the number of oral drug prescriptions prescribed for and received by patients on IV antimicrobial therapy. The number of oral drug prescriptions issued to patients on IV antimicrobial therapy was 48. Furthermore, the fact that near to half of patients 45.07 %(32/71) received oral drugs while on IV antimicrobial therapy this indicated that more than half of patients had gastrointestinal absorption problems or it might not be required IV medication. However, all community acquired pneumonia patients were taking oral doxycycline from the beginning.

CHAPTER SIX:

DISCUSSION

6.1. Discussion on clinicians' results

The decision about the timing of conversion from intravenous (IV) to oral (PO) antimicrobial is crucial while managing patients with moderate to severe infections. The aim of conversion should be to provide better quality of care at lower cost. In comparison with IV therapy, oral administration is safer, more acceptable to the patient, facilitates early discharge from hospital and reduces the cost of consumables and workloads to healthcare providers.

This study was designed to evaluate the clinicians' knowledge, belief, acceptance and current practice of IV- to-oral antimicrobial therapy conversion among hospitalized patients at medical and surgical ward. Insights from this survey and patient follow-up can be used as a preliminary resource to devise protocols as well as to introduce corresponding reinforcement strategies.

The clinicians identified the ability to maintain oral intake, normal temperature, absence of unstable co-morbid disease and a mental status at baseline as the most important clinical determinants in deciding when to convert patients from IV to oral antimicrobials. These were found to be in line with the previous works by Lee S L *et al* in Malaysia (19) and Halm *et al* in Pennsylvania (32) those identified the similar factors as those found in the current study with the addition of normalization of blood pressure , absence of positive blood culture and general appearance that were found only moderately rated in this study.

The results from the present study were not entirely in accordance with prior work where high CURB-65 (confusion of new onset, urea >7 mmol.L $^{-1}$, respiratory rate of ≥30 breaths.min $^{-1}$, blood pressure < 90 mmHg or diastolic blood pressure ≤60 mmHg, and age ≥ 65 yrs) score were shown to be vital indicators for judging overall clinical stability in pneumonia (18, 38).

There was a general consensus among clinicians about the importance of most of the clinical factors for conversion decision except in the case of a normalized white cell count and heart rate at baseline, whereby specialists/consultants were found to have a lower rate on these items. This probably indicates that specialists/consultants would treat patients based on clinical judgment rather than to be tied down to the traditional teaching about the importance of a normalized white cell count that lacks supportive evidence (32). This was found to be consistent with the prior works by Lee S L *et al* (19) and could probably suggest that clinicians' with long years in practice or specialization focused on patient specific factors instead of following general principles before any antimicrobial prescribed. However, this finding is contradictory a report that clinicians with more years in practice are inclined to hold on to more traditional practice beliefs (32, 39). This could be explained by the fact that the current study participants' specialists were both academicians and service providers.

The current study identified that high proportion of clinicians' 81.1% (96/109) opinions were found to be similar on traditional clinical rule that patient should be afebrile for 24 hours before IV to oral conversion. This finding is coincide with the previous works by Lee S L *et al (19),* as well as it is strengthen in accord with study findings by Halm et al(36) indicating that the risk of subsequent clinical deterioration critical enough to require intensive care or coronary care was minimal (1% of cases or fewer) once overall stability (which includes temperature ≤ 38°C or 101°F or less) is achieved. Subsequently, they concluded that it would be safe for conversion to oral antimicrobials once patients are clinically stable for 24 hours and allow discharge shortly thereafter provided that there are no active complaints (36). Besides that, a previous study on pneumonia (40) and pyelonephritis (41) had demonstrated that patients do not benefit from in-hospital observation instead of discharge after conversion from intravenous to oral antimicrobials. Significant majority, 85.3 %(93/109) of clinicians in the current study agreed with the rule (patient should be afebrile for 24 hours), 7.3 %(8/109) of them disagreed with it. The possible reason for this small proportion clinicians do not fully agree either with the timing (24 hrs) or the explicit temperatures (≤38°C) that were stated (or both) before which the conversion could be performed.

The current study identified differences of beliefs among clinicians of various specialties for four of the five clinical practice statements. The overall tendency was that gynecology and obstetrics, and internal medicine were relatively more inclined to hold the belief that patients should be afebrile for 24 hours prior to the conversion as compared to other specialties (including ophthalmology, psychiatry, anesthesiology and dermatology). This difference could have resulted from the nature of the disease managed by the respective specialties. Some specialties possibly manage more complicated and life-threatening cases as a result they give great attention to normalized temperature besides other clinical factors before antimicrobial conversion. On top of that, bioavailability of oral antimicrobials also the main concern while the patient would have an impaired gastrointestinal function.

Significant minority of clinicians 14.7% (16/109) felt that patients should always have a complete IV course of antimicrobials as a standard practice. The current finding was decreased from the previous works that had nearly half of the clinicians reported by Lee S L *et al* (19). This conservative practice is guaranteed to severe and more complicate infections; otherwise it is difficult to generalize for all cases. For reasons that, several studies have shown that short courses of IV therapy are safe and effective, especially for pneumonia (27, 42-43) and urinary tract infections (41, 44).Also, most of the oral antimicrobial agents have excellent bioavailability in addition to having spectra of antimicrobial activity similar to those of parenteral agents, this allows achievement of satisfactory serum drug level in the shortest time possible (provided that gastrointestinal tract is functional for optimal absorption).

Interestingly, this study discovered that clinicians of gynecology and obstetrics specialty (yielded mean rank=42.12) showed to be less predisposed to agree that patients should always complete IV course as a standard practice. In contrast to, clinicians in the area of practicing surgical procedures (general surgery, yielded mean rank=69.60) are more inclined towards continuation of IV antimicrobials. It could be explained the fact that all post-surgery patients may not be appropriate to be administered oral antimicrobials (45). Secondly the kinetic study , it was noticed that reduction of oral bioavailability of ciprofloxacin for peritonitis surgery patients (46). This finding point out major surgery may impair absorption

of ciprofloxacin, however, it needs further studies using different antimicrobials are required to clarify this issue.

In the current study, Over half (57.8%) of the clinicians agreed that patients should not be converted to oral antimicrobials if one of the following vital signs for clinical instability is present. These include HR $\geq$ 100 beats min^{-1}, RR $\geq$ 20 BPM, BP $\leq$ 100 mmHg or white cell count < 4 x 10^9/L or >12 x 10^9/L. Our findings are consistent with previous studies that reported two thirds of the clinicians agreed that patients should not be converted to oral antibiotics if one of the above vital signs for clinical instability is present(19). In a study by Halm *et al* (36), it was revealed that, for assessment of clinical outcomes after reaching clinical stability for CAP, the risk of subsequent deterioration is minimal once a patient had stabilized. However, there were still some of clinicians (30.2%), in the current study, who did not agree with the clinical thresholds for instability, particularly the pediatric clinicians. This could be due to the fact that pediatric cases management relied on different set of criteria because of varying pharmacokinetic profile. Besides, in the area of antimicrobial converting, pediatric studies have been scant and lacking(47) . In spite of that , it is as yet relevant that clinicians come up an agreement about a minimum standard set of criteria for antimicrobial converting as Halm *et al* (36) also interestingly found that different definitions of stability can result in greater than two-fold differences in the target length of stay.

More than half the clinicians (54.1%) were disagreeing and 23.9% of them were agreeing to the belief that white cell count should return to the reference range before IV-to-oral converting could be performed. This finding varying to the prior works by Lee S L *et al* (19) as it was discovered that equal proportion of clinicians agreeing and disagreeing. Indeed, normalization of the white cell count, while a sensible physiological marker of infection, has never been independently associated with mortality in the case of CAP (32, 48). However, additional studies needed to be carry out to validate this finding in infection other than community acquired pneumonia.

Majority of the clinicians (97.2%) recognized clinical instability of the patient was one of the main reasons that they would continue on IV antimicrobials. This is consistent with the previous two works by Lee S L *et al* (19) and Wong-Beringer *et al* (33) by which both were also rated as the primary reasons for IV continuation. In consideration of this, patient eligibility criteria for convertion should be judiciously developed to assure appropriate patient selection (9). Slightly over three quarters of the clinicians (78.0%) were uncertain about whether the oral alternatives would achieve effective tissue levels as accomplished converting and they were reassured that IV treatment would achieve effective tissue levels as compared to oral alternatives (69.7%). These two reasons could be explained that, clinicians were seemed to be as inevitable idea that IV antimicrobials are better than the oral ones, similarly it was described by Cunha in his review article (49).Nevertheless, such belief is understandable as an existence and continued development of potent oral antimicrobial with promising pharmacokinetic profile and those in selected populations, remarkably in pediatric patients are still lacking the data (9, 47). Over three quarter of the clinicians (84.4%) itemized that being uncertain about patients' gastrointestinal function is also one of the main reasons for antimicrobial non-converting practice. This finding showed that absorption of the drugs in the gut is the main concern before deciding IV to oral conversion. For the reason that follows, as Wetzstein (50) had mention, although oral antimicrobials are preferred for several advantage, certain patients are not candidate IV to oral conversion because of unreliable therapeutic response or patients whose disease state does not permit conversion. This is to avoid ineffective treatment and modestly cost even more than the money that could be saved from the converting program (51). Forty five percent (45.9%) of the clinicians justified that on uncertain about the availability of oral alternative in stock, to a certain extent, hindered them from converting IV to oral dosing. This barrier could be solved by developing guidelines; participating in major round and providing in person and over - the-phone information by the clinical pharmacists.

The current study discovered that clinicians' gender, specialty training do not interfere in their knowledge about antimicrobial conversion practice. However, there were differences in the knowledge score between the resident clinicians and specialists/consultants. As well,

there were differences among groups of clinicians' opinion told on departmental practice, awareness and knowledge of IV-to-oral antimicrobial conversion on response rating of low and average practice. It was not surprising that resident clinicians inclined to be less familiar with the practice principles (reflected in their lower knowledge scores) as compared to specialists/consultants, possibly, owing to their shorter years of clinical practice. Moreover this, over half of the clinicians 65(59.6%) got a knowledge score of greater than four in at least four of the five questions designed to assess their knowledge. Considering that resident clinicians have lower mean total knowledge scores, for that reasons extra educational strategies need to be taken up to heighten their level of awareness and reinforce their knowledge on such practice. Guidelines are "good educational tools" that may be most beneficial to those with less experience and expertise (52-53).

The justifications stated by the small proportion of clinicians (22%) who opposed the idea of antimicrobial converting guideline implementation were acceptable as those are applicability of individual patients, inefficiencies of the health care system, level of local participation and authorization by health institution leaders while deciding definitive criteria of patient eligibility for converting. Seeing as the encouraging response as general in considers to development and implementation of clinical practice guidelines as a means of improving IV to oral antimicrobial converting practice. However, the documented practice guidelines do not always guide practice, unless the heterogeneous forces participating on converting practice. Guidelines should always be looked upon as advisory rather than obligatory tools to guide clinicians towards the best practice of care. On top of this, the current study finding showed that, there were no differences between residents and specialists/consultants on toward supportive of a guideline being incorporated in to practice. However, this results contrary to the previous works by Lee S L *et al* (19) that denoted the differences between them.

6.2. Discussion on patients' results

To our knowledge, this is the second study conducted in Africa with greatest challenge to the effective treatment of infections due to antimicrobial resistance and escalating costs of antimicrobials with the suitability of converting antibiotic therapy from the IV to the oral route.

The higher proportion of admission diagnosis was community acquired Pneumonia (67.6%) and the most common chronic diseases present before admission was cardiovascular disease (54.9%).Those findings are consistent with the previous work by Van Niekerk *et al* (26). The number of converted patients 20.8 % (10/71) in this study was higher from the reported by Van Niekerk *et al* (13%) (26), conversely , it was decreased more than by half from other study finding by Servinc *et al* (54%) (23).

The mean time to clinical stability in this study (6.04 ± 3.25 days) was slightly increased from the previous studies in pre-implementation phase (4.7±2.5) by Van Niekerk *et al* (26) and that also reported 2.0–4.0 days as the appropriate time for IV therapy to be reassessed (25, 27, 35). The increased in time to clinical stability might raise the inquiry of whether antimicrobials were given for either too long (unnecessary use) or too short (risk of relapse) a period. However, the decision to conversion was left to the attending physicians and, thus, it was assumed that patients were appropriately converted according to the discretion of the physician with the help of the conversion criteria. After conversion, most of the converted patients were observed in hospital. This could be linked to the high incidence of co-morbid conditions, such as cardiovascular disease, tuberculosis and diabetes mellitus, or socioeconomic factors (a lack of money, absence of reliable family members and/or the absence of equipped facility for continued care). Other reasons could include: (i) physicians reluctant to discharge patients; (ii) patients not assessed on a daily basis; and (iii) physicians waiting for further diagnostic workup, similar to previous studies (25, 34).

The median length of hospitalization for patients in this study (11.0days) (See Table 10) was slightly higher to the median length of hospitalization reported by Van Niekerk *et al* (26) (9.2 days) at pre-implementation phase. The number of prescriptions for which IV antimicrobials duration was specified by physicians in this study 7(n=87) was decreased from the prior work by Van Niekerk *et al* (26) 40(n=204) at pre-implementation phase. The possible reasons for its difference is (i) the variation of number of patients involved in the studies (71 versus 119) and (ii) the less availability of alternative medication in the current study area. The median duration of IV antimicrobial in the present study (7 days) was close to the previous study by Mertz *et al* (25) (6 days) at control phase. The mean time of IV therapy after clinical stability for non-converted patients in this study (3.23 ± 2.09 days) was consistent with the prior work by Van Niekerk *et al* (26) (3.8 ± 2.4). In the current study , the considerable decrease in the duration of IV therapy led to substantial drug-acquisition cost savings of up to 1537.42 birr (n=10) or $ 81.50 (n=10) in the converted patients. This result was slightly increased from the prior work by Van Niekerk *et al* (26) $ 113.63 (n=19) at pre-implementation phase.

In this study, all community acquired pneumonia patients at the time of admission were taking simultaneously IV ceftriaxone or ceftazidime with oral doxycycline, even if the patient was not candidate for oral medication, due to the absence of first line IV medication that could be substitute oral doxycycline. A recent survey discovered that pharmacists in the USA regard gastrointestinal functionality as one of the most important criteria for converting from IV to oral therapy (54). The current study, near to half of patients 45.07 % (32/71) received oral drugs while on IV antimicrobial therapy this indicated that more than half of patients had gastrointestinal absorption problems or it might not be required PO medication. However, all community acquired pneumonia patients were taking oral doxycycline from the beginning. This implies that since, 45.0% of patients in received oral medication while on IV antimicrobial therapy, the number of patients converted could have been even higher than the current finding(20.8%). This study has taken into account that certain clinical conditions, such as infective endocarditis, meningitis, deep abscess, cystic fibrosis, infection

of a prosthetic device and neutropenia require IV therapy even though the patient can take oral medication (due to the pharmacokinetic/ pharmacodynamic criteria of the antimicrobial).

Perceived barriers to an early-conversion strategy by case specific response (patient specific checklist) from the treating physicians, included mainly the presence of co-morbid disease 28.6 % (8/28), should be received standard duration of intravenous antimicrobials 25.0 % (7/28) and forgetting to conversion to oral agents 21.4% (6/28). Those findings were inconsistency with the theory response (physician specific questionnaire) about reasons of continuing IV therapy comprises clinical instability 97.2% (106/109), uncertain about gastrointestinal function 84.4 (92/109) and uncertainty as to whether the oral alternatives achieve effective tissue level 78.0% (85/109). It is therefore likely that the majority of the barriers identified in this study could be reduced by means of an educational intervention (55-56).

CHAPTER SEVEN:

CONCLUSION AND RECOMMENDATION

7.1 CONCLUSION

Over half of the clinicians had adequate knowledge. Specialists/consultants were found to be more knowledgeable about the converting practice as compared with residents.

Clinicians believed that patients with moderate to severe infection could be converted from IV to oral antimicrobials once they are able to tolerate orally intake, the temperature had normalized and after stabilized co-morbid conditions. There was substantial variation in several practice beliefs among clinicians of various characteristics such as specialty and current position.

The lowest rate of timely converting patients to oral antimicrobials was observed during this study. About two third 48(67.8%) of patients who were found to be candidate for IV to oral antimicrobial conversion only 20.9% were timely converted, while 45.8% of them non-converted.

The converted patients had shortened IV duration than the non-converted one. Besides, the conversion from IV to oral antimicrobials is often unnecessarily delayed in patients hospitalized with moderate to severe infection; this is mostly due to the presence of co-morbidity, needed IV therapy as standard duration and forgetting to convert to oral agents.

7.2 RECOMMENDATION

It is useful to design and implement physician education programs focused on the advantage of timely intravenous to oral antimicrobial therapy conversion. Obtaining support from medical, administrative, and nursing staffs are instrumental in obtaining buy-in prior to implementation.

Overall, guidelines that are carefully developed regarding IV to oral antimicrobial therapy conversion are essential to address the heterogeneity in the practice beliefs we observed.

Clinicians should consider conversion of IV to oral therapy based on standard guidelines for treatment of specific disease.

In effect, the preliminary finding of this research is open a road map for further exploration of practice and perceived barriers for effective implementation of IV to PO conversion at hospitals.

Clinical pharmacist and treating physicians should come together to work hand –in-hand to improve the practice of antimicrobials therapy.

As the impact of IV to oral conversion on the incidence of IV device-related infections and rate of relapse, and cost containment issue were not assessed in the current study, it is also clear that further studies are necessary to investigating these aspects.

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ANNEX

ANNEX I: - QUESTIONNAIRE. Code Number_____

The objective of the present study is to explore clinicians' baseline knowledge, practice beliefs and acceptance of intravenous-to-oral antimicrobial therapy conversion at Jimma University Specialized Hospital and it is self administered questionnaire to be filled and returned within maximum of 5 days.

First of all I am grateful and acknowledge you for your willingness in participation to the present study.

Instruction

A. Select your answer for the questions by marking "√" in the box provided
B. If your answer is out of the choice provided; write your answer in the space provided.
C. For clinical perspective questions, consider moderate to severe infection.

I. Demographic and practice characteristics of study respondents

1. Age: _____

2. Sex Male ☐ Female ☐

3. Practice Characteristics ☐

3.1. Current Position

Resident 1…… ☐

Resident 2…….. ☐

Resident 3 or 4 …… ☐

Specialist/ Consultant……. ☐

3.2. Specialty

Internal medicine ☐ Ophthalmology ☐
Surgery ☐ Psychiatry ☐
Obstetrics & Gynecology ☐ Pediatrics ☐
Orthopedics ☐ Anesthesiology ☐
Dermatologist ☐
Others ☐ specify_____

4. Length of service in clinical practice (i.e. including the practice of as general practitioner (GP), residence and senior physician) _____

II. On the scale of importance indicate how much the following statements are important for early conversion (Clinical stable patients convert on day 2 to 4 of hospital admission) IV to PO antimicrobial therapy conversion.

	Clinical factor	Very unimportant	unimportant	neutral	important	Very important
1	Able to maintain oral intake					
2	Microbiology etiology					
3	No evidence of suppurative (i.e. pus-producing) infection					
4	Afebrile or Temperature returned to normal and stable over 24 hr period					
5	Co-morbid conditions stabilized					
6	General appearance					
7	No positive blood cultures					
8	White cell count returned to baseline					
9	Heart rate returned to baseline					
10	Mental status returned to baseline and no loss of consciousness					
11	Respiratory rate returned to baseline					
12	Oxygenation returned to baseline					
13	Blood pressure returned to baseline					

III: On the level of agreement indicate how much you agree/disagree that the following statements are true for early IV to PO antimicrobial therapy conversion or with hold the conversion.

	Clinical Practice Statement	Strongly disagree	Disagree	Neutral	Agree	Strongly Agree
1	Patients should be afebrile for 24 hours before IV-to-oral switch (Temperature >36^{o}C and <38^{o}C)					
2	Patients should always have a complete IV course of antibiotics as standard practice					
3	Patients should **not** be converted if **more than one** of the following is present- I. Heart rate ≥ 100 BPM II. Respiratory rate ≥ 20BPM III. Blood pressure ≤ 100mmHg IV. White cell count < 4 x 10^{9}/L or >12 x 10^{9}/L					
4	The white cell count should always return to the reference range before IV-to-oral switch					
5	The oral route should not be compromised when considering IV-to-oral switch					

IV. Based on priority, select 5-points with order of importance (by ranking from 1 to 5) among the following list of reasons for continuing IV therapy?

	Type of main reasons	Order of importance
1	Clinical instability of the patient	
2	Uncertainty about gastrointestinal function	
3	Uncertainty as to whether the oral alternatives achieve effective tissue levels	
4	Reassurance that IV treatment achieves effective tissue levels	
5	Uncertainty about availability of oral alternatives (in stock)	
6	Liability for unsuccessful treatment outcomes	
7	Others specify:	

Note. Others specify, simply not think about it at a time; ☐
Diagnosis is not confirmed; ☐ Comorbidity delaying the switch; ☐
Need senior physicians consult (only for residents); ☐
and_____

V. Knowledge assessment about the IV to PO converting practice.

	Type of baseline knowledge question	Extremely sure	Very sure	Some-what sure	Very unsure	Not sure at all
1	Could you describe the potential benefits of conversion from IV to PO therapy?					
2	Could you describe the ideal characteristics of a medication that is included in an IV to PO therapy conversion program?					
3	Could you identify patients who are appropriate candidates for IV to PO therapy conversion?					
4	Could you differentiate between the type of IV to PO therapy conversion, like:-**Sequential therapy** (conversion made within the same medication e.g Cloxacillin IV to Cloxacillin PO), **Switch therapy** (within the same class, but is a different compound e.g. Ceftriaxone IV to Cephalexine PO) , and **Step-down therapy**(Conversion made between different compound e.g Gentamicin IV to Ciprofloxacin PO)?					
5	Could you identify **excellent**, **good** & **poor** bioavailability of medications & their dosage calculation for IV to Oral therapy conversion					

VI. a). Does your hospital has a protocol for conversion of IV to Oral therapy for different types of moderate to severe infections? Yes ☐ No ☐ Not Applicable ☐

b). If "No" Do you agree with the introduction of an IV- to-Oral antibiotic conversion protocol/guideline in your hospital? Yes ☐ No ☐

If your answer is "No" for question number VII, Reasons of objection include

_____

VIII. In your opinion, what is the level of practice, awareness and knowledge of medical doctors in this hospital (specifically your department) about IV to PO antimicrobial therapy conversion?

None ☐ Low ☐ Average ☐ High ☐ Not Applicable ☐

ANNEX-II: PATIENT DATA ABSTRACTION TOOL.

Checklist for IV to PO Antimicrobial Conversion at Jimma University Specialized Hospital in Medical Ward and Surgical Ward

Patient card No _____ Date _____

Admission date _____ Discharge date _____

Instruction:-

This check list is prepared for patients receiving intravenous antimicrobial therapy for treatment of Community-acquired pneumonia (CAP), Urinary tract infection (UTI), skin and soft tissue infection, and/or bone and joint infection.

A. Select your answer for the questions by marking "√" in the box provided
B. If your answer is out of the choice provided; write your answer in the space provided.

I. Patient socio-demographic data

1. Age _____

2. Sex Male ☐ Female ☐

3. Educational level Illiterate ☐ Primary School ☐
Secondary School ☐ College and above ☐

4. Residence Urban ☐ Rural ☐

5. Monthly income (birr) <501 ☐ 501-1000 ☐ 1001-2000 ☐ Above 2000 ☐

6. Patient admitted ward Surgery ☐ Internal medicine ☐

II. Diagnosis and prescribed drugs

1. Apparent indication for antibiotic therapy (Diagnosis):-
Pneumonia ☐ Urinary tract infection (e.g Pyelonephritis) ☐
Skin and soft tissue infection (e.g. Cellulitis, Soft tissue laceration, Pyomyositis etc) ☐
Bone and joint infection (e.g Osteomyelitis) ☐
2. Chronic diseases present before admission: CV disease ☐ HIV ☐ TB ☐
liver disease ☐ and, if other co-morbid specify_____
3. Patient is receiving intravenous therapy with one or more of the following antibiotics:
   - Ampicillin 500mg- 1gm (bid - qid) ☐
   - Ceftazidime 1gm ☐
   - Ceftriaxone 0.5/1g ☐
   - Chloramhenicol 1g ☐
   - Clinindamycin 150mg/5ml ☐
   - Cloxacillin 500mg ☐
   - Fluconazole ☐
   - Gentamicin 80mg/2ml ☐
   - Metronidazole 5mg/ml ☐
   - Penicillin G sodium crystalline 1mIU ☐

- Vancomycine 1gm ☐
- Other antibiotics administered on the day of admission

_____

III. Patient Eligibility Criteria and incidence of conversion

1. Criteria for patient eligibility

i. Inclusion criteria for IV to PO therapy conversion

- Intravenous antimicrobial for > 24 hrs
- Clinical improvement (Temp. $< 37.8^0$C, 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
- Continuing sepsis (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 (24) .
- Febrile with neutropenia (ANC less than 1 x 10^9 /L)
- Serious deep seated infection that requires IV therapy as a co-morbid (e.g. meningitis ,endocarditis, deep abscess, cystic fibrosis, infection of a prosthetic device.

2. Instead of IV drugs, start oral medication without fulfilling of eligibility criteria**.**
   Yes☐ No ☐
   If you answer "Yes", Reasons…….
   i. Absence of first line IV medication ☐
   ii. Patient doesn't tolerated IV routes ☐
   iii. Others ☐ specify
   _____
3. Which oral medication is used because of absence of first line IV medication
   _____
4. Are there any other oral drug prescriptions prescribed for and received by patients while on IV antibiotic therapy. Yes☐ No ☐
   If you answer yes, list the drugs and its indication_____
   _____
5. Additional IV antibiotics for admitted patients without changed/revised the first established diagnosis. Yes ☐ No ☐
   5.1) 1st time:-Start date & time _____End date & time _____
   Name of antibiotics, Dose, Frequency: _____
   Duration._____
   Cost._____
   5.2) 2nd time :- Start date & time _____End date & time _____
   Name of antibiotics, Dose, Frequency.1) _____

Duration._____

Cost._____

6. Proceedings of diagnosis and order of medications after the first established diagnosis. Yes ☐ No☐

A.) Revised/changed diagnosis (2nd time), Specify._____

Start date & time,_____ End date & time _____

Name of antibiotics, Dose, Frequency._____

2)_____

Duration._____ Cost._____

B.) Revised/changed diagnosis (3rd time), Specify._____

Start date & time _____End date & time _____

Name of antibiotics, Dose, Frequency._____

2)_____

Duration._____ Cost._____

7. **Was conversion made after fulfilling of eligibility criteria**? Yes☐ No ☐
8. If answer "Yes" for question number 7.Which to which?

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

9. 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'.

10. Follow-up patient status after IV to PO conversion (at least 72 hours).
    i. Continued PO until discharged. Yes ☐ No ☐
    ii. 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_____
    iii. Converted back to IV agents to previous one ☐ OR other agent ☐
    Name, dose, frequency _____
    Reason/Indication_____
    Duration_____ Cost_____
11. If answer **"No"** for question number **7**(No conversion made after fulfilling of eligibility criteria) and **continuation of IV therapy on day 3 or more than 3 days of treatment** .Why?

IV. Barriers an early IV to oral conversion after clinical stability

Choose among the following suggested barriers to conversion after clinical stability or write other reasons on the space provided for non-conversion.

- A conversion to oral agents was possible but not performed ☐
- For pneumonia , patient factors delaying the conversion on day 3 of antibiotic treatment ,specify reasons
    - ✓ Respiratory rate _____
    - ✓ Blood pressure _____
    - ✓ Pulse rate_____
    - ✓ Confusion of new onset_____
    - ✓ Oxygen (O_2) saturation _____
    - ✓ WBC_____
- For COPD patients, patient factors delaying the conversion on day 3 of antibiotic treatment ,specify reasons
    - ✓ Presence of dyspnea and cough ☐
    - ✓ Oxygen (O_2) saturation $\leq$ 90% ☐
- Patient should receive a standard duration of intravenous antibiotics ☐
- Liability for unsuccessful treatment outcomes ☐
- Absence of major round for clinical decision ☐
- Decision was made by senior physicians ☐
- Comorbidity delaying the switch ☐
- Absence of similar or alternative oral drugs ☐
- Diagnosis isn't still confirmed ☐
- Believe IV superior to PO antimicrobial therapy ☐
- Decision waiting by expecting other discipline ☐
  Specify:-_____
- Other reasons :-1)_____
  2) _____

V. 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. $< 37.8^0C$, 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) _____

vii. Length of hospital stay : - Admission date & time _____
Discharge date & time _____

VI. Vital sign follow–up sheet.

Day/ Date	Temp (^0C)	Pulse rate (PR)	BP (mmHg)	Respira -tory Rate (RR)	O_2 satu- ration	Mental Status	Route of administ ration (IV /PO)	Remark
1								
2								
3								
4								
5								
6								
7								

Note:-1. If the patient is discharge, write the date & put the letter "D" on remark column.

2. If the patient is on oxygen treatment, classified either with O_2 (w) or without O_2 ($\bar{w}$) and put on the remark column.

ANNEX III: -

I. PATIENT INFORMATION SHEET

Name of the principal investigator: Alemseged Beyene Berha

Name of study area: Jimma University Specialized Hospital

Research budget covered by: Jimma University

Research objective**:** The objective of this study is to explore clinician's baseline knowledge, belief, acceptance and current practice of IV to PO antimicrobial therapy conversion among hospitalized patients at medical and surgical ward of Jimma University Specialized Hospital, between March –June 2013.

Significance of the study**:** The findings are used as primary and important sources of reference prior to the implementation of IV to PO antimicrobial conversion guidelines at institutional level. After documenting this research as a baseline, forward practicable recommendations for policy makers and service providers to create confidence and gives clue for health policy maker for designing appropriate use of antimicrobials pertinent to IV to PO antimicrobial therapy conversion.

Study procedure: The data collectors were filled the data from patient card, vital sign sheet and some number of interview questions were responded by the subjects after obtaining consent from the patient.

Risks**:** No risks except the time that patient spend during the interview.

Participant right**:** The patient has a right to stop the interview at any time, or to skip any question that he/she does not want to answer.

Beneficial**:** The study is beneficial for patient's quality service delivery for future encounters.

Incentives**:** Nothing was provided as a specific incentive for taking part in the research other than acknowledgment.

Confidentialities: The study result was not including patient's name and address.

Agreement: Patients are expected to be fully voluntary to participate in the study.

Whom to contact**:** If you have any kind of inconveniencies about the study, you can contact the following individual:

- Mr. Alemseged Beyene (principal investigator)
    - Tel: +251920017618
    - Email: alembeyene98@gmail.com

II. CONSENT FORM FOR STUDY PARTICIPANTS (ENGLISH VERSION)

Name…….…..…….. Card no…..……

Ward……..…… Code no……..

I had been informed that the objective of this study is to explore clinician's baseline knowledge, belief, attitude and current practice of intravenous to oral antimicrobial therapy conversion among hospitalized patients at medical and surgical ward. The results of this study have importance to treat me and other patients and to use as a guide for decreased cost and safer use of antimicrobials. I had been also informed about the confidentiality of the checklist. The principal investigator requested me to participate in the study that would require my willingness to respond to an interview, and to provide information. Therefore, with full understanding of the importance of the study, I agreed voluntarily to provide the requested information.

I_____ hereby give my consent for providing the requested information.

Signature: _____ Date_____

Thank you for your participation!!!

CERTIFICATE

This is to certify that the thesis entitled **"Intravenous-to-Oral Antimicrobial Therapy Conversion: Clinicians' Knowledge, Beliefs, Acceptance and Current Practice at Jimma University Specialized Hospital, South West Ethiopia"** was carried out by **Alemseged Beyene** under direct supervision of advisor(s) listed below. Further, the advisor(s) certify that this work has not been submitted in part or full in any University or Institution for any Degree or Diploma.

1. Name: _____ Signature: _____ Date: _____

2. Name: _____ Signature: _____ Date: _____

DECLARATION

I hereby declare that the work embodied in this thesis was carried out by me under direct supervision of **Mr.Gizat Molla and Dr.Sintayehu Fekadu**, Department of Pharmacy, College of Public Health and Medical Sciences, Jimma University. This work has not been submitted in part or full in any University or Institution for any Degree or Diploma. I further endorse that this work is the property of Jimma University and all rights in this regard are reserved with Jimma University.

Name: _____ Signature: _____

Examiners:-

External examiner _____

Internal examiner _____