تغييم الأنواع المختلفة للميكروبات المسببة الإلتمابب الرئوي و حساسيتما للمضاحات الحيوية في مرضي وحدة الرغاية المركزة للصدر بمستشفيات جامعة عين شمس

رسالة توطئة للحصول علي درجة الماجستير في الأمراض الصدرية والتدرن

مقدمة من الطبيب / محمود محمد محمود الحميد

تحت إشراف

أ • د / ليلي عاشور محمد

استاذ الأمراض الصدرية كلية الطب – جامعة عين شمس

د / إبراهيم علي دويدار مدرس الأمراض الصدرية كلية الطب – جامعة عين شمس

كلية الطب- جامعة عين شمس ٢٠١٠

Assessment of different pathogens causing pneumonia and antibiotic sensitivity in patients admitted to Respiratory Intensive Care Unit in Ain Shams University Hospitals

Thesis

Submitted for partial fulfillment of master degree in Chest Diseases and Tuberculosis

Presented by Mahmoud Mohammad Mahmoud Abd Elhameed M.B., B.CH.

Under supervision of **Prof. Laila Ashour Mohammad**

Professor of chest diseases Faculty of Medicine Ain Shams University

Dr. Ibraheem Aly Dwidar

Lecturer of chest diseases Faculty of Medicine Ain Shams University

Faculty of Medicine Ain Shams University 2010

Äcknowledgment

Thanks first and last to **Allah** for granting me to accomplish this work, as we owe to him for his support and guidance in every step in our life.

I would like to express my cordial appreciation and infinite gratitude to *Prof. Laila Ashour*, Professor of Chest Diseases, Faculty of Medicine, Ain Shams University, for her guidance and advice along the entire course of the study.

I am also grateful to *Dr. Ibraheem Dwidar*, lecturer of Chest Diseases, Faculty of Medicine, Ain Shams University, for his willing assistance and continues encouragement.

Lastly, I would like to express my deep thanks to all the staff of Chest Department, Ain Shams University for their encouragement and helpful advices.

Abbreviations

\$	Dollargian
	Dollar sign
<u>≥</u> ≤	More than or equal to
	Less than or equal to
ADH	Anti-Diuretic Hormone
AE	Acute Exacerbation
AIDS	Acquired Immune Deficiency Syndrome
ARDS	Adult Respiratory Distress Syndrome
ATS	American Thoracic Society
BA	Bronchial Asthma
BAL	Broncho-Alveolar Lavage
BTS	British Thoracic Society
CAP	Community Acquired Pneumonia
CFT	Complement Fixation Test
CFU	Colony Forming Unit
CMV	Cytomegalovirus
COPD	Chronic Obstructive Pulmonary Disease
CT	Computed Tomography
DNA	Deoxyribonucleic Acid
EGNB	Enteric Gram Negative Bacilli
ELISA	Enzyme-Linked Immunosorbent Assay
ETA	Endotracheal Tube Aspirate
FG	French Gauge
HAP	Hospital Acquired Pneumonia
HCAP	Heath Care Associated Pneumonia
HIV	Human Immune Deficiency Virus
ICU	Intensive Care Unit
IDSA	Infectious Diseases Society Association

IFAT	Immuno-Florescent Antibody Test
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IV	Intra-Venous
LDH	Lactate Dehydrogenase
LRT	Lower Respiratory Tract
LRTIs	Lower Respiratory Tract Infections
MDR	Multi-Drug Resistant
MOTT	Mycobacterium Other Than Tubercle bacilli
MRSA	Methicillin Resistant Staph. aures
MSS	Methicillin Sensitive Staph. aures
MV	Mechanical Ventilation
NNIS	National Nosocomial Infection Surveillance System
NPV	Negative Predictive Value
P	Probability
PaO ₂	Partial Oxygen Pressure
PC	Personal Computer
PCP	Pneumocystitis carinii pneumonia
PCR	Polymerase Chain Reaction
PPV	Positive Predictive Value
PSB	Protected Specimen Brush
RMAT	Rapid Micro-Agglutination Test
SD	Standard Deviation
SPP.	Species
ТВ	Tuberculosis
VAP	Ventilator Associated Pneumonia

List of Tables

No.	Title	Page
Table 1	Classifications of pneumonia.	11
Table 2	The most common pathogens implicated in	20
	CAP and their relative contributions.	
Table 3	Patients with mild to moderate HAP, no	29
	unusual risk factors, onset any time or patients	
	with severe HAP with early onset.	
Table 4	Patients with mild to moderate HAP, with risk	30
	factors, onset any time.	
Table 5	Patients with severe HAP with risk factors,	31
	early onset or patients with severe HAP, late	
	onset.	
Table 6	Criteria of severe HAP.	34
Table 7	The common pathogens causing pneumonia in	38
	immunocompromised individuals.	
Table 8	ATS&BTS guidelines in management of CAP.	62
Table 9	Initial empiric antibiotic therapy for HAP and	66
	CAP in patients with no known risk factors for	
	MDR pathogens, early onset and any disease	
	severity.	
Table 10	Initial empiric antibiotic therapy for HAP and	67
	VAP in patients with late onset disease or risk	
	factors for MDR pathogens and all disease	
	severity.	
Table 11	Initial intravenous, adult doses of antibiotic for	68
	empiric therapy of HAP and VAP in patients	
	with late onset disease or risk factors for MDR	
	pathogens.	

No.	Title	Page
Table 12	Description of personal and clinical characteristics of all study participants.	81
Table 13	Description of Prevalence and types of isolated organism, sensitive and resistant Antibiotic among all study participants.	85
Table 14	Description and comparison of personal and clinical characteristics in-between mechanically and normally ventilated patients.	89
Table 15	Description and comparison between mechanically and normally ventilated patients regarding types of isolated organism, sensitive and resistant Antibiotics.	92
Table 16	Description of sensitive and resistant antibiotic for Pseudomonas spp.	95
Table 17	Description of sensitive and resistant antibiotic for E.coli.	95
Table 18	Description of sensitive and resistant antibiotic for Methicillin Sensitive Staph. aureus (MSS).	96
Table 19	Description of sensitive and resistant antibiotic for Methicillin Resistant Staph. aureus (MRSA).	97
Table 20	Description of sensitive and resistant antibiotic for Acinetobacter spp.	97
Table 21	Description of sensitive and resistant antibiotic for Klebsiella spp.	98
Table 22	Comparison of personal and clinical characteristics in-between improved and died patients.	99

List of Figures

No.	Title	Page
Figure 1	Algorithm for Classifying patients with	26
	hospital-acquired pneumonia (HAP).	
Figure 2	Distribution of all patients in the study	82
	according to gender.	
Figure 3	Distribution of all patients in the study	83
	according to type of ventilation.	
Figure 4	Distribution of all patients in the study	84
	according to diagnosis.	
Figure 5	Distribution of all patients in the study	85
	according to fate.	
Figure 6	Distribution of all patients in the study	87
	according to the isolated organisms.	
Figure 7	Distribution of all antibiotics according to	88
	their sensitivity against different isolated	
	organisms.	
Figure 8	Distribution of all antibiotics according to	89
	pathogen Resistance.	
Figure 9	Comparison between mechanically and	91
	normally ventilated patients regarding their	
	diagnosis.	
Figure 10	Comparison between mechanically and	92
	normally ventilated patients regarding fate.	
Figure 11	Comparison between mechanically and	94
	normally ventilated patients regarding	
	isolated organism.	

Contents

Introduction		
Aim of work		
Review of literature		
 Pneumonia 		
-Definition	6	
-Epidemiology of pneumonia	7	
-Classification of pneumonia	11	
-Pathology & pathogenesis	12	
-modes of transmission of pneumonia	13	
-Risk factors of pneumonia	16	
-Microbiology of pneumonia	18	
Microbiology of community acquired pneumonia	18	
Microbiology of hospital acquired pneumonia	25	
Microbiology of Ventilator-Associated Pneumonia	36	
Microbiology of pneumonia in immunocompromised patients	37	
Microbiology of pneumonia in elder patients	42	
-clinical presentation of pneumonia		
- Diagnostic studies in pneumonia		
-Management of pneumonia		
Subjects and methods	74	
Results	81	
Discussion	101	
English summary	114	
Conclusion		
Recommendations		
References		
Arabic summary		

INTRODUCTION

Pneumonia continues to be a major clinical problem in term of morbidity, mortality and use of hospital resources. It is well recognized that a delay in making the diagnosis and instituting appropriate antibiotic treatment is associated with an increased mortality (*Andrews*, 1987).

Diagnosis of pneumonia is easily made in the presence of typical symptoms, physical signs and radiological features. However, the clinical picture may not be so well defined in the presence of co-existing lung disease or if the patient presents in the early stages before radiological picture becomes apparent. In addition, other traditional markers may not be elevated. If making the diagnosis has not been easy, then assessing treatment response is likely to be difficult (*Falsey et al.*, 1995).

Ventilator-associated pneumonia (VAP) is the main cause of nosocomial infection in an intensive-care setting. VAP diagnosis is difficult, due both to the lack of well-defined clinical criteria and the overlap of symptoms with those of nosocomial pneumonia. American medical literature states that the mean incidence rate of VAP is 7 cases per 1,000 days of mechanical ventilation, ranging from 1 to over 20 cases per 1,000 days of mechanical ventilation (*Richards*, 1999).

Though an etiological investigation, composed of quantitative cultures from VAP patients (bronchoalveolar lavage fluid obtained through bronchoscopy with or without a protected catheter or simply collected by tracheal aspiration) is important for the optimization of antibiotic use, this recommendation is not universally accepted due to the lack of objective studies that demonstrate the benefit of these procedures. There have been few trials made with critically ill-patient populations concerning the importance of such data for clinical practice (*Ravindra*, 2002).

Mini-BAL sampling in the previous literature usually depends on using a prepackaged dedicated catheters that is not available in the developing countries and if imported it would be extremely expensive (*Levy*, 1994). Therefore, this study employed a new, cheap method in acquiring mini-BAL samples in the diagnosis of VAP.

AIM OF THE WORK

The aim of this study was to assess the incidence of different pathogens causing pneumonia and their antibiotic sensitivity in patients admitted to the respiratory intensive care unit in Ain Shams University Hospital during the period from 1/12/2009 to 31/5/2010.

PNEUMONIA

During the early years of medical science, beginning somewhere in the 1840s with the great University of Vienna School of Medicine, pneumonia was relatively simple to diagnose because most cases were found at autopsy. Although Laennec's invention, the stethoscope, was in use, relatively few people were experts in its application. Autopsies were the great learning tool of the second half of the 19th century, and modern medicine truly began with the careful study of autopsy material. In those times, pneumonia was defined as inflammation and consolidation of lung tissue, and the various stages of consolidation were well studied and characterized histopathologically e.g. terms as "red hepatization" and "gray hepatization". Although they are not longer used much, physical examination was done by the more advanced practitioners. Results were fairly well described and correlated with autopsies, but an average patient seeing an average physician was unlikely to obtain any relief. Specific causes of pneumonia were simply not understood because the germ theory had not yet been developed (Sarosi, 1999).

Proposal of the germ theory led various physicians to attempt isolation of the organisms responsible for pneumonia. In 1880, Pasteur isolated an organism that was later called Streptococcus pneumoniae. Unfortunately,

Pasteur did not do very much with his discovery, and further characterization awaited Frankel's work in 1884, at which time the microorganism was named Diplococcus pneumoniae. (This designation persisted in the literature, and only in the last 40 years or so has the official name been changed to Streptococcus pneumoniae). After these discoveries, pneumonia was similar thought to synonymous with infection caused by D. pneumoniae. That thinking held, even though in 1882 Friedlander described for acute pneumonia: another organism Klebsiella pneumoniae or Friedlander's bacillus. For the next 50 years or so, pneumonia was assumed to be an infection caused by pneumococci, even after a new pneumonia organism, Haemophilus influenzae was isolated in 1920s as a result of the worldwide epidemic of influenza A, or Spanish flu, H. influenzae was originally thought to be the cause of influenza (hence its name); it is well known now that this assumption was erroneous. Other agents causing pneumonia were gradually identified, more by their associated epidemiologic circumstances than by microbiologic methods. Pneumonia associated with tularemia and the plague had been well defined, and even typhoid fever had a pneumonic component. By the middle of the 20th century, however, these entities were of medical curiosities (Raafat, 2002).

Definitions

When the word 'pneumonia' is used in medical practice, it almost always refers to a syndrome caused by acute infection, usually bacterial, characterized by clinical and/or radiographic signs of consolidation of a part or parts of one or both lungs. However, the use of the term has been greatly extended to include non-bacterial infection of the lungs caused by a wide variety of microorganisms. Pneumonitis is occasionally used as a synonym for pneumonia, particularly when inflammation of the lung has resulted from a non-infectious cause, such as chemical or radiation injury (*Seaton*, 2000).

Hospital acquired (Nosocomial) pneumonia has been defined as an infection of the lung parenchyma that was neither present nor incubating at the time of hospital admission. Health care—associated and nosocomial pneumonias are the second leading cause of hospital-acquired infections and are increasing in proportion to the use of assisted ventilation and with prolonged care of critically ill patients (*Gaynes*, 2005).

Heath care associated pneumonia [HCAP] is a category includes patients who a] receive home intravenous antibiotics, home nursing, or home wound care; b] patients who reside in nursing homes or long-term care facilities; c] patients who have been hospitalized for > 2 days in the past