# Health care–associated Infections with *Acinetobacter* Species in Intensive Care Units at Ain Shams University Hospital

**Thesis**
Submitted for partial fulfillment of Master Degree *in*
*Medical Microbiology and Immunology*


By
**Fatma Mohamed Saad**
M.B.B.Ch
Faculty of medicine-Ain Shams University


**Under Supervision of**

Prof. Amany Tharwat Abdel Rahman
*Professor of Medical Microbiology and Immunology*
*Faculty of Medicine-Ain Shams University*

Dr. Shereen El-Sayed Mohamed Taha
*Lecturer of Medical Microbiology and Immunology*
*Faculty of Medicine-Ain Shams University*

Dr. Sara Mahmoud Abd EL-Hakam
*Lecturer of Tropical Medicine*
*Faculty of Medicine-Ain Shams University*


**Faculty of Medicine**
**Ain Shams University**
**2013**

# Acknowledgment

My deepest gratitude and thanks to **ALLAH** the most merciful for guiding me through and giving me the strength to complete this work the way it was.

My outmost thanks and deepest gratitude and appreciation go to **Dr. Amany Mostafa,** Head of department of Medical Microbiology and Immunology.

It is my pleasure to express my deepest thanks and profound respect to my honored professor, **Dr. Amany Tharwat Abdel Rahman** professor of Medical Microbiology & Immunology, Faculty of Medicine, Ain Shams University for her useful scientific supervision and valuable remarks during every step of this work., without which this work could never have seen the light.

My deep appreciation and deepest sense of obligation to **Dr. Shereen El-Sayed Mohamed Taha** lecturer of Medical Microbiology & Immunology Faculty of Medicine, Ain Shams University for her sincere advice during the whole work. She offered me every guidance and support

I would like to express my thanks to **Dr. Sara Mahmoud Abd EL-Hakam**, lecturer of Tropical Medicine Faculty of Medicine, Ain Shams University for her great cooperation in the practical part of this work.

Words cannot suffice to express my gratitude to my family especially my mother and my husband, without their patience and great love I would never been able to finish this work.

Fatma

# Contents

# List of Tables

# List of Figures

# List of Abbreviation

| | |
|---|---|
| *A. baumannii* | *Acinetobacter baumannii* |
| *Acinetobacter* spp | *Acinetobacter spieces* |
| AFLP | Amplified fragment length polymorphism |
| *AGS 13TU* | *Acinetobacter genomic species 13TU* |
| AMEs | Aminoglycoside modifying enzyme |
| AMs | Alveolar macrophages |
| APCs | Antigen-presenting cells |
| ARDRA | Amplified ribosomal DNA restriction analysis |
| A-site | Aminoacyl site |
| ASUHs | Ain Shams University Hospitals |
| BIs | Blood stream infections |
| *C. albicans* | *Candida albicans* |
| CDC | Centers for disease control and prevention |
| CFU | Colony forming unit |
| CFU | Colony forming unit |
| CLED | Cystine-Lactose-Electrolyte-Deficient Agar |
| CONS | Coagulase-negative staphylococci |
| *E. coli* | *Escherichia coli* |
| *EPA* | United states environmental protection agency |
| ETA | Endotracheal tube aspirate |
| FH | Factor H |

ت

| | |
|---|---|
| **HAP** | Hospital-acquired pneumonia |
| **HAI** | Health care–associated infections |
| **ICUs** | Intensive care units |
| **IDSA** | Infectious Diseases Society of America |
| **LPS** | Lipopolysaccharide |
| **MCP** | Macrophage chemotactic protein |
| **MDR** | Multidrug resistant |
| **MDR-Ab** | Multidrug resistant Acinetobacter |
| **MHA** | Mueller-Hinton agar |
| **MICs** | Minimum inhibitory concentrations |
| **MIP** | Macrophage inflammatory protein |
| **NHS** | Normal human serum |
| **NNIS** | National Nosocomial Infection Surveillance |
| **NO** | Nitric oxide |
| **OMPs** | Outer membrane proteins |
| ***P. aerugenosa*** | *Pseudomonas aeruginosa* |
| **PCR–ESI-MS** | PCR-electrospray ionization mass spectrometry |
| **PDR** | Pandrug resistant |
| **PLC** | Phospholipases C |
| **PPE** | Personal protective equipment |
| **ROS** | Reactive oxygen species |
| **RTIs** | Respiratory tract infections |
| ***S. aureus*** | *Staphylococcus aureus* |

| | |
|---|---|
| **SHEA** | Society for Healthcare Epidemiology of America |
| **SOM** | Somatostatin |
| **TLR** | Toll-like receptor |
| **TNF-α** | Tumor necrosis factor alpha |
| **UTI** | Urinary tract infections |
| **VAP** | Ventilator-associated pneumonia |
| **XDR** | Extensive drug resistant |

# Introduction

Members of the genus Acinetobacter are ubiquitous, free living, small aerobic Gram negative cocco-bacilli that prefer moist environment and can be easily obtained from soil, water, food and sewage (Gerner-Smidt, 1995). They are normal inhabitants of human skin and are frequently isolated from the throat and respiratory tract of hospitalized patients **(Fournier and Richet, 2006).**

More than 30 named and unnamed species of *Acinetobacter* have been described **(Nemec et al.,2009),** some of which are of clinical importance, including *Acinetobacter baumannii* (*A.baumannii)*, *Acinetobacter gen. sp. 3*, and *Acinetobacter gen. sp. 13TU*, while other species, like *A. junii, A. johnsonii, A. ursingii,* and *A.schindleri*, can also incidentally be associated with infections **(Dijkshoorn et al., 2007).** Much attention has been paid to outbreaks caused by *Acinetobacters* **(Villegas and Hartstein, 2003),** which in most cases are caused by *A. baumannii*. The crude mortality (at any age) for *Acinetobacter spp.* ranges from 23 - 73% **(Jain and Danziger, 2004).**

*A. baumannii* is capable of causing both community and health care–associated infections (HAIs) and it has recently emerged as a major cause of HAI, because of its propensity to

accumulate mechanisms of antimicrobial resistance that lead to pan-drug resistance**(Fournier and Richet, 2006)**. It has become one of the top nine pathogens threatening the current health care delivery system, particularly the intensive care units (ICUs) **(Talbot et al.,2006)** *A. baumannii* mainly causes pulmonary, urinary tract, bloodstream or surgical wound infections **(Fournier and Richet, 2006)**.

A number of risk factors have been shown to be associated with *Acinetobacter* nosocomial infections. They include advanced age, immunosuppression, surgery, previous treatment with broad-spectrum antibiotics, use of invasive devices, burns, fecal colonization with *Acinetobacter*, and prolonged hospital or ICU stays. Environmental contamination of various hospital items has been often identified, ranging from suctioning equipment to pillows and mattresses. The role of hands has also been investigated, showing that hand-carriage rates among staff members (nurses and physicians) ranged from 3% to 23% and that the carriage was usually transient, except in the case of damaged skin **(Rungruanghiranya et al., 2005).**

*Acinetobacters* may be identified presumptively to the genus level as Gram-negative, catalase-positive, oxidase-negative, non motile, non fermenting coccobacilli. *Acinetobacter* species of human origin grow well on solid media that are routinely used in clinical microbiology laboratories aerobically at a 37°C incubation temperature.

Leeds Acinetobacter medium facilitate the isolation of *Acinetobacters* from mixed bacterial populations. Of the few methods that have been validated for identification of Acinetobacter species, DNA-DNA hybridization remains the reference standard. There are other molecular methods that have been developed and validated for identification of *Acinetobacters* as amplified 16S rRNA gene restriction analysis, high-resolution fingerprint analysis by amplified fragment length polymorphism (AFLP), ribotyping etc. More recent developments include the identification of *A. baumannii* by detection of the blaOXA-51-like carbapenemase gene intrinsic to this species, PCR-electrospray ionization mass spectrometry (PCR–ESI-MS) **(Peleg et al., 2008).**

*A.baumannii* is intrinsically multidrug resistant. Relatively few antibiotics are active against this organism. While colonization should not be treated, infection should. Medications to which *Acinetobacter* is usually sensitive include the following: Meropenem, Colistin, Polymyxin B, Amikacin, Rifampin, Minocycline, and Tigecycline. In general, first-, second-, and third-generation cephalosporins, macrolides, and penicillins have little or no anti-*Acinetobacter* activity, and their use may predispose to *Acinetobacter* colonization (**Peleg et al., 2007**).

.

To prevent the occurrence and transmission of this organism in the ICU, infection control measures are essential. Measures described in the clinical trials include hand disinfection and contact isolation using glove, gown, and barrier precautions. Specialized infection control measures are indicated in numerous studies, the major focus is the antibiotic control strategy, which consists of restricted use of third generation cephalosporins and carbapenems, antibiotic cycling schedules and implementation of antimicrobial prescribing guidelines. Other measures include rigorous cleaning and disinfection of the ICU environment. Surveillance cultures of patients, environmental surfaces, and staffs; continuous educational and quality control programs for all ICU personnel; and adequate ICU staffing **(Rungruanghiranya et al., 2005)**.

# Aim of the Work

The aim of this work is to study the pattern of health care associated infections and antimicrobial susceptibility of *Acinetobacter* species in Intensive Care Units at Ain Shams University Hospitals.

# ACINETOBACTER

The genus Acinetobacter has undergone significant taxonomic modification over the last 30 years. Its most important representative, *Acinetobacter baumannii (A. baumannii),* has emerged as one of the most troublesome pathogens for health care institutions globally. Its clinical significance has been propelled by its remarkable ability to up regulate or acquire resistance determinants, making it one of the organisms threatening the current antibiotic era. *A. baumannii* strains that are resistant to all known antibiotics have now been reported, signifying a sentinel event that should be acted on promptly by the international health care community **(Peleg et al., 2008).**

Acting in synergy with this emerging resistance profile is the uncanny ability of *A. baumannii* to survive for prolonged periods throughout a hospital environment, thus potentiating its ability for nosocomial spread. The organism commonly targets the most vulnerable hospitalized patients, those who are critically ill with breaches in skin integrity and airway protection. As reported from reviews dating back to the 1970s, hospital-acquired pneumonia is still the most common infection caused by this organism. However, in more recent times, infections involving the central nervous system, skin, soft tissue and bone have emerged as highly problematic for certain