قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ

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Tuberculous patients in Respiratory Intensive Care Unit: Characteristics and Outcome

Thesis

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مرضى الدرن فى وحدة الرعاية المركزة للجهاز التنفسى : محددات ونتائج

رسالة

توطئة للحصول على درجة الماجستير فى الامراض الصدرية والتدرن

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Abbreviations

ABG	Arterial blood gases
ADA	Adenosine deaminase
AFB	Acid fast bacillus
AIDS	Acquired immunodeficiency syndrome
APACHE II score	Acute Physiology and Chronic Health Evaluation II scores
ARDS	Acute respiratory distress syndrome
BAL	broncho alveolar lavage
BCG	Bacille Calmette–Guerin
CAP	Community acquired pneumonia
Cat I	Category I
Cat II	Category II
CD4	cluster of differentiation 4
CDC	Center for disease control and prevention
CI	confidence interval
CMI	Cell mediated immunity
CNS	Central nervous system
COPD	Chronic Obstructive Pulmonary Disease
CPD	Chronic pulmonary diseases
CT	Computed tomography
CX-R	chest X-ray
DIC	Disseminated intravascular coagulation
DM	Diabetes mellitus
DNA	Deoxyribonucleic acid
DR-TB	Drug resistant tuberculosis
DST	Drug sensitivity testing
DTH	Delayed-type hypersensitivity
ECMO	Extracorporeal membrane oxygenation
ELISA	Enzyme-linked immunosorbent assay
FM	Florescent microscope
GCS	Glascow coma scale
Gm	Gram
Hb	Heamoglobin
HEPA	High-efficiency particulate air
HIV	Human immunodeficiency virus
HLA	Human leukocyte antigen
HRCT	High resolution computed tomography
HRZES	Isoniazid, Rifampicin, Pyrazinamide, Ethambutol And, Streptomycin

ICU	Intensive care unit
IFN-γ	Interferon gamma
IGRA	Interferon gamma release assay
INR	International normalized ratio
IRB	Institutional Review Board
IV	Intravenous
K	Potassium
Kpa	Pascal
LMIC	Low and middle-income countries
LTBI	Latent tuberculosis infection
MDRTB	Multi drug resistant tuberculosis
Mg	Milligram
MGIT	Mycobacterial Growth Indicator Tube
MmHg	millimetre of mercury
MOF	Multi organ failure
MTB	Mycobacterium tuberculosis
MTB/RIF	Mycobacterium / rifampicin
MV	Mechanical ventilation
Na	Sodium
NAATs	Nucleic acid amplification tests
NAATS	Nucleic acid amplification testes
NIPSV	Noninvasive pressure support ventilation
NIV	Noninvasive ventilation
Non-TB	Non Tuberculosis mycobacterium
NPV	Negative predictive value
OR	Odds Ratio
PA	Posterior – anterior
PAS	Para-aminosalicylic acid
PLT	Platelets
PPD	Purified protein derivative
PPV	Positive predictive value
PT	Prothrombin time
PTT	Partial thromboplastin time
QFT-GIT	QuantiFERON®-TB Gold In-Tube
RD-1	region of difference-1
RICU	Respiratory ICU
RNA	Ribonucleic acid
RR-TB	Rifampicin-resistant tuberculosis
SD	standard deviation
SDGS	Sustainable Development Goals
SGOT	Serum glutamic-oxaloacetic transaminase

SGPT	Serum glutamic pyruvic transaminase
SLIDs	Second-line injectable drugs
SPSS	Statistical Package the Social Sciences
SR	Standard error
TB	Tuberculosis
TB/HIV	Tuberculosis / Human immunodeficiency virus
TLC	Total leucocytic count
TST	Tuberculin skin test
VAP	Ventilator-associated-pneumonia
WHO	World health organization
XDR	Extended drug resistant tuberculosis
Xpert MTB/ RIF	Xpert Mycobacterium tuberculosis/rifampicin assay
ZN	Ziehl-Neelsen stain

INTRODUCTION

Introduction

Tuberculosis (TB) remains a major health problem worldwide. TB affects 10 million people each year and is one of the top ten causes of death for the past 5 years. In 2015, WHO estimated 1.4 million TB-related deaths with an addition of 0.4 million deaths resulting from TB/HIV co-infection. Multidrug-resistant TB (MDRTB) (clinically defined as TB resistance to at least isoniazid and rifampicin) is a high burden TB variant which is progressively emerging due to improper management of TB (e.g. lack of adherence to medications), or person-to-person transmission **(Duro RP et al, 2017)**. WHO recently reported 480,000 new cases of MDRTB in addition to 100,000 new cases of rifampicin-resistant TB (RR-TB) who are at risk to develop MDRTB **(WHO, 2017).**

In 1990, the WHO estimated the prevalence and incidence of tuberculosis in Egypt to be 82/100,000 and 35/100.00, respectively. Effective diagnosis and treatment reduced TB prevalence and incidence in 2015 to 27 /100,000 and 15 / 100.00 cases population (a half of the 1990 estimate) **(Egyptian Guidelines, 2017).**

TB is an air-born infectious disease caused by the bacillus Mycobacterium tuberculosis. It typically affects the lungs (pulmonary TB) but can also affect other sites (extra-pulmonary TB). The probability of developing TB disease is much higher among people infected with HIV, and also higher among people affected by risk factors such as under-nutrition, diabetes, smoking and alcohol consumption **(WHO, 2017).**

The classic symptoms of active TB are chronic cough with blood containing sputum, fever, night sweats, and weight loss. Diagnosis of TB is generally based on chest-x ray finding, sputum smear microscopy for acid fast bacilli, and TB sputum culture (Löwenstein–Jensen medium and BACTEC MGIT TB system). in addition to new high tech-based diagnostic strategies of which, GeneXpert is the most powerful breakthrough. The most common clinical variants of TB infection are active pulmonary, latent TB, extra-pulmonary TB (e.g., *Miliary* TB, TB meningitis), multi-drug resistant TB, (MDRTB), TB-HIV co-infection **(Lewinsohn DM et al, 2017)**.

Early diagnosis and treatment are crucial milestones for TB control, since delayed diagnosis and/or treatment increases mortality rates and evolve aggressive clinical forms of the disease. Moreover, late diagnosis and treatment contribute to disease dissemination with dramatic public health implications **(Lewinsohn DM et al, 2017)**.

Severe forms of TB usually presents with respiratory failure and requires admission at Intensive Care Unit (ICU). Despite the availability of efective therapies, mortality rates remain between 15.5 and 65.9% **(Duro RP et al, 2017)**. Previous studies reported multiple risk factors of TB mortality in ICU. The most frequent factors are: old age **(Kim YJet al ,2008)**, respiratory failure/need for mechanical ventilation **(Erbes R et al ,2006)**, co-morbidities (e.g., HIV, diabetes) **(Dos Santos RP et al, 2011)**, acute renal failure **(Erbes R et al, 2006)**, sepsis **(Loh W et al, 2016)**, and other infections (e.g., ventilator associated pneumonia) **(Silva DR et al, 2012)**.