شبكة المعلومات الجامعية

التوثيق الإلكتروني والميكروفيلم

بسم الله الرحمن الرحيم

HANAA ALY

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جامعة عين شمس

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HANAA ALY

Characterization of Some Antibiotic Resistant Genes Isolated from Pathogenic *Staphylococcus aureus*

Thesis
Submitted for a PhD. Degree in Science in (Microbiology)

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2022

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Declaration

This dissertation has not been previously submitted for any degree at this or at any other university

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Acknowledgment

First of all, everlasting thanks to" ALLAH " to whom I relate any success in life.

It gives me pleasure to express my deep thanks to Microbiology Department, Faculty of Science, Ain-Shams University.

Sincere gratitude to Dr. Nagwa Ahmed Abdullah, Professor of microbiology, microbiology Department, Faculty of Science, Ain Shams University, for her continuous supervision, reading the manuscript and criticizing the results.

My deep thanks and everlasting gratitude goes to Dr. Sahar Tolba Mohamed, Assistant Professor of Microbiology, Faculty of Science, Ain Shams University, for her supervision, valuable advice, continuous encouragement and all the facilities offered during the investigation which made the completion of this work possible.

I am also profoundly grateful to Dr. Einas Hamed El-Shatoury, Professor of Microbiology, Faculty of Science, Ain Shams University, for her supervision, constructive criticism and continuous encouragement throughout this work.

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aad : aminoglycoside adenyltransferase gene cassettes
ABC gene : ATP binding cassette
ACCs : N-acetyl transferases
ADHs, aphs : O-phospho transferases
AMEs : aminoglycoside modifying enzymes
AMP : ampicillin
AMPs : Antimicrobial peptides
ANTs : nucleotidyl transferases
attI : attachment site of the integron integration
attC : attachment site of the gene cassette
betA, *bet*B : betaine aldehyde dehydrogenase
CALIN : cluster of attC site lacking integron-integrase
BC : benzalkonium chloride
Ccr : unique cassette of recombinase genes
CDC : Center for Disease Control and prevention
CIP : ciprofloxacin
CLSI : Clinical and Laboratory Standards Institute
3′ or 5′-CS : 5′-conserved segment
CS1 : class1 integron
DA : clindamycin
DEPC : diethylpyrocarbonate
dfr : dihydrofolate reductase
DNA : deoxyribonucleic acid
DNTPs : deoxynucleotide5-triphosphate
DO : doxacycline
E : erythromycin
EmrE : ethidium multidrug resistance protein E
EDTA : ethylene diamine tetra-acetic acid
G island : genomic island
HGT : Horizontal gene transfer
intI : integrase gene
In0 : elements have integrase gene without *attC* sites
Kbp : kilo base pair
KCL : potassium chloride

MDR : multidrug resistance
MDRP : multidrug reflux pump
*Mec*A : methicillin resistance gene
*Mec*I : methicillin resistance gene transducer
*Mec*R1 : methicillin resistance gene repressor
MIC : minimal inhibitory concentration
MRS : methicillin resistant *Staphylococci*
MRSI : methicillin resistant *Staphylococci* isolate
MRSA : methicillin resistance *Staphylococcus aureus*
MSSA : methicillin sensitive *Staphylococcus aureus*
NaCl : sodium chloride
NCCLS : National Committee for Clinical Laboratory Standards
ORF : open reading frames
PBP2a : penicillin binding protein 2a
PCR : polymerase chain reaction
P_c & P_2 : constitutive promoters for the genes cassettes integrated at the *attC* site
P-gp : P-glycoprotein transporter
P_{intI} : integrase gene promoter
QAC : Quaternary ammonium compound
qacEΔ1 : quaternary ammonium resistant gene
Rpm : revolution per minute
SA : *Staphylococcus aureus*
SCC : staphylococcal cassette chromosome
SMR : small multidrug resistance family
*sul*1 : dehydropetroate synthase sulfonamide resistance gene
TAE : Tris acetate-EDTA buffer
TE : Tris-EDTA buffer
*Tet*A : tetracycline structural efflux genes
*tet*R : tetracycline resistant gene
TetR : repressor protein
Tris : Tris hydroxymethyl amino methane
TM : transmembrane
Tn3 : transposon family
VA : vancomycin

YdeI/OmpD: polymyxin B resistant gene cassette

OmpD : trimeric β-barrel outer membrane general porin family

16S-RMTase: methyltransferase

Abstract

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Characterization of some resistant genes isolated from antibiotic resistant *Staphylococcus aureus*

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Two hundred and twenty clinical *Staphylococcus aureus* (SA) isolates were collected from 3 Egyptian hospitals (Ain-shams hospital, Cairo hospital and Abbassia fever hospital). All isolates were multidrug resistant (showing resistance to two or more antibiotic groups), antimicrobial susceptibility test showed that 81.8% of isolates were resistant to methicillin, 65% were resistant to trimethoprim-sulphamethaxole, 60% were resistance to amikacin, 46.3% were resistance to ciprofloxacin, 44.5% were resistance to erythromycin, 44% were resistance to clindamycin, 43.6% for doxacycline, 40% for vancomycin, 36.3% for imipenem and 11% of isolates were resistant to all tested antibiotic groups. Minimal inhibitory concentration of amikacin and imipenem showed that 65% and 58% of isolates were resistant. One hundred of isolates were examined for the presence of *mec*A gene, (*intI1*) integrase gene and class1 integron by PCR amplification; forty two percent of the isolates were found to carry class1 integron gene cassettes with variable amplicon, 36% of isolates carry (*intI1*) integrase gene and 80% of MRSA isolates were positive to the methicillin resistance *mec*A gene. Non classic class1 integron gene cassettes were detected in our MRSA isolates encoding resistance to quaternary ammonium compound (Qac resistance gene *emr*E), *emr*E gene is a small multidrug resistant (SMR) acting as osmoprotectants such as betaine aldehyde dehydrogenase (*bet*B).

This study highlights the prevalence of multidrug resistant *Staphylococcus aureus* in Egyptian hospitals in the presence of integron and the role of integron in the dissemination of antibiotic resistance.

Keywords: *Staphylococcus aureus*, *mec*A, (*intI1*) integrase gene, Class1 integron.