Screening of Reduced Susceptibility to Glycopeptides among Staphylococcus aureus isolates

Thesis

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Presented by

Noha Salah Eldein Elsayed Ali Soliman

M.B.B.Ch - Faculty of Medicine

Cairo University

Under supervision of

Prof.Dr.Sahar M. Khairat

Professor of Clinical and Chemical Pathology

Faculty of Medicine

Cairo University

Prof.Dr.Mervat G. ElAnany

Assistant Professor of Clinical and Chemical Pathology

Faculty of Medicine

Cairo University

Faculty of Medicine
Cairo University

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Abstract

Staphylococcus aureus is a leading nosocomial pathogen of major worldwide importance. Furthermore, it has been recently implicated in serious community acquired infections. This problem is further confounded by the appearance of S.aureus strains exhibiting reduced susceptibility to vancomycin. Since emergence of methicillin-resistant S.aureus, the glycopeptide (vancomycin) has been the only effective treatment for staphylococcal infections. However, lately S.aureus has developed resistance to glycopeptides and this was associated clinically with treatment failure. This work aimed at studying the prevalence of reduced susceptibility of S.aureus to glycopeptides (vancomycin). In this study, 500 S.aureus isolated from different sample sources were collected over a period of 5 years from hospitalized patients as well as outpatients and staff members. These isolates were subjected to methods of identification and testing methods for the susceptibility to vancomycin in the form of drug agar dilution and E-test. Among the 500 S.aureus isolates, 1.6% showed S.aureus with reduced susceptibility to vancomycin (hVISA) with MIC $\geq$ 2µg/ml of which the majority 87.5% were hospital acquired. Also a tendency to an increase in vancomycin MICs (glycopeptide creep) had been observed over the 5 years. Strict measures of infection control should be applied and increased awareness of the physicians about antibiotics abuse which is essential to combat spread of s.aureus with reduced susceptibility to vancomycin.

Key Words:

Staphylococcus aureus

Vancomycin - glycopeptide

Susceptibility - hVISA

Contents

Abbreviations

BHI : Brain heart infusion agar

BHIV4or6 : Brain heart infusion with vancomycin concentration 4 or 6µg/ml

CA : Community acquired

CDC : Centers of Disease Control and Prevention

CLSI : Clinical and Laboratory Standard Institute

CUH : Cairo University hospitals

C.V.L : Central Venous Line

DM : Diabetes Mellitus

DNase : Deoxyribonuclease test

Eap : Extracellular adherence protein

EARRS : European Antimicrobial Resistance surveillance

E/M : Electron Microscope

FnBP : Fibronectin-binding protein

FTIR : Fourier transform infra-red spectroscopy

GISA : Glycopeptide intermediate S.aureus

HA : Hospital acquired

hGISA : Heterogeneous glycopeptides intermediate S.aureus

HICPAC : Hospital Infection Control Advisory Committee

hVISA : Heterogeneuos vancomycin intermediate S.aureus

ICU : Intensive care unit

IDSA : Infectious Disease Society of America

LOS : Length of hospital stay

MAP : Major histocompatibility complex class II analogous protein

MET : Macrodilution method E-test

MH : Mueller-Hinton agar

MHT5 : Mueller-Hinton agar with teicoplanin concentration 5µg/ml

MIC : Minimal inhibitory concentration

MRSA : Methicillin-resistant S.aureus

PAP : Population analysis profile

PBP : penicillin-binding protein

PCR : Polymerase chain reaction

PVL : Panton-Valentine Leucocidin

TEM : Transmission electron microscopy

TMP-SXT : Trimethoprim-sulfamethoxazole

TP : Teicoplanin

TSS : Toxic shock syndrome

TSST-1 : Toxic shock syndrome toxin-1

V0.5,1,2,4 : Mueller-Hinton agar with different vancomycin concentrations

VA : Vancomycin

VISA : Vancomycin-intermediate S.aureus

VRSA : Vancomycin-resistant S.aureus

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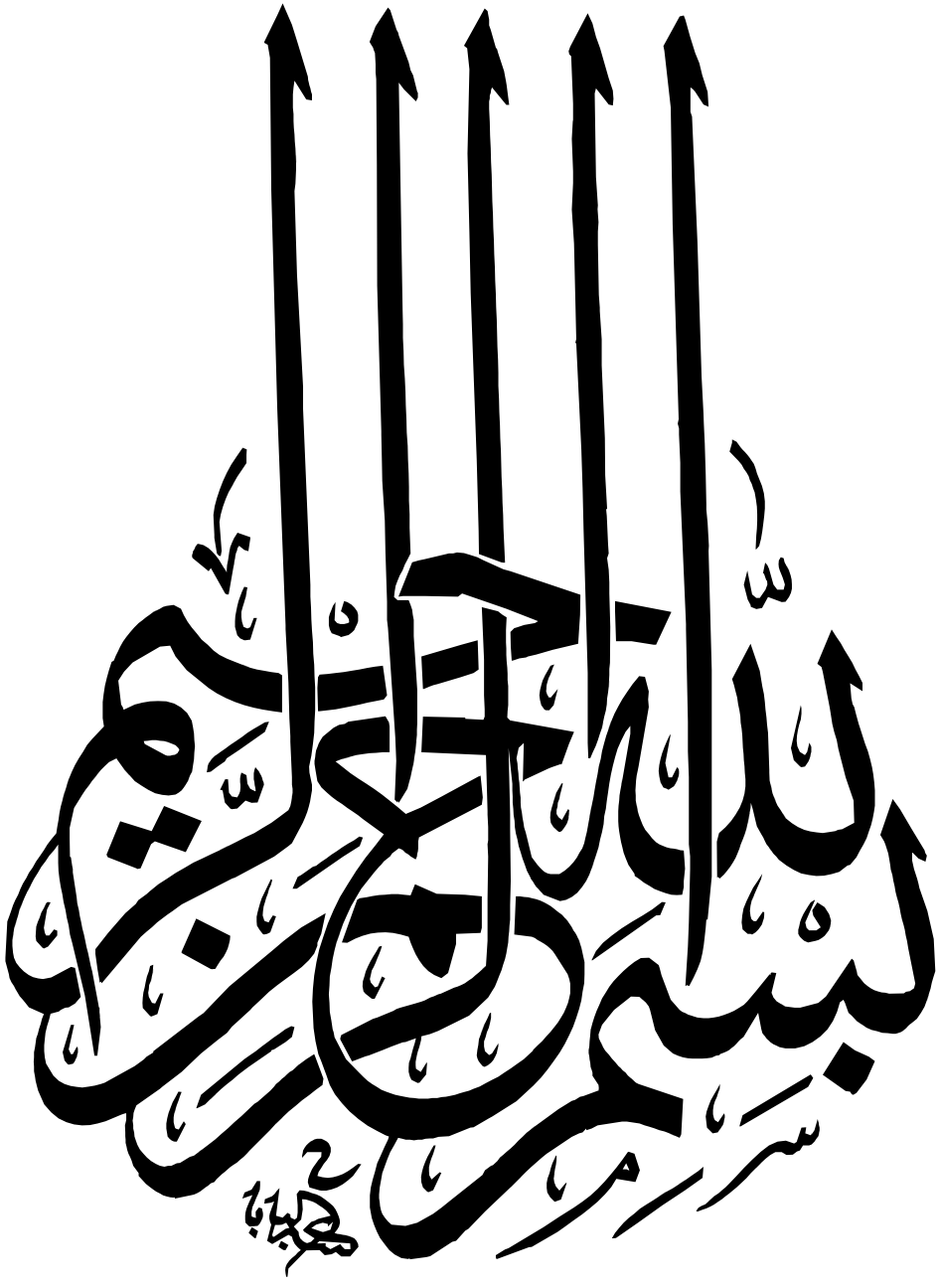
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INTRODUCTION

Introduction

Staphylococcus aureus is one of the most common causes of community acquired and hospital acquired infections.

After initial success of penicillin in treating staphylococcus aureus infections, resistance to this drug began to emerge, then methicillin and other semisynthetic methicillins were successful in treating penicillin resistant staphylococcus aureus until 1980 when methicillin resistant staphylococcus aureus (MRSA) became endemic in hospitals **(Oliveira et al., 2002)**.

Since emergence of MRSA, the glycopeptide (vancomycin) has been the only effective treatment for staphyloccal infections.

Lately, Staphylococcus aureus has developed resistance to glycopeptides (vancomycin) and the degree of resistance was determined by minimal inhibitory concentration (MIC) testing of the drug **(Hiramatsu et al., 1997)**.

Staphylococcus aureus with reduced susceptibility to glycopeptides or vancomycin (VISA or GISA) was first discovered in Japan 1996 and since then, reports of VRSA & VISA among staphylococcus aureus isolates have been increasing **(Hiramatsu et al., 1997).**

The clinical significance of emergence of reduced susceptibility to vancomycin among staphylococcus aureus represented in appearance of cases with treatment failure, not responding to the drug.

Aim of the work:

This work aimed at studying the prevalence of reduced susceptibility to glycopeptides represented in vancomycin among staphylococcus aureus isolates collected from hospitalized patients as well as outpatients and staff members in Cairo University Hospitals.

REVIEW OF LITERATURE

CHAPTER (1)

Staphylococcus aureus

Staph aureus has long been recognized as one of the major human pathogens responsible for a wide range of infections. It is a common pathogenic commensal bacterium found in warm moist areas of the body, particularly the nose, axilla, perineum. The basic human habitat of S.aureus is the anterior nares with a nasal carriage of about 20%-50% of the population, but it does not cause harm and does not require treatment. However, some S.aureus carriers constitute a source of infection by disseminating the organism to others **(Haddadin et al., 2002).**

Pathogenesis and Virulence factors:

Staph aureus expresses many potential virulence factors that contribute to its ability for attachment, colonization, cell-cell interaction, immune evasion and tissue damage. The virulence factors can be classified as cell wall associated and extra-cellular component **(Novick et al., 2001).**

***A)Cell wall components*:(Brooks et al., 2004)**

1)Protein A:

It is a cell wall component of many S.aureus strains. It is an important virulence factor because it binds to the Fc portion of IgG, preventing the activation of complement. As a consequence, no C3b is produced, and the opsonization and phagocytosis of the organisms are greatly reduced.

2)Techoic acids :

They are polymers of ribitol phosphate. They mediate adherence of the Staphylococci to mucosal cells and play a role in the induction of septic