Sole Zinc Oxide and Titanium Dioxide nanoparticles antimicrobial activity versus their association with different antibiotics on Methicillin-Resistant *Staphylococcus aureus*

Treatment and prevention of wound infection continue to be a challenging issue. *S.aureus* is one of the most significant human pathogens that cause wound infections. MRSA is a significant global health problem that impacts patients in both community and health care settings associated with considerable morbidity and mortality**.**

Methicillin resistant *S.aureus* is a multidrug resistant organism, being not only resistant to β-lactam antibiotics, but also resistant to other antimicrobial agents. Therefore, many new therapeutic strategies against MRSA are urgently needed such as new antimicrobial drugs based on nanoparticles which have many advantages compared with conventional antibiotics.

The aim of this study was to isolate and identify MRSA strains and detect the antimicrobial activity of ZnO and TiO2 NPS on them then evaluating the effect of the nano-antibiotics association.

This study was conducted in Medical Microbiology and Immunology Department, Faculty of medicine, Benha University, during the period from June 2020 to March 2021.The study was carried out on 150 pus samples collected from patients with infected wounds in different wards. Their ages ranged from 21 years to 64 years.

The collected specimens were examined microscopically by Gram stain, cultivated on nutrient agar and mannitol salt agar and tested by conventional biochemical reactions (catalase test and coagulase test) for

full identification of *S. aureus* isolates. Then identification of MRSA isolates was performed by chromogenic media and cefoxitin disc diffusion test. All MRSA isolates were tested for antibiotic susceptibility testing using the disk diffusion method.

The antibacterial activity of ZnO and TiO2 NPs was tested by measuring their inhibition zones on MRSA isolates. Then the effect of their combination with antibiotics (Azithromycin, clindamycin, linezolid, and vancomycin) was evaluated by determination of inhibition zones of nano-antibiotics association on MRSA isolates. The effect of NPs on MRSA was visualized by using electron microscope.

The prevalence of *S.aureus* among samples in the present study was 61 isolates (40.6%) and the percentage of MRSA among *S.aureus* isolates was 60.7%.

Concerning the demographic and clinical data of patients enrolled in this study as sex, age, antibiotic administration, hospitalization, and comorbidities, there was no significant difference between patients infected by MRSA and those infected with MSSA.

As regards the antibiotic susceptibility testing of MRSA isolates, it was found that the highest antibiotic resistance rates were recorded for ciprofloxacin (48.6%), gentamycin (37.8%), and chloramphenicol (35.1%), while the lowest resistance rates were recorded for linezolid, clindamycin (8.1%) and rifampin (10.8%) respectively. The percentage of MDR among MRSA isolates was 27%.

The present study detected the antibacterial activity of ZnO and TiO2 with the mean diameters of inhibition zones of ZnO and TiO2 NPs on MRSA isolates which were 8.16 mm and 6.08 mm respectively.

There was a high significant increase in the mean diameters of the inhibition zones of tested antibiotics on MRSA isolates when they were conjugated with ZnO and TiO2 NPs. Moreover, distortion in structure and arrangement of MRSA after treating with ZnO and TiO2 NPs was detected by TEM.

Conclusions:

- The prevalence of MRSA is prominently high among wound infection samples from patients in different wards of hospitals.
- There is high resistance rate of MRSA isolates towards many antibiotics (MDR isolates) and there is spread of resistance among critical drugs like linezolid.
- Results of this study support marked antibacterial activity of ZnO and TiO2 NPs against MRSA isolates.
- Results of this study support marked synergy between NPs (ZnO and TiO2) and antibiotics (Azithromycin, clindamycin, linezolid, and vancomycin) when both combined against MRSA isolates.