

الآية

قال الله تعالى:

﴿ فَتَعَالَى اللَّهُ الْمَلِكُ الْحَقُّ وَلَا تَعْجَلْ بِالْقُرْآنِ مِنْ قَبْلِ أَنْ يُقْضَىٰ

إِلَيْكَ وَحْيُهُ وَقُلْ رَبِّ زِدْنِي عِلْمًا ﴾

(طه: 114)

صدق الله العظيم

Dedication

For my lovely parents, for their advices, patience, faith and support

Because they always understood.

Along with all hard working and respected teachers, and for all gentle readers.

For me

Acknowledgment

Firstly the hall thanks to Almighty to **Allah** for giving me faith for completion of this research. Am deeply grateful to **Prof. Yousef Fadalla Hamed Elneel** for his gaudiness, sharing his knowledge, valuable comments and suggestions that really helped me in the completion of this study, it is truly an honor. I would like to pay my special regards to **Dr. Hisham Noreldayem Altayeb** for helping me through all the practical part. I wish to thank all the people whose assistance was a milestone in the completion of this project.

Abstract

Colistin belongs to last resort antibiotic for the treatment of carbapenems resistant Gram-negative bacteria. Until recently, the resistant to colistin was restrictedly due to chromosomal mutations which cannot be transferred between organisms. However, identification of plasmid transfer *mcr-1* colistin resistant gene is considered as a source of threat. The resistance of *K.pneumoniae* to antibiotics led to longer hospitalization, high cost, and increased mortality.

It's a descriptive cross sectional and hospital-based study, the main objective is to identify the presence of *mcr-1* gene in *K.pneumoniae* using Polymerase chain reaction (PCR).

The PCR was performed at research laboratory in Sudan University of Sciences and Technology, during the period from June to November, 2019. A total of (50) isolates were collected from Military hospital, Police University Hospital, Royal Care Hospital hospitals at Khartoum State. Laboratory tests such as colony growth characteristics and basic biochemical tests were performed to confirm identification of *K.pneumoniae*, antibiotic sensitivity test against colistin, DNA extraction and PCR tests for identification of *K.pneumoniae* and *mcr-1* gene.

Only 8(16%) isolates showed resistance against colistin, 42(84%) were susceptible to colistin. PCR results revealed that 2 (4%) out of (50) *K.pneumoniae* isolated from clinical specimens were positive for *mcr-1* gene.

This study confirm the presence of *mcr-1* gene among clinical isolates of *K.pneumoniae* in Khartoum state, Sudan was 2 (4%). Out of (50) *K.pneumoniae* clinical isolates carried the *mcr-1* gene, also the study revealed that the genotypic positive isolates of *mcr-1* gene do not reflect phenotypic resistance to Colistin, and there were about 1(2%) *mcr-1* gene positive *K.pneumoniae* isolates still susceptible to Colistin antibiotic by disk diffusion test.

المستخلص

المضاد الحيوي كولستين ينتمي الي الملاذ الاخير من المضادات الحيوية لعلاج البكتريا سالبة الغرام المقاومة للكاربابينيم، حتى وقت قريب كانت المقاومة للكولستين محدودة ونتاجة بسبب الطفرات الكروموسومية التي لايمكن نقلها بين الكائنات الحية, ولكن فإن انتشار جين *mcr-1* المقاوم للكولستين الذي ينتقل عن طريق البلازميد، يعتبر مصدرا للتهديد. تؤدي مقاومة بكتريا الكلبسيلا الرئوية الي زيادة حدة المرض و تقليل نسبة الشفاء وايضا ارتفاع تكلفة العلاج، بالاضافة الي زيادة معدل الوفيات.

الهدف الرئيسي من الدراسة هو التحقق من وجود جين *mcr-1* في العينات السريرية لبكتريا الكلبسيلا الرئوية.

تم جمع ٥٠ عينة من عينات سريرية مختلفة من عدة مستشفيات في ولاية الخرطوم من مستشفى رويال كير، مستشفى السلاح الطبي ومستشفى الشرطة الجامعي في الفترة من شهر يونيو الي سبتمبر ٢٠١٩ تم اجراء الاختبارات المعملية المختلفة مثل نمو المستعمرة واختبار الكيمياء الحيوية لتحديد وتاكيد بكتريا الكلبسيلا الرئوية. وايضا تم اختبار حساسية البكتريا للمضاد الحيوي الكولستين ومن ثم استخلاص الحمض النووي واختبار البلمرة التسلسلي.

اثبتت الاختبارات وجود بكتريا الكلبسيلا الرئوية في جميع العينات المجموعة ، يوجد ٨ منها مقاومة للكولستن و ٤٨ لديها حساسية تجاه الكولستين. كما اوضح جهاز البلمرة التسلسلي وجود عينيتين من اصل ٥٠ تحتوي على جين *mcr-1*.

اوضحت النتائج وجود جين *mcr-1* في سلالة بكتريا الكلبسيلا الرئوية المعزولة من عينات المرضى التي خضعت للدراسة، ضرورة اتخاذ الاجراءات اللازمة للتخفيف من انتشار هذا الجين قبل استفحاله في المستشفيات وضرورة اتباع اللوائح بخصوص تناول المضادات الحيوية في السودان.

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List of Abbreviations

Abbreviations	Complete words
ABR	Antibiotic Resistance
AMR	Antimicrobial Resistance
AST	Antimicrobial Susceptibility Test
CAUTIs	Catheter Associated Urinary Tract infections
CBC	Complete Blood Count
CLED	Cysteine lactose Electrolyte Deficient
CLSI	Clinical and Laboratory Standards Institute
CPS	Capsular Polysaccharides
CRE	Carbapenems-Resistant Enterobacteriaceae
CT	Computerized Tomography
DNA	Deoxy Ribonucleic Acid
DW	Distilled Water
ESBL	Extended Spectrum Beta-Lactamase.
EUCAST	European Committee on Antimicrobial Susceptibility Testing
FQs	Fluoroquinolones
HGT	Horizontal Gene Transfer
ICU	Intensive Care Unit
Kb	kilobases
KIA	Kliger Iron Agar
KPC	<i>Klebsiella pneumoniae</i> Carbapenemase
LPS	Lipopolysaccharides

<i>mcr-1</i>	Mobile Colistin Resistance Gene-1
MDR	Multi-Drug Resistance
MGEs	Mobile Genetic Elements
<i>NDM-1</i>	New Delhi metallo-beta-lactamase 1 (NDM-1)
OTC	Over the Counter
<i>OXA</i>	Oxacillinase-type β -lactamase
PCR	Polymerase Chain Reaction
TLR-4	Toll Like Receptors-4
UTIs	Urinary Tract Infections
WHO	World Health Organization