

List of Contents

Title	Page No.
<i>List of Abbreviations</i>	<i>ii</i>
<i>List of Figures</i>	<i>v</i>
<i>List of Tables</i>	<i>vii</i>
<i>Introduction</i>	<i>1</i>
<i>Aim of the Work</i>	<i>4</i>
<i>Review of Literature</i>	
▪ <i>Beta-Lactamases</i>	<i>5</i>
▪ <i>Ambler Class C β-Lactamases</i>	<i>25</i>
▪ <i>Laboratory Diagnosis of AmpC β-Lactamases</i>	<i>41</i>
▪ <i>Treatment of AmpC β-Lactamases</i>	<i>68</i>
▪ <i>Prevention and Control</i>	<i>73</i>
<i>Materials and Methods</i>	<i>76</i>
<i>Results</i>	<i>101</i>
<i>Discussion</i>	<i>126</i>
<i>Summary</i>	<i>133</i>
<i>Conclusions and Recommendations</i>	<i>138</i>
<i>References</i>	<i>140</i>
<i>Arabic summary</i>	<i>-</i>

List of Abbreviations

ACC	: Ambler class C
ACT	: AmpC type
Ala	: Alanins residue
AMC	: Amoxicillin/Clavulanate
AmpC	: Ambler class C enzyme
AmpCs	: Ambler class C enzymes
APB	: Aminophenyl boronic acid
BA	: Boronic acid
BIL-1	: Bilal
bla	: Beta-lactamase
bp	: Base pair
BZBTH2B	: Benzo (β) thiophene-2-boronic acid
CA	: Clavulanic acid
CAM	: Cefoxitin agar medium
CAZ	: Ceftazidime
CC-DD	: Cloxacillin combined disk diffusion
CC-DDS	: Cefoxitin-Cloxacillin double-disk synergy
CFU	: Colony forming unit
<i>C. freundii</i>	: <i>Citrobacter freundii</i>
CIAT	: Ceftazidime-imipenem antagonism test
CLA	: Clavulanate
CLOX	: Cloxacillin
CLSI	: Clinical and laboratory standards institute
CMY	: Cephamycins
CTT	: Cefotetan
CTX	: Cefotaxime
CTX-M	: Cefotaximase
DAP	: Diaminopimelic acid
DD	: Disk diffusion
DDS	: Double-disk synergy
DHA	: Dhahran
DMSO	: Dimethyl sulfoxide
DSDT	: Double senergy differential test
EDTA	: Ethylene-diamine-tetra-acetic acid
<i>E. cloacae</i>	: <i>Enterobacter cloacae</i>
<i>E. coli</i>	: <i>Escherichia coli</i>
ESAC	: Extended-spectrum AmpC

ESBL	: Extended-spectrum β -lactamase
ESBLs	: Extended-spectrum β -lactamases
E-test	: Epsilometer test
FOX	: Cefoxitin
FOX-CTX	: Cefoxitin-cefotaxime
GES	: Guiana extended-spectrum β -lactamase
Glu	: Glucine residue
HPLC	: High-performance liquid chromatography
IEF	: Isoelectric focusing
IMI	: Imipenem hydrolyzing β -lactamase
IPM	: Imipenem
IMP	: Inner membrane protein
<i>K. pneumoniae</i>	: <i>Klebsiella pneumoniae</i>
KPC	: <i>Klebsiella pneumoniae</i> carbapenemase
LAT	: Latamoxef
LTCFs	: Long-term care facilities
LysR	: Lysine residue
M3D	: Modified three dimensional test
MBL	: Metallo β -lactamase
MBLs	: Metallo β -lactamases
MCA	: MacConkey agar
MDRO	: Multi-drug resistance organisms
MHA	: Mueller Hinton agar
MIC	: Minimal inhibitory concentration
MICs	: Minimal inhibitory concentrations
MIR-1	: Miriam
MOX	: Moxalactam
MRSA	: Methicillin resistant <i>Staphylococcus aureus</i>
NCCLS	: National committee for clinical laboratory standards
NMC-A	: Non-metallo carbapenemase of class A
OB disk	: Cloxacillin disk
OXA	: Oxacillinase
<i>P. mirabilis</i>	: <i>Proteus mirabilis</i>
PBP	: Penicillin binding protein
PBPs	: Penicillin binding proteins
PC1	: Penicillinases
PCR	: Polymerase chain reaction
pI	: Isoelectric point

PMABL	: Plasmid mediated AmpC β -lactamase
PMABLs	: Plasmid mediated AmpC β -lactamases
SME	: <i>Serratia marcescens</i> enzyme
<i>S. marcescens</i>	: <i>Serratia marcescens</i>
Spp.	: Species
SHV	: Sulfhydryl variable
TAE	: Tris Acetate EDTA
TDET	: Three dimensional extract test
TE	: Tris EDTA
TEM	: Temoneira
UV	: Ultraviolet
VIM	: Verona integron encoded metallo- β -lactamase
Zn⁺⁺	: Zinc

List of Figures

Fig. No.	Title	Page No.
1	Outer wall of Gram-positive and Gram-negative species and detail of porin channels of Gram-negative bacteria. Antimicrobial agents diffuse easily through the loose outer wall of Gram-positive bacteria, but must go through the narrow channels of the Gram-negative species	19
2	β -Lactamase found in bacteria and their classification and synthesis, whether chromosomally or plasmid mediated.	21
3	Scheme of the AmpC induction process.	33
4	Methods designed for detection of AmpC enzymes.	47
5	Modified Three Dimensional Test.	48
6	Tris-EDTA (AmpC) Disk Test	49
7	CAM Assay.	50
8	E-Test. cefotetan/cefotetan with cloxacillin.	51
9	Detection of AmpC β -lactamases using CIAT. Bacterial strains and the respective enzymes are indicated.	52
10	Cefoxitin-Cefotaxime Antagonism Test.	53
11	Results of Cefoxitin-Boronic Acid method.	54
12	Inhibitor Based Test.	57
13	Cloxacillin-Based Double Disk Senergy Test.	58
14	Representative results using the DSDT.	61
15	Growth patterns of the <i>bla</i> _{CMY-1} -allele-positive and negative isolates in the Cephamycin Hodge test.	62

16	Algorithm for scoring the Cica- β -Test.	64
17	Specimen results with the Cica β -Test Strip.	65
18	CC-DDS test, CC-DD test & FOX resistance.	87
19	CIAT.	88
20	Cefoxitin-Cefotaxime Antagonism Test.	89
21	Modified Three-Dimensional Test.	91
22	Modified Three-Dimensional Test.	91
23	DDS test.	92
24	Agarose gel electrophores.	99
25	Results of Cefoxitin (FOX) DD method among all examined isolates.	102
26	Results of different tests among all examined isolates.	103
27	Flow charts for the results of different tests compared to the results of M3D test among M3D-positive isolates.	104
28	Flow charts for the results of different tests compared to the results of M3D test among M3D-negative isolates.	105
29	Results of multiplex-PCR among 40 examined isolates.	106
30	Flow charts for the results of different tests compared to the results of multiplex-PCR among PCR-positive isolates.	107
31	Flow charts for the results of different tests compared to the results of multiplex-PCR among PCR-negative isolates.	108
32	<i>AmpC</i> genes among 13 PCR-positive isolates.	109

List of Tables

Table No.	Title	Page No.
1	Classification schemes for β -lactamases.	8
2	Genetics of β -Lactamases.	15
3	Primar sequences of PMABL genes.	82
4	Components of PCR tube (25 μ l).	96
5	Results of different tests among all examined isolates.	102
6	Results of multiplex-PCR among 40 examined isolates.	106
7	Description of detected genes among 13 PCR-positive isolates.	109
8	PMABLs genes among 13 PCR-positive isolates (Per case).	110
9	Sensitivity, specificity and agreement between FOX disk resistance (DD) and M3D test.	111
10	Sensitivity, specificity and agreement between FOX disk resistance (DD) and multiplex-PCR.	112
11	Sensitivity, specificity and agreement between CC-DD test and M3D test.	113
12	Sensitivity, specificity and agreement between CC-DD test and multiplex-PCR.	114
13	Sensitivity, specificity and agreement between CC-DDS test and M3D test.	115
14	Sensitivity, specificity and agreement between CC-DDS test and multiplex-PCR.	116
15	Sensitivity, specificity and agreement between CIAT and multiplex-PCR.	117

16	Sensitivity, specificity and agreement between FOX-CTX antagonism test and multiplex-PCR.	118
17	Diagnostic performance of different tests for detection of AmpC production.	119
18	Sensitivity, specificity and agreement between ESBL detection and cloxacillin/augmentin synergy test.	120
19	Raw data of samples.	121



Introduction





Aim of the Work





Review of Literature





Materials and Methods





Results





Discussion





Conclusion and Recommendations

