Prevalence of Carbapenem-Hydrolyzing β-Lactamase Gene carrying *Klebsiella pneumoniae* and its Clinical Implication

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Introduction

- *Klebsiella pneumoniae* – The 4th and 5th most common cause of pneumonia and bacteremia in the ICU.
- UsuallyTreated with broad spectrum β-lactam antibiotics.
- Resultant increased resistance to β-lactam antibiotics and extended spectrum β-lactamase
- Drug of choice for resistant infection are Carbapenems, (Imipenem,Meropenem and Ertapenem).

Introduction

- First strain of *Klebsiella pneumoniae* resistant to Carbapenems (KPC) 2001 in North Carolina.
- Now spread to Russia, Central Europe
- KPC resistance has mostly been reported from tertiary care centers.
- Lack of data
  - On prevalence from community hospitals
  - Clinical outcomes

Evolution of Drug Resistance in Klebsiella

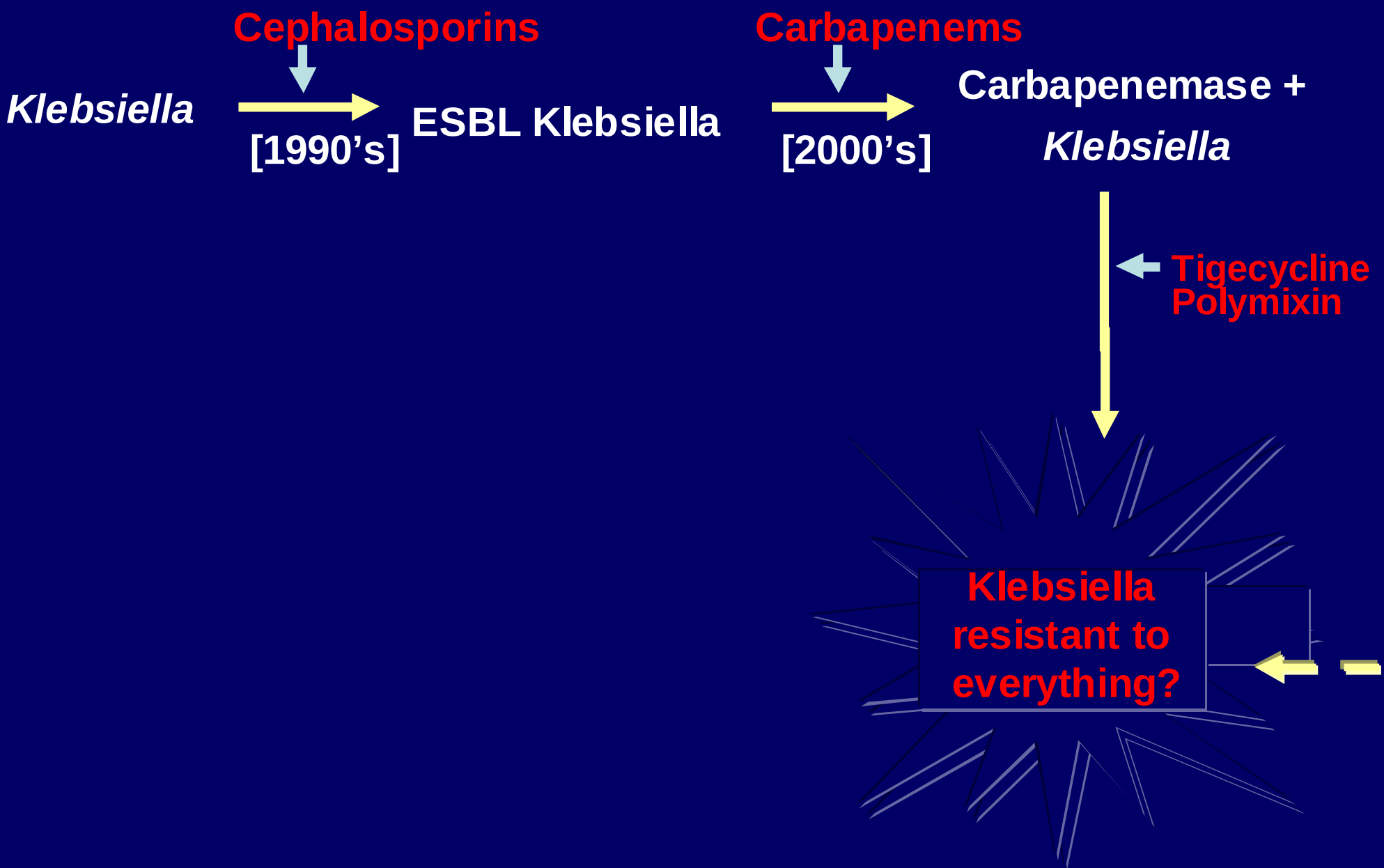
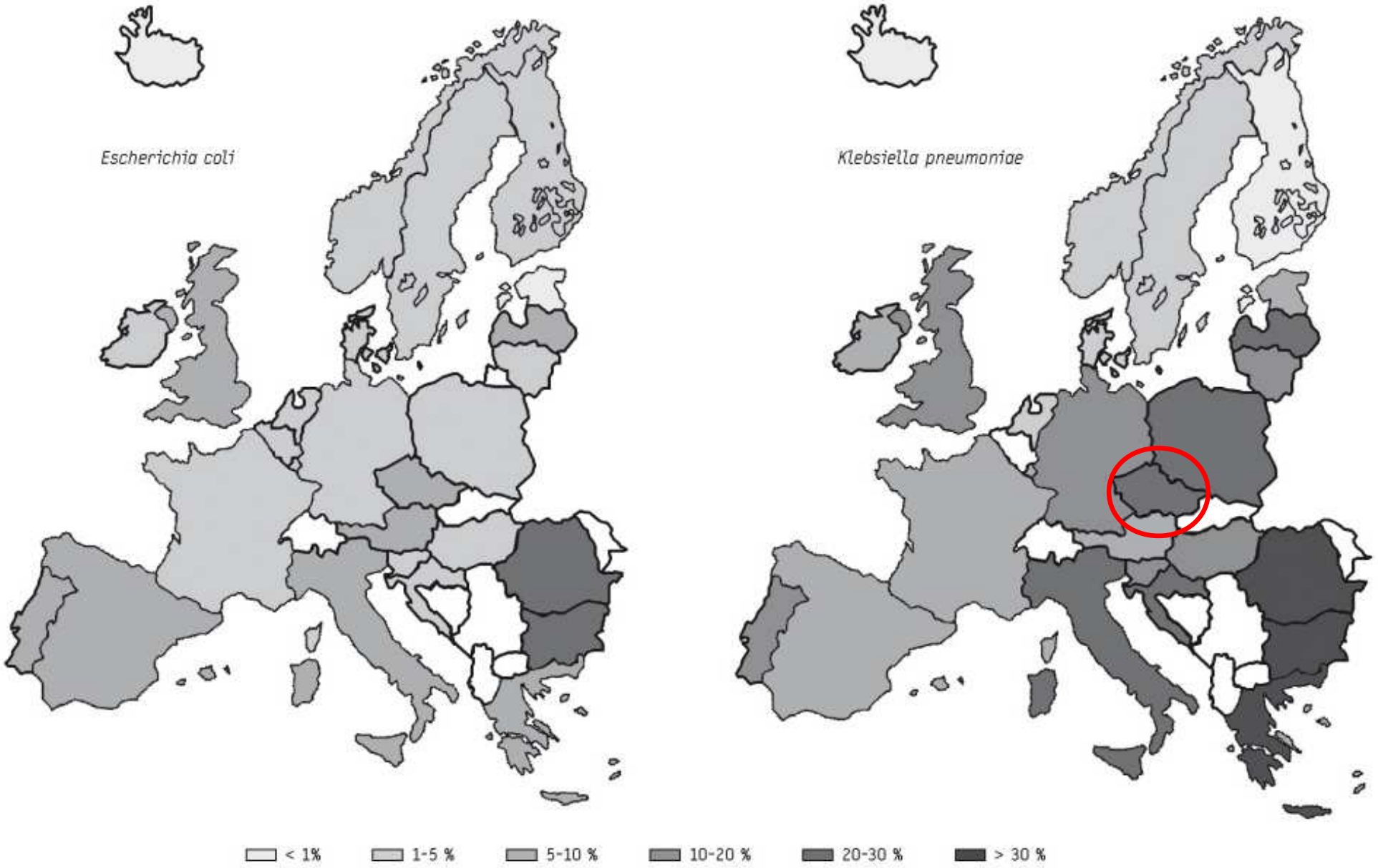


FIGURE 1

Proportion of invasive *Escherichia coli* and *Klebsiella pneumoniae* isolates resistant to third generation cephalosporins in 2006 (EARSS study)



EARRS: European Antibiotic Resistance Surveillance System

Introduction

- Method of testing antibiotics sensitivity- Disk Diffusion method.
- Gold standard to diagnose *Klebsiella pneumoniae* resistant to Carbapenem
  1) Modified Hodge test
  2) PCR for the blaKPC gene

Klebsiella pneumoniae Blood Isolate by Automated Susceptibility

Patient A persistent fever bacteremia being treated with Imipenem

Agent	MIC (mcg/mL)	Interpretation
Amikacin	≥32	R
Ampicillin	≥32	R
Cefazolin	≥32	R
Ceftazidime	≥32	R
Ceftriaxone	≥32	R
Cefepime	≥32	R
Ciprofloxacin	≥4	R
Gentamicin	4	S
Imipenem	4	S
Meropenem	4	S
Piperacillin-Tazobactam	≥128/4	R
Tobramycin	≥16	R
Trimethoprim-Sulfamethoxazole	≥4/76	R
Automated ESBL test:		**negative**

When to Test for Carbapenemase Gene

1.) one or more carbapenem results are susceptible, with MIC or disk diffusion zone diameters that are close to the standard CLSI susceptible breakpoints (see below), and

2.) one or more third-generation cephalosporin results are resistant.

	Standard CLSI susceptible breakpoints		Values suggesting carbapenemase activity*	
	MIC (mcg/mL)	Disk (mm)	MIC (mcg/mL)	Disk (mm)
Ertapenem	≤2	≥19	2	19-21
Imipenem	≤4	≥16	2-4	N/A†
Meropenem	≤4	≥16	2-4	16-21

* Isolates with intermediate or resistant carbapenem results need not be tested for carbapenemase activity.

† N/A, not applicable (poor test performance)

Aim of the study

- Primary Objective –

  To identify the prevalence of *Klebsiella pneumoniae* resistant to carbapenems over a period of two years.

- Secondary Objective –

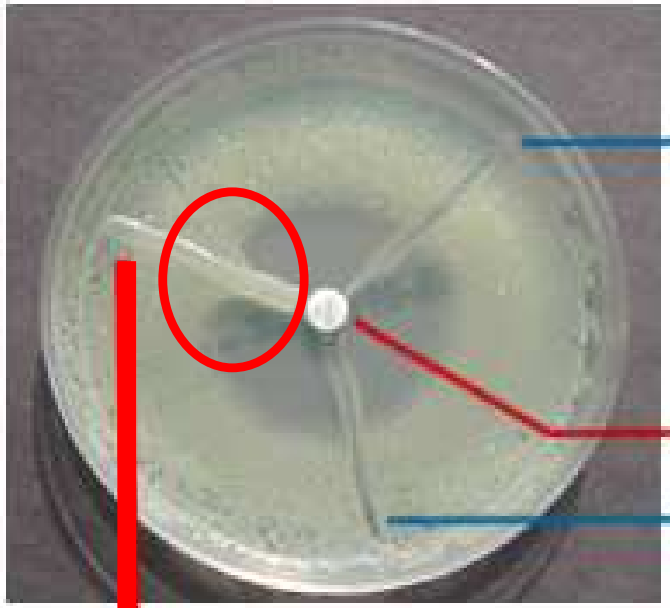
  To identify the clinical implication of treating KPC strain as recommend by disk diffusion method.

Method

1) Hospital IRB approval.
2) Duration of study – 2 years (Oct 1, 2007-Sept 30, 2009).
3) All specimens were identified as *Klebsiella pneumoniae* (KP).
4) All KP were tested for KPC by Modified Hodge test .
5) Chart review was conducted on KPC +ve infected patients for clinical outcomes..

Method

- What is Modified Hodge test



MHT Using MircroBioLogics Quality Control Microorganisms

Method

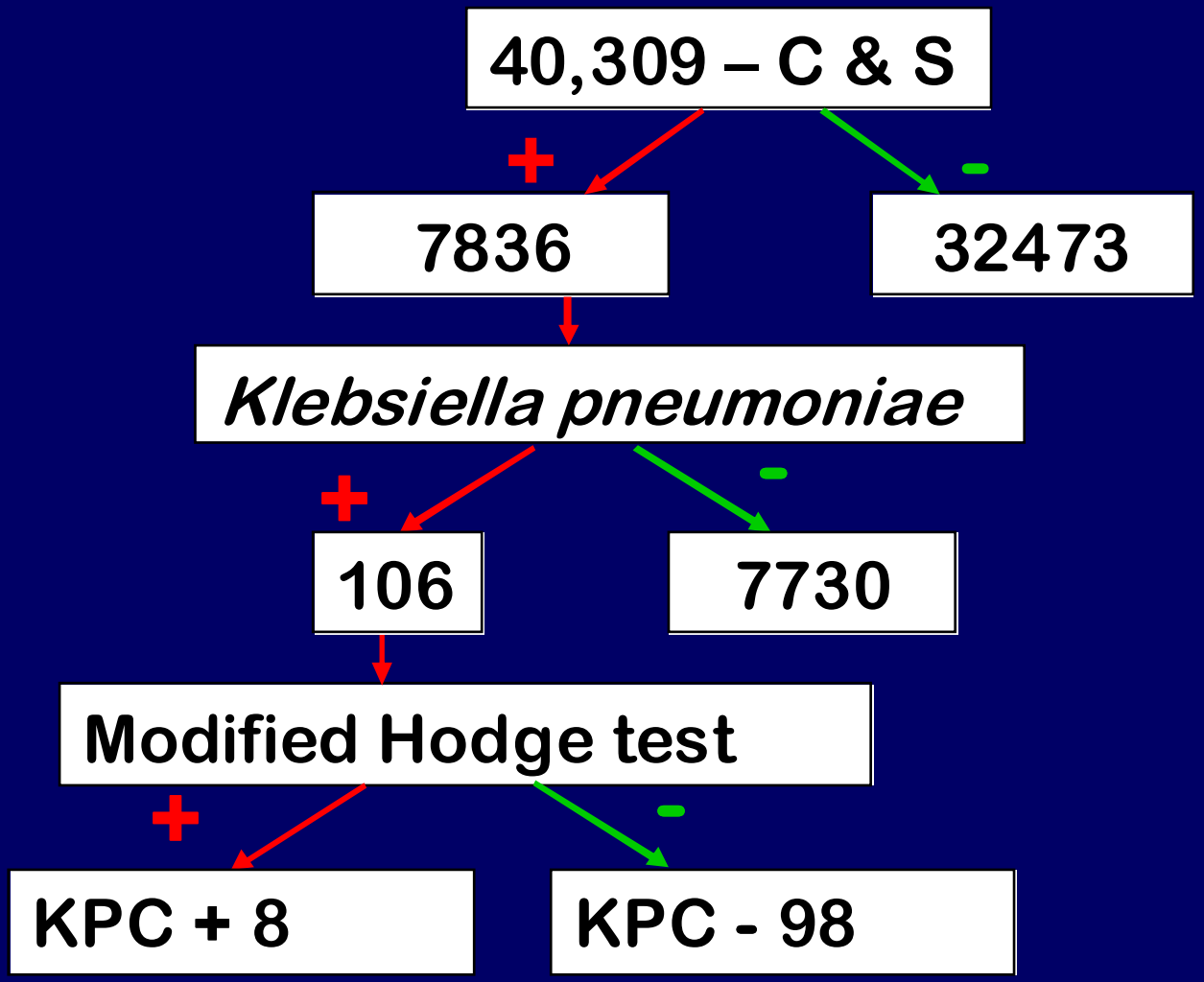
- The prevalence of KPC gene among *Klebsiella pneumoniae*

$$= \frac{\text{Total number of Hodge test positive}}{\text{Number of Klebsiella Pneumonia samples}}$$

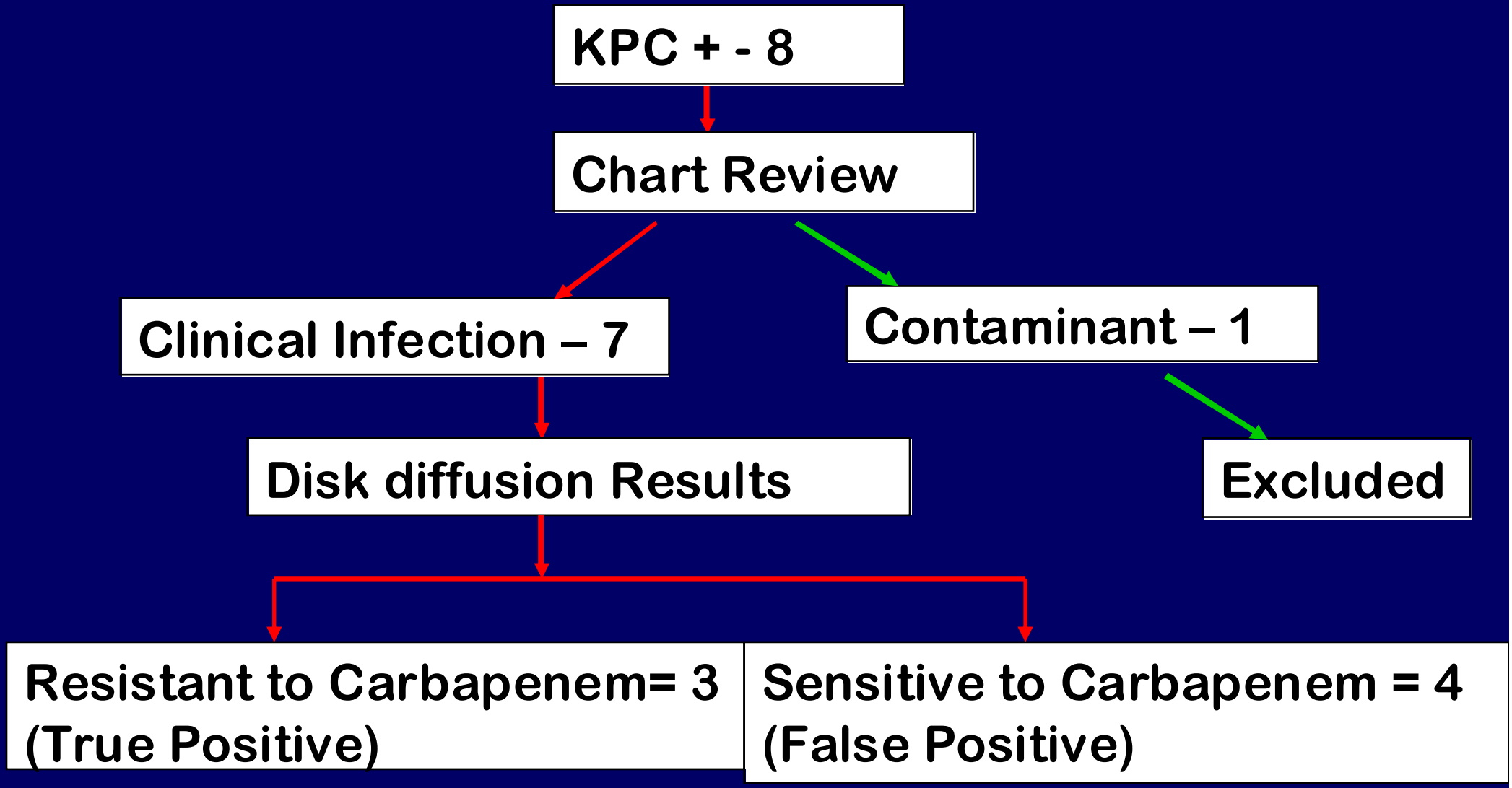
Method

- Mortality due to improper treatment of infection as patient dying due secondary to sepsis or bacteremia .
- Death due to other causes such as MI, PE were excluded.
- Clinical outcomes –
- a) recovered clinically
- b) Death

Results


40,309 – C & S
+
-
7836
32473
Klebsiella pneumoniae
+
-
106
7730
Modified Hodge test
+
-
KPC + 8
KPC - 98

Results


KPC + - 8
Chart Review
Clinical Infection – 7
Contaminant – 1
Disk diffusion Results
Excluded
Resistant to Carbapenem= 3 (True Positive)
Sensitive to Carbapenem = 4 (False Positive)

Results

Resistant to Carbapenem= 3
(True Positive)

Antibiotic changed to Tigecycline and Polymyxin

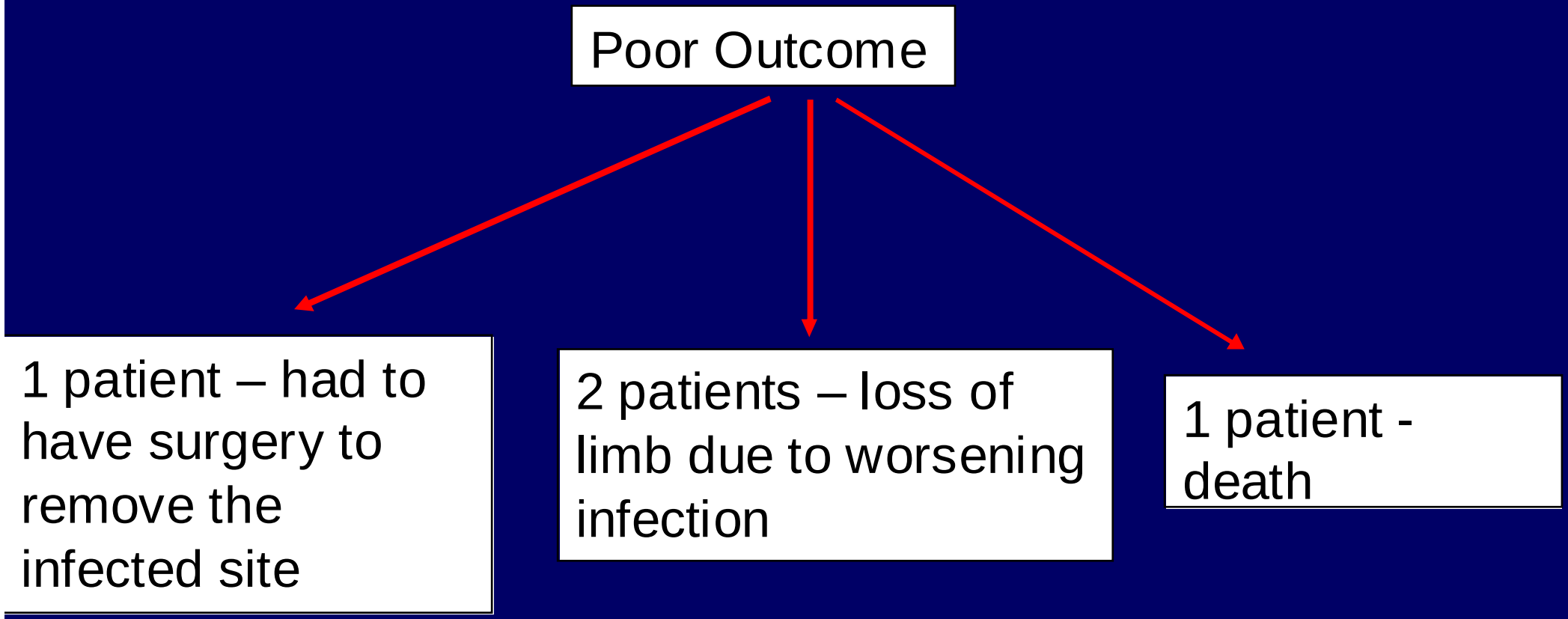
Clinical Improvement

Sensitive to Carbapenem = 4
(False Positive)

Carbapenem Continued

Poor Outcome

Results


Poor Outcome
1 patient – had to have surgery to remove the infected site
2 patients – loss of limb due to worsening infection
1 patient - death

•Results

- Gender M – 2
  F - 8
- Length of stay in the hospital - 16.5±21 days.

  – Antibiotics prior to isolation - Piperacillin/Tazobactam and Vancomycin

- Prevalence of KPC = 7.5%.
- Clinical outcome – 100% morbidity mortality if continued carbapenem

Discussion

- This is the first study showing the prevalence and clinical outcome of KPC in a community hospital.
- KPC – Emerging pathogen – present at Saint Peter's Hospital.
- KPC infection is associated with increased length of stay.

Discussion

- The prevalence of KPC strain is 7.5%.
- Modified Hodge test should be used to identify KPC since the disk diffusion method is not sensitive in detecting KPC.
- Clinical outcomes are poor in patients with KPC strain infection if appropriate changed to the antibiotics are not made.

Conclusion

- Prevalence KPC is 7.5% at Saint Peter's Hospital.
- As a result of this study all *Klebsiella pneumoniae* samples at Saint Peter's hospital are tested for KPC gene using Modified Hodge test.