NATIONAL HEALTH LABORATORY SERVICE

MICROBIAL AETIOLOGY OF COMMUNITY ACQUIRED PNEUMONIA AT A TERTIARY HOSPITAL

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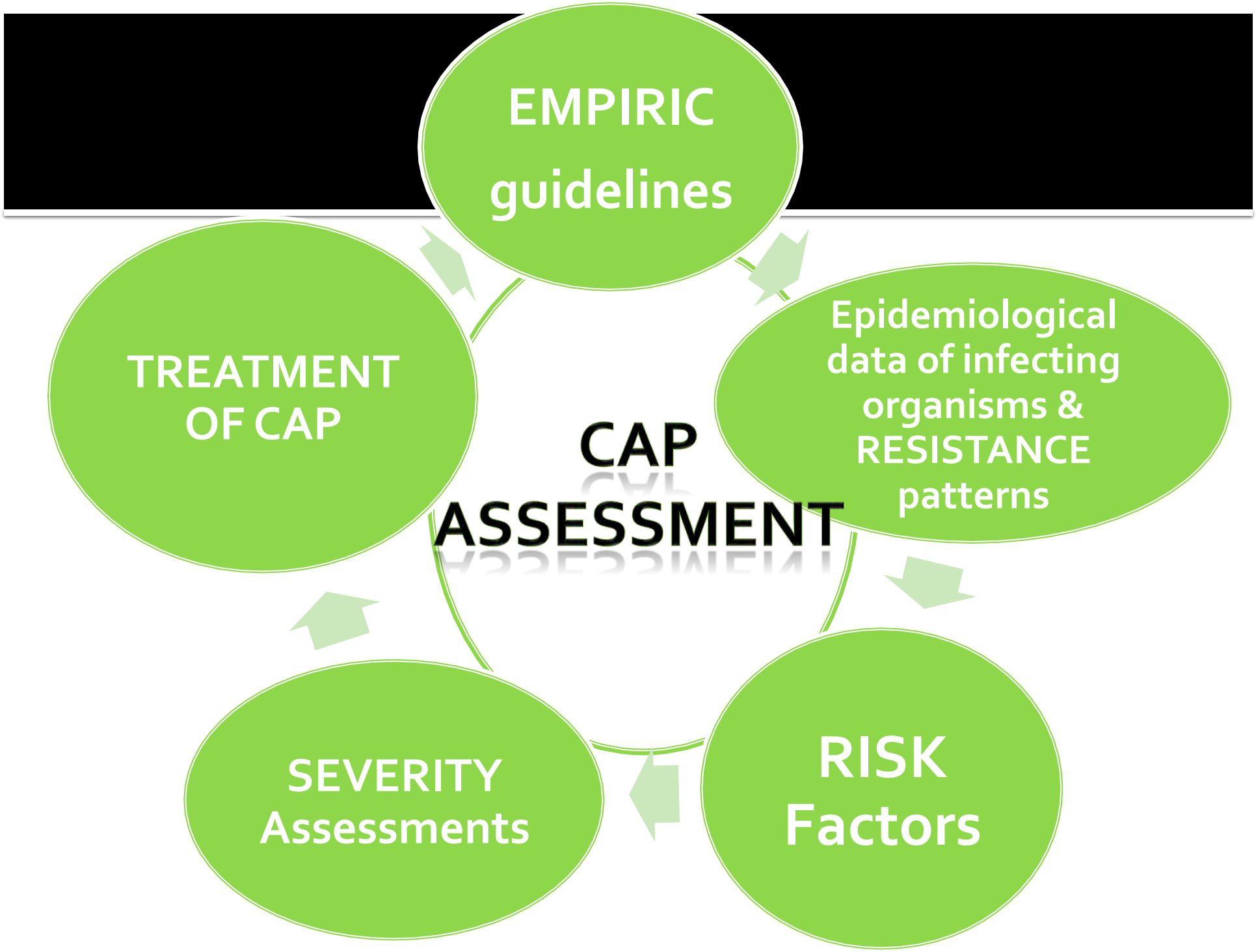
EMPIRIC guidelines
Epidemiological data of infecting organisms & RESISTANCE patterns
RISK Factors
SEVERITY Assessments
TREATMENT OF CAP
CAP ASSESSMENT

Rationale for Study

- Increased mortality in patients with severe CAP & a pathogen-directed therapy is associated with a better outcome in patients with severe disease.
- The main argument against a pathogen directed approach is the lack of sensitivity and specificity of the routine culture based methods currently employed.
- Provide potentially important epidemiologic information.

PrimeStore MTM

- The collection system, PrimeStore MTM, inactivates microbes and maintains RNA stability and preservation compared to other storage and transportation media.
- It is temperature stable and suitable for outbreak surveillance.
- The pathogen specific detection system, PrimeMix, is an all inclusive, one-step PCR reagent mix from point of collection to detection.

Study Objectives & Design

- **Primary aim:** was to describe the microbial etiology of CAP in adults presenting to an urban tertiary-care hospital in Gauteng, South Africa.
- **Secondary aim:** was to ascertain by PCR detection the DNA/ RNA preserved/stabilized in PrimeStore MTM from nasopharyngeal swabs from patients that met the inclusion criteria of the study prior to their first dose of antibiotics.
- **Design:** This was a prospective, observational clinical and microbiological investigational study.
- Acutely ill patients were enrolled as they were admitted to casualty, and thereafter to the infectious diseases ward or ICU.
- Patient enrollment was sequentially begun: June 2010 and completed at the end of November 2010.

Materials & Methods

- 104 patients were screened for the study and 48 patients met the inclusion criteria.
- All adult patients (age ≥ 18 years) with CAP were screened for inclusion in the study.
- Participants signed a consent form and were then further screened for inclusion in the study.
- All patients were assessed by an infectious disease clinician to confirm CURB 65 severity assessment score, as well as the clinical and radiological proven case definition criteria.
- Signs & symptoms of TB was an exclusion criteria.

Microbiological Evaluation

- Sputum for MC&S
- Sputum for PJP IF
- Sputum for AFB and TB C&S
- Blood for bacterial culture
- Blood Urea
- Beta D Glucan assay
- Urine Ag for *Legionella pneumophila S1*
- PCR (PrimeStoreMTM nasopharyngeal swabs)
- Serotyping and antimicrobial susceptibility of significant isolates

Molecular Diagnostics

- The Seeplex RV5 ACE Screening for the detection of adenovirus; influenza A&B; respiratory syncytial virus A&B; metapneumovirus; parainfluenzavirus 1, 2, 3; rhinovirus A/B; coronavirus 229E/NL63; coronavirus OC43/ HKU1 and bocavirus was used (multiplex RT-PCR).

- The second kit was for the same number of nasopharyngeal swabs which were analysed for *Streptococcus pneumoniae, Haemophilus influenzae, Mycoplasma pneumoniae, Chlamydophila pneumoniae, Bordetella pertussis and Legionella pneumophila* called the Seeplex Pneumobacter multiplex PCR kit.

CHARACTERISTICS	NUMBER	PERCENTAGE
Total Patients	48	
Median Age	37	
Male	21	43.7%
Female	27	56.2%
Smoking	5	10.4%
Site of Care		
General Pulmonology Ward	33	68.7%
Intensive Care Unit	15	31.2%
Co-morbidity		
HIV positive	29	60.4%
COPD	5	10.4%
Asthmatic	2	4.1%
Cardiac failure	3	6.2%
Diabetes mellitus	3	6.2%
Alcohol abuse	5	10.4%
Radiologic confirmation		
Consolidation	30	62.5%
Pleural Effusion	7	14.5%
Reticular infiltrate	6	12.5%
Ground Glass appearance	5	10.4%
Significant Laboratory findings		
Beta-D-Glucan>500	5	10.5%
Pneumocystis Jerovicii IF	1	2%
Negative Urine Leg. Antigen	48	100%

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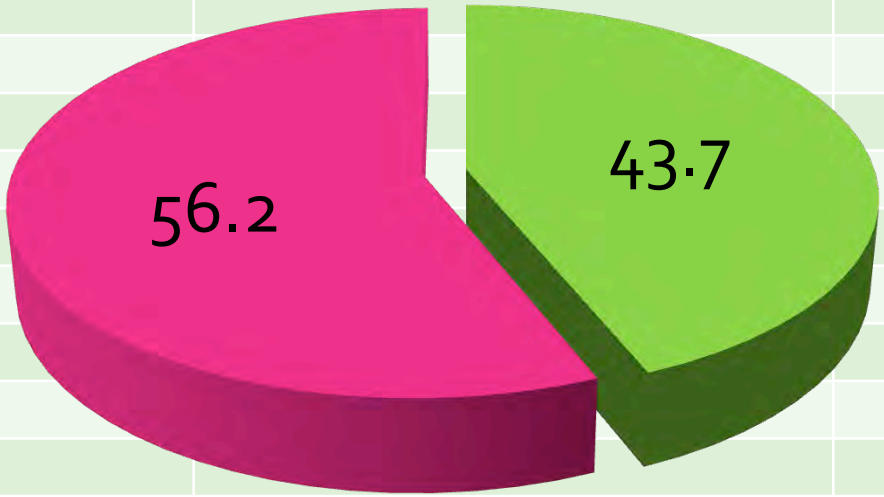

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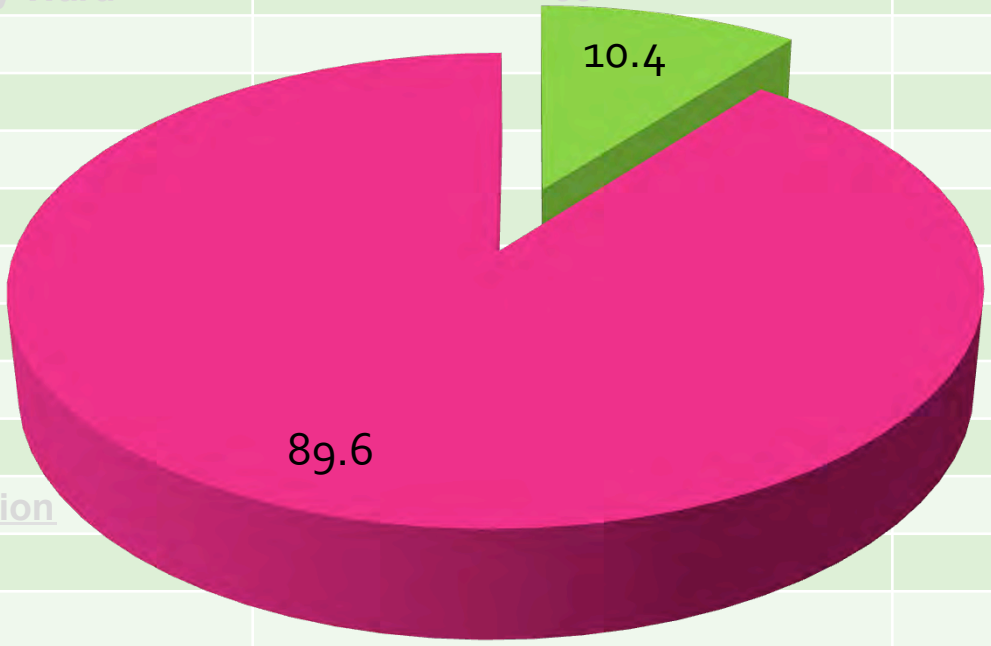

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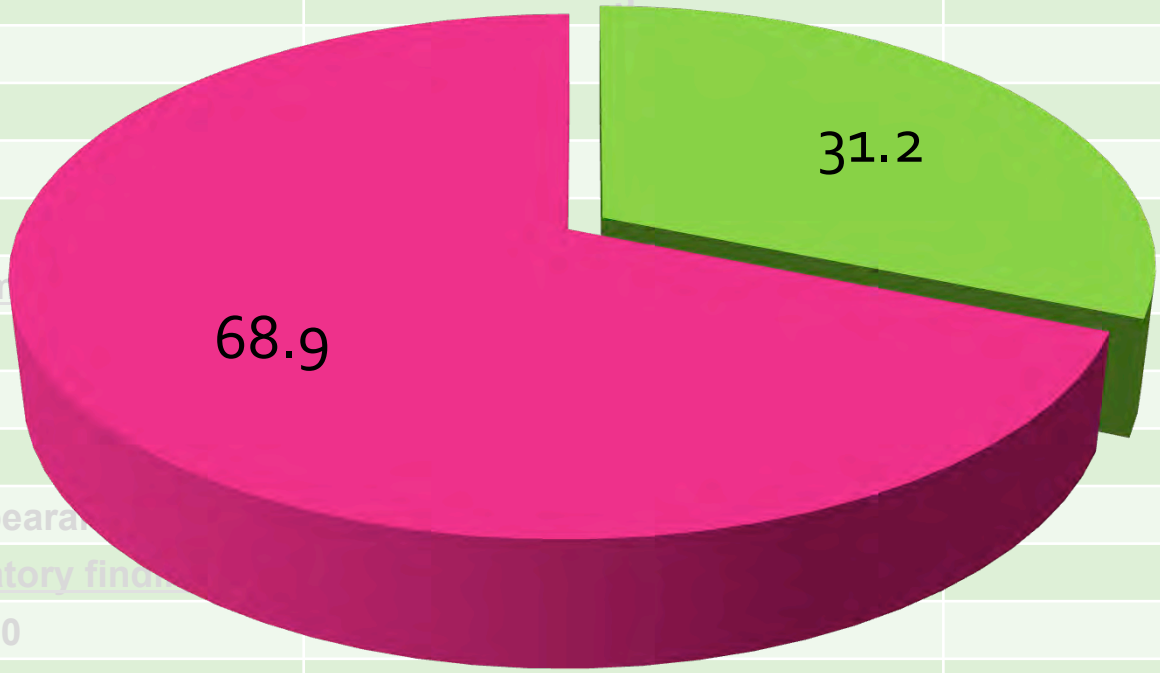

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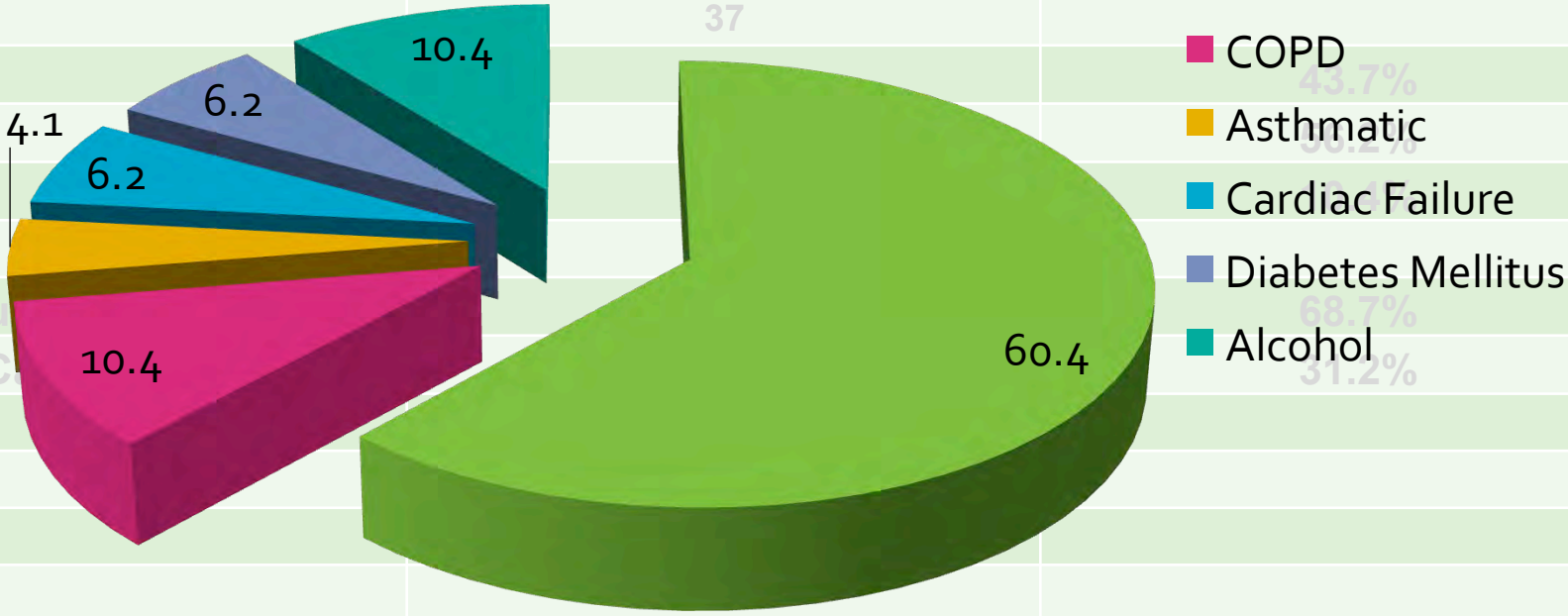

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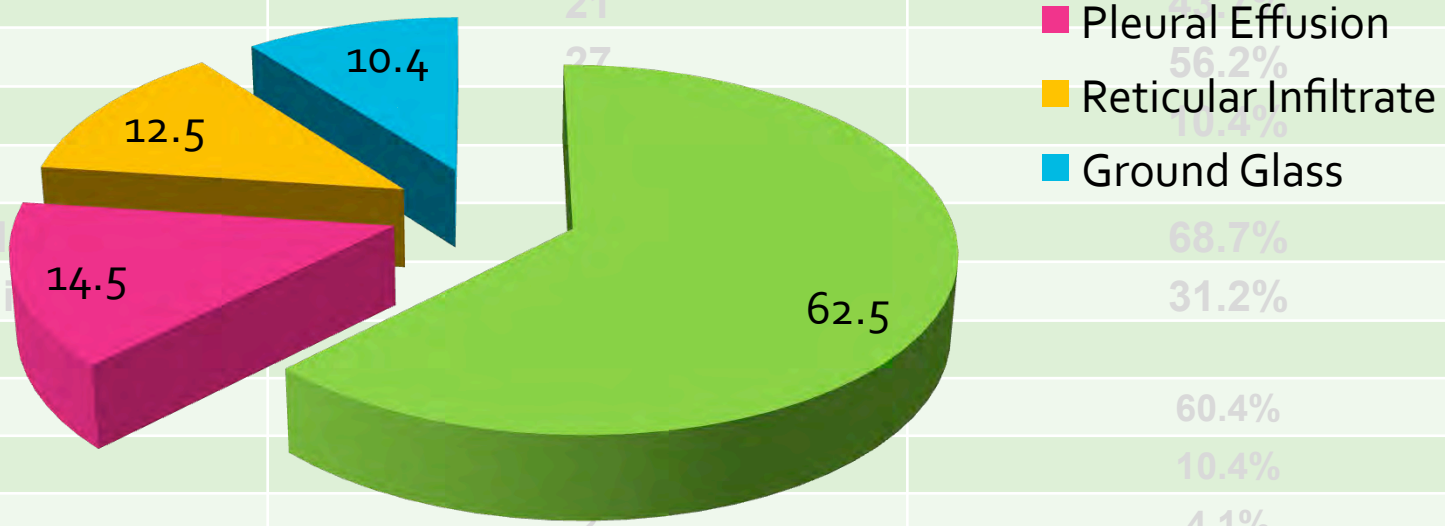

Results

PROBABLE BACTERIAL AETIOLOGY	PROBABLE MICROBIAL AETIOLOGY (PCR)	DEFINITE MICROBIAL AETIOLOGY
7 (14.5%)	38 (79.1%)	8 (16.7%)

Microbial Aetiology

S.pneumoniae	*H. Influenzae*	MPV Rhinovirus A/B Coronavirus	Influenza A/B
41.7%	29.2%	16.7%	14.6%

PATHOGEN	NUMBER OF PATIENTS WITH POSITIVE FINDINGS	POSITIVE BLOOD CULTURE	POSITIVE SPUTUM CULTURE	POSITIVE PCR NASOPHARYNGEAL SECRETION SAMPLE (PNEUMOBACTER)	POSITIVE PCR NASOPHARYNGEAL SECRETION SAMPLE (RV5)
M. pneumoniae	1	0	0	1	-
L. pneumophila	0	0	0	0	-
S. pneumoniae	23	8	4	20	-
H. influenzae	14	0	3	14	-
B. pertussis	0	0	0	0	-
C. pneumoniae	0	0	0	0	-
Adenovirus	3	-	-	-	3
Influenza A	6	-	-	-	6
Influenza B	1	-	-	-	1
Respiratory syncytial virus A/B	1	-	-	-	1
Metapneumovirus	8	-	-	-	8 *
Parainfluenza1,2,3	1	-	-	-	1
Rhinovirus A/B	8	-	-	-	8 *
Coronavirus 229E/ NL63/ OC43/HKU1	8	-	-	-	8 *
Bocavirus	1	-	-	-	1
S. pneumoniae and ***H. influenzae*** co-infection	8	3**	2***	8	3****
Negative PCR and negative cultures but BDG>500	5 *****	-	-	-	-

S. pneumoniae Serotypes&Pen MIC

SEROTYPE	N=8	ICU	PENICILLIN MIC
9N	1	1	0.38ug/ml
8	1	-	0.008ug/ml
1	1	1	0.38ug/ml
19A	3	3	0.38ug/ml (all 3)
4	1	1	0.5ug/ml
MISSING ISOLATE	1	1	0.5ug/ml

Aetiology in ICU

AETIOLOGY	%	n = 15
S. pneumoniae	47%	7
H. influenzae	27%	4
MPV/HRV/COV	20%	3
Influenza A/B	20%	3
Pneumocystis Jerovicii pneumonia	0.6%	1
Adenovirus	0.6%	1

CURB65 VS ICU ADMISSIONS

CURB SCORE	N=15
CURB 65 ≤ 2	3
CURB 65 = 3	6
CURB 65 = 4	5
CURB 65 = 5	1

Major Findings

- The total microbial yield was significantly elevated than those reported previously .
- The yield improved with the implementation of nasopharyngeal secretion samples that were then stored in PrimestoreMTM for further analysis by PCR for respiratory virus and bacterial and atypical pathogens
- S. *pneumoniae* was the leading causative agent.
- Despite respiratory viruses being found at a high frequency as part of a mixed infection, usually in combination with *S. pneumoniae* and *H. influenzae;* they still attributed for 9 out of 48 clinically and radiologically confirmed CAP cases (19%).

Of Note

- Our study's aetiological spectrum was different from the previous studies in South Africa.
- One possibility is that those studies included patients with co-morbid pathology known to be associated with invasive Gram negative disease.
- Another possibility is that the method of diagnosis makes a difference.
- Our study population does differ from some other studies in that the majority of our cases were HIV positive (60.4%)
- The recognition of the aetiological pathogens of CAP should alert the clinician to the need of appropriate empiric antibiotic therapy.

Limitations

- Due to the unavailability of a routine viral diagnostic laboratory, traditional viral culture methods were not undertaken in our patients. It would have been valuable to be able to compare those yields with the PCR method that was undertaken.
- Urine test for *Streptococcus pneumoniae* antigen detection was not performed.
- Quantification of the amount of target present with a defined threshold value that correlates with infection rather than colonization may be necessary to provide confidence in molecular results.

Conclusion

- Perhaps the greatest shift in our understanding of the impact of pneumonia on the host has been the continuing excess mortality for more than 2 years after surviving an episode of CAP.
- The switch from treating CAP as an acute illness to one that has long-term health implications is a profound shift in our current treatment paradigms.
- Guidelines should support the recommendation from this study that the cornerstone of treatment of patients with severe CAP is based on the knowledge of etiological agents, which increases the urgency for more sensitive diagnostic tests such as PCR.