

# “Race Against Resistance: The Looming Threat Of Superbugs And Humanity’s Struggle!!” A Descriptive Study Of The Clinico-Radiological Characteristics And Treatment Outcomes Among Patients With Respiratory Isolates Of Carbapenem Resistant Acinetobacter Baumannii Acquired In The Community And In The Hospital.

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## **Abstract:**

Antibiotics have historically been hailed as monumental advances in medicine, yet the emerging challenge of antibiotic resistance represents a new pinnacle of concern. The emergence of multidrug-resistant (mdr) and extensively drug-resistant (edr) strains of acinetobacter baumannii has significantly complicated the treatment landscape for infections attributed to this pathogen, effectively turning a once dependable therapeutic ally into a daunting foe. The notable proficiency of a. Baumannii to develop resistance to antibiotics has markedly limited treatment options. The advent of carbapenem-resistant acinetobacter baumannii (crab) further aggravates this scenario, rendering carbapenems, previously cornerstone agents in treatment regimens, as nearly defunct. Initially confined to hospital environments, crab isolates are now emerging in community settings, amplifying the global public health challenge of escalating antibiotic resistance. In response to this escalating threat, we propose a cross-sectional descriptive study to be conducted at a tertiary care hospital from march 2022 to december 2023. This study aims to elucidate the clinical and radiographic presentations, as well as treatment outcomes, of patients with respiratory isolates of crab acquired both within the community and hospital settings. Our objective is to shed light on the rising prevalence of crab, identified by the world health organization as a leading superbug on the global priority list of antibiotic-resistant pathogens. This investigation seeks to pave the way for more effective treatment strategies and underscore the critical role of antimicrobial stewardship programs

**Background:** carbapenem-resistant acinetobacter baumannii (crab) a serious nosocomial pathogen leading the who global priority list of antibiotic resistant bacteria for which new antibiotics are urgently needed. Although most antibiotic-resistant bacteria first appeared in hospitals, drug-resistant strains are becoming increasingly prevalent in the community due to inappropriate use of antibiotics, ineffective infection control and hygiene practices with increase in antibiotic use in food industry. Difficulties in treating crab infections stem from a formidable resistance profile that leaves only a few antibiotics with questionable efficacy. The global impact of antibiotic resistance is potentially devastating, threatening to set back progress against certain infectious diseases to the pre-antibiotic era. We hereby propose the first ever case study which compares the diverse clinico-radiological manifestations and treatment outcomes in patients with respiratory isolates of crab from the community and the hospital, thereby drawing attention to the growing emergence of crab now in the community which highlights the importance of urgent infection control measures and strict antimicrobial stewardship programs.

**Materials and methods:** this is a retrospective cross sectional analytical study conducted at pondicherry institute of medical sciences between march 2022 and december 2023. 68 patients who presented with respiratory secretions of carbapenem resistant acinetobacter baumannii were recruited for the study. Patients were divided into hospital acquired and community acquired pneumonia based on standard definitions. Clinical characteristics, radiographic patterns of presentation such as ground glass opacities, unilobar consolidation, multilobar consolidation and treatment outcomes were analyzed. We subdivided treatment regimens into 5 subdomains such as patients who received single antibiotic or combination antibiotics combining colistin with

carbapenem or tetracycline or ceftazidime avibactam or colistin with carbapenem and tetracycline and results were interpreted.

**Results:** of the 68 patients analyzed, 61 patients belonged to the hospital acquired crab pneumonia category and 7 patients belonged to community acquired crab pneumonia.

In the hap group, 72% of patients had immunosuppression with overlapping co-morbidities, with 22.9% presenting structural lung disease. Recent hospital admission within the last year was noted in 44.26%, and 29.5% were current smokers. Ground-glass opacity was the most common radiographic finding in 93.44%, with multilobar and unilobar consolidation in 47.54% and 42.62%, respectively. Treatment outcomes showed recovery rate of 85% in the colistin-tetracycline combination outperforming the colistin-carbapenem pair at 54.5%, indicating superior efficacy of the former. The average hospital stay was 22.62 days, with an overall recovery rate of 57.37%.

In the cap group, all patients exhibited immunosuppression and concurrent comorbidities, highlighting increased susceptibility to multidrug-resistant organisms from community among immunosuppressed individuals. A significant 71.42% had structural lung disease, and 14.28% were smokers. Ground-glass opacities and multilobar consolidation were the primary radiographic findings in 71.42%. Treatment approaches showed patients managed with either colistin-tetracycline or colistin-carbapenem combinations achieved a 100% recovery rate with uneventful follow-ups. The average hospital stay was 11.86 days, with an 85.71% recovery rate.

Comparative analysis of treatment outcomes across various antibiotic regimens, utilizing binary logistic regression, revealed an odds ratio (or) of 3.22. This indicates a significantly higher likelihood of recovery, approximately 3.22 times greater, with the colistin-tetracycline combination compared to regimens excluding this therapy. Recovery odds were notably reduced with alternative antibiotic combinations, suggesting their less favorable impact on patient recovery outcomes.

**Conclusion:** in summary, antimicrobial resistance represents a complex and pressing global issue. Our retrospective case analysis reveals that immunosuppression significantly influences mortality rates, with ground-glass opacities and multilobar consolidation emerging as the primary radiographic features. Consequently, we advocate for the adoption of a dual-antibiotic therapy combining colistin and tetracycline. This regimen has shown superior efficacy in improving treatment outcomes, including reduced mortality and enhanced recovery rates, in patients afflicted with crab pneumonia, compared to monotherapy approaches

**Key word:** antibiotic resistance, crab, cap, hap, antimicrobial stewardship, strict infection control.

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## I. Introduction

Carbapenem-resistant *Acinetobacter baumannii* (CRAB) a serious nosocomial pathogen leading the WHO Global priority list of Antibiotic Resistant bacteria for which new antibiotics are urgently needed <sup>(1)</sup>. Although most antibiotic-resistant bacteria first appeared in hospitals, drug-resistant strains are becoming increasingly prevalent in the community due to inappropriate use of antibiotics, ineffective infection control and hygiene practices with increase in antibiotic use in food industry <sup>(2)</sup>. Difficulties in treating CRAB infections stem from a formidable resistance profile that leaves only a few antibiotics with questionable efficacy. The global impact of antibiotic resistance is potentially devastating, threatening to set back progress against certain infectious diseases to the pre-antibiotic era <sup>(3)</sup>. We hereby propose the first ever case study which compares the diverse clinico-radiological manifestations and treatment outcomes in patients with respiratory isolates of CRAB from the community and the hospital, thereby drawing attention to the growing emergence of CRAB now in the community which highlights the importance of urgent infection control measures and strict antimicrobial stewardship programs.

## II. Material And Methods

This retrospective Cross sectional descriptive study was carried out on patients presenting to our Institute with Respiratory Isolates of Carbapenem Resistant *Acinetobacter baumannii* between March 2022 and December 2023. A total 68 eligible patients were recruited.

**Study Design:** A Retrospective Cross sectional descriptive study.

**Study Location:** The study was conducted at a 720 bedded tertiary hospital and teaching Institute, Pondicherry Institute of Medical Sciences, Puducherry, India.

**Study Duration:** March 2022 and December 2023.

**Sample size:** 68 patients.

**Sample size calculation:** This is a retrospective analysis of case records from medical database conducted at our Institute between March 2022 and December 2023 which included 68 eligible subjects.

**Subjects & selection method:** The study group comprised of all patients who presented to our Institute with Respiratory isolates of Carbapenem Resistant Acinetobacter baumannii and were grouped into Community acquired or Hospital acquired pneumonia based on inclusion and exclusion criteria.

**Inclusion criteria:**

Patients who presented to our Institute with Respiratory isolates of Carbapenem Resistant Acinetobacter baumannii.

**Exclusion criteria:**

At the time of study, any patients with

- ✓ Multiple organisms isolated from sputum at the time of study.
- ✓ Pregnancy.
- ✓ Malignancy.
- ✓ Children < 12 years of age

**Procedure methodology**

**Ethics:**

The present study was carried out after clearance from ethical committee (rc/2024/07) the authorized researchers were granted the right to extract data from our hospital database with waiver of consent owing to the retrospective nature of the study.

**Data collection:**

The study was conducted at a 720 bedded tertiary care hospital and teaching institute. It is a hospital based retrospective descriptive study design conducted between march 2022 to december 2023. The study group included patients presenting to our hospital or diagnosed during course of stay at hospital with respiratory isolates of carbapenem resistant acinetobacter baumannii. Patients with multiple organisms isolated from respiratory secretions at the time of study was excluded from the study group. The demographic and clinical data were retrieved from the medical database retrospectively and entered in a case report form. The demographic variables included age, gender and indication for admission. Clinical variables included predominant respiratory symptom at the time of isolation, comorbid medical illness, underlying structural lung disease, addictions, immune status, previous hospital admission, radiographic pattern, antibiotic resistance pattern, antibiotic used during hospital stay, average duration of hospital stay and treatment outcome. The radiological patterns were subdivided into 3 groups: ground glass opacity, unilobar consolidation and multilobar consolidation. We categorized the treatment regimens into 5 subdomains: patients who received single antibiotic or combination antibiotics combining colistin with carbapenem or tetracycline or ceftazidime avibactam or colistin with carbapenem and tetracycline. Data obtained was statistically analyzed and the results were interpreted.

**Statistical analysis:**

Data was entered in microsoft excel spreadsheet and descriptive data were analyzed using spss software (version 23.0). Descriptive statistics were used. Mann whitney u test was used for comparing the continuous variables such as age, duration of hospital stay and spo2 levels. Chi square test was used to compare between the categorical data. Binary logistic regression was used to assess the association between the treatment outcome and administration of combination antibiotics. For all statistical tests, a p- value of < 0.05 is to be considered statistically significant.

### **III. Results**

A total of 68 eligible patients with respiratory isolates of CRAB were included in our study. Of the 68 patients, 7 patients were community acquired isolates and 61 patients were hospital acquired isolated (Table 1).

In the **HAP group**, the average age of presentation was 53.42 years with male predominance. 72 % of patients were immunosuppressed with overlapping co-morbidities. 22.9% of patients had underlying structural lung disease. 44.26% of patients had recent hospital admission within the past 1 year and 29.5% of patients were current smokers. The predominant radiographic abnormality was Ground glass opacity in 93.44% followed by Multilobar consolidation in 47.54% and Unilobar consolidation in 42.62% of patients. Among the treatment regimens followed, 14.75% of patients received single antibiotic and 85.24% of patients received combination antibiotic regimens. The recovery rate in single antibiotic usage was 11.1% compared to 66.17% in combination antibiotics. Of the combination antibiotic regimens used, Colistin with Tetracycline showed a recovery rate of 85% followed by Colistin with Carbapenem with a recovery rate of 54.5% suggesting Combination antibiotics of Colistin with Tetracycline had better treatment efficacy. The average duration of hospital stay was 22.62 days with a recovery rate of 57.37%.

In the **CAP group**, the average age of presentation was 59.71 years with male predominance. All patients were immunosuppressed with overlapping co-morbidities suggesting that immunocompromised patients are more

prone to acquire multidrug resistant organisms from the community. 71.42% of patients had underlying structural lung disease. 14.28% of patients were current smokers. The predominant radiographic abnormalities were Ground glass opacities and multilobar consolidation in 71.42% of patients. Among the treatment regimens followed, single antibiotic was used in 16.66% of patients and dual antibiotics in 83.33% of patients with Community acquired isolates. Better treatment outcome was observed in patients receiving combination antibiotics. Among the combination antibiotics, patients who received Colistin with Tetracycline or Carbapenem showed equal treatment recovery rate of 100% with uneventful follow up. The average duration of hospital stay was 11.86 days with recovery rate of 85.71%.

**Table 2: comparison of antibiotic used with treatment outcomes in hap vs cap crab pneumonia**

	Group	Treatment outcome			Total
			Recovered	Mortality	
Combination antibiotic colistin + carbapenem	Hap	Frequency	18	15	33
		%	54.50%	45.50%	100.00%
	Cap	Frequency	2	0	2
		%	100.00%	0.00%	100.00%
Colistin + tetracycline	Hap	Frequency	17	3	20
		%	85.00%	15.00%	100.00%
	Cap	Frequency	2	0	2
		%	100.00%	0.00%	100.00%
Colistin + ceftazidime avibactam	Hap	Frequency	2	2	4
		%	50.00%	50.00%	100.00%
	Cap	Frequency	1	0	1
		%	100.00%	0.00%	100.00%
Colistin + carbapenem + tetracycline	Hap	Frequency	3	3	6
		%	50.00%	50.00%	100.00%
Single antibiotic (colistin)	Hap	Frequency	1	8	9
		%	11.10%	88.90%	100.00%
	Cap	Frequency	0	1	1
		%	0.00%	100.00%	100.00%

On comparing the final treatment outcomes among different antibiotic regimens, Binary Logistic regression analysis showed us an odds ratio (OR) of 3.22 which suggests that there is a notable increase in the odds of recovery associated with the combination of colistin and tetracycline which suggests that this combination therapy have approximately 3.22 times higher odds of recovery compared to those not receiving the treatment. The odds of recovery are significantly lower in the groups receiving other antibiotic combinations. This suggests a potential negative impact on recovery associated with these combinations.

**Table 3: binary logistic regression analysis**

		B	Std error	Exp(b) Odds ratio	Wald	Sig.
Step 1 <sup>a</sup>	Colistin + carbapenem	-.067	1.004	0.94	0.00	0.95
	Colistin + tetracycline	54.131	11463.079	3.22	0.00	1.00
	Colistin + cephalosporin	-.997	1.389	0.37	0.52	0.47
	Colistin + carbapenem + tetracycline	-54.390	11463.079	0.00	0.00	1.00
	Single antibiotic	-36.552	8466.126	0.00	0.00	1.00
	Group (type of pneumonia)	-18.772	5802.172	0.00	0.00	1.00
Constant		56.321	13140.430	2.88	0.00	1.00

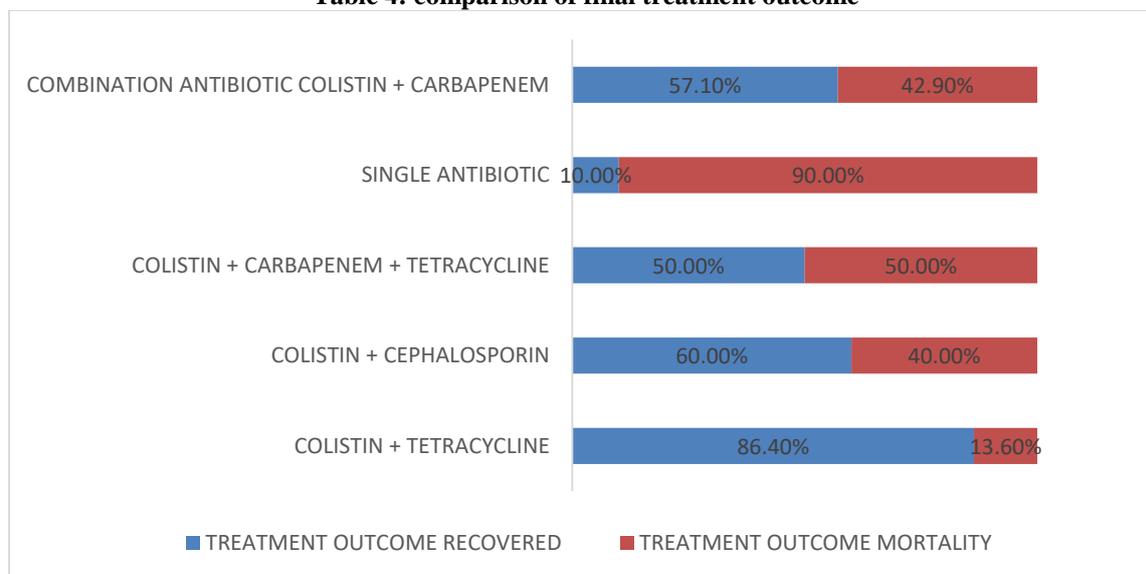
**Colistin + carbapenem:** The odds ratio (Exp(B)) is 0.94 with a p-value of 0.95. This suggests a non-significant decrease (6% reduction) in the odds of recovery for this combination compared to the constant (reference category).

**Colistin + tetracycline:** The odds ratio is 3.22 with a p-value of 1.00. This indicates a significant increase in the odds of recovery for this combination. However, the very high p-value might indicate some issues or uncertainty in this estimate.

**Colistin + cephalosporin:** The odds ratio is 0.37 with a p-value of 0.47. This suggests a significant decrease (63% reduction) in the odds of recovery for this combination compared to the constant.

**Colistin + carbapenem + tetracycline:** The odds ratio is 0.00 with a p-value of 1.00. This suggests a non-significant effect on recovery.

**Table 4: comparison of final treatment outcome**



#### IV. Discussion

*Acinetobacter baumannii* are serious nosocomial pathogens known for its potential to cause multidrug resistant infections through its inherent antibiotic resistance profile as described by Nordmann et al <sup>(5)</sup>. Carbapenems are considered as effective antibiotics for Gram negative pathogens but the rise of Carbapenem resistance in *Acinetobacter baumannii* is one step closer to the global challenge of extreme drug resistance in gram negative organisms <sup>(6)</sup>. Selecting an appropriate antibiotic regimen in managing drug resistant *Acinetobacter* infections has been always challenging <sup>(7)</sup>.

On navigating through the available treatment options in CRAB, recent IDSA Guidelines suggested that combination antibiotics are preferred over single agents <sup>(8)</sup>. Colistin, known for its potent activity against Enterobacteriales is warranted to be used in combination with another potent antibiotic <sup>(10)</sup>. One such combination adverts the use of Tetracyclines with Colistin. Si-Ho Kim et al. concluded in his study that Tetracycline containing regimens were independently associated with lower 30-day mortality compared to other regimens and suggested that tetracyclines might be an effective treatment option for CRAB infections, especially when coupled with other antibiotics. Specifically, the tetracycline-colistin combination had a greater 30-day survival rate than either drug alone <sup>(11,12)</sup>.

Through our retrospective study, we evaluated the clinico-radiological patterns of presentation and the treatment outcomes of patients with CRAB pneumonia acquired from the Hospital and from the Community. Our study demonstrated that

- ✓ Immunosuppression is an important factor contributing to the disease as 72% of patients in HAP group and 100% of patients in the CAP group were immunocompromised.
- ✓ The predominant radiographic pattern of presentation were Ground glass opacities followed by Multilobar consolidation in both the groups.
- ✓ Combination antibiotics showed better treatment efficacy compared to single antibiotic.
- ✓ Among the combination antibiotics, Colistin with Tetracycline showed better treatment outcome in the HAP group and Colistin with Tetracycline or Carbapenem showed good treatment outcome in the CAP group.

#### V. Conclusion

In conclusion, antimicrobial resistance is a global multifaceted problem, a question of serious concern. Through our retrospective case study, we conclude that Immunosuppression is an important factor contributing to disease mortality with Ground glass opacities and Multilobar consolidation as predominant radiographic presentation. Hence, we recommend use of dual antibiotics with Colistin and Tetracycline as an efficient treatment regimen which demonstrated better treatment outcome over single antibiotic use in terms of mortality and recovery rate in patients with CRAB pneumonia. Our study also highlights the increasing incidence of multidrug-

resistant organisms in the community, an alarming issue which warrants strict infection control measures and antimicrobial stewardship programs.

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