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Research Article

Clinico-Bacteriological Profile and Antibiotic Resistance Pattern in Patients with Acute Exacerbation of COPD in a Tertiary Care Hospital

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A B S T R A C T

Background: Chronic Obstructive Pulmonary Disease (COPD) is a leading respiratory illness characterised by frequent infectious exacerbations that increase morbidity and mortality.

Aim: To identify bacterial pathogens responsible for acute exacerbations of COPD (AECOPD) and analyse antibiotic resistance patterns and prescribing trends.

Methods: A prospective observational study was conducted among 93 AECOPD patients in Kerala. Sputum samples were processed for microbial culture and antimicrobial susceptibility testing using CLSI guidelines. Demographic and prescription data were statistically analysed.

Results: Males comprised 75.3% of participants with a mean age of 64.5 years. Klebsiella pneumoniae (42%) was the predominant isolate, followed by Streptococcus pneumoniae and Pseudomonas aeruginosa. Gram-negative pathogens exhibited marked resistance to cephalosporins, aminoglycosides, and β-lactams. Clarithromycin and cefoperazone–sulbactam were most frequently prescribed empirically. Post-culture adjustments improved clinical outcomes in resistant infections.

Conclusion: Gram-negative bacteria dominate AECOPD aetiology in Kerala, showing extensive resistance. Rationalised antibiotic use and culture-guided therapy are vital to control emerging resistance.

Keywords: COPD, acute exacerbation, bacteriological profile, antibiotic resistance, prescription pattern.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a major global health burden, contributing significantly to chronic morbidity, mortality, and healthcare utilisation. This also has heavy economic burdens, with 90% in the middle-income countries and low-income countries.[1] While age-standardised mortality rates have declined in some high-income regions, absolute numbers of cases, deaths, and disability-adjusted life years (DALYs) remain high worldwide due to ageing populations and persistent exposure to risk factors such as tobacco smoking, biomass fuel, and air pollution.[2] However, in India, COPD prevalence is especially concerning, with high estimates among both smokers and non-smokers and substantial regional heterogeneity. The non-smokers also express an increased prevalence by 7% upon exposure to biomass and air pollution.[3] Chronic obstructive pulmonary disease (COPD) is a major global health challenge and a leading cause of morbidity and mortality worldwide. It is a progressive respiratory disorder characterised by persistent airflow limitation, abnormal inflammatory responses, and structural remodelling of the airways and lung parenchyma.[4] The condition develops primarily due to long-term exposure to harmful particles and gases such as cigarette smoke, biomass fuel, and occupational pollutants.[5] Traditionally regarded as a non-communicable disease, COPD is increasingly recognised to have a communicable dimension because infectious agents—particularly bacteria and viruses—play a critical role in triggering acute exacerbations.[6] These exacerbations not only accelerate disease progression but also contribute significantly to hospitalisations, health-care costs, and mortality.[7] Understanding the pathophysiological mechanisms and the role of communicable factors in COPD is essential for effective prevention, clinical management, and public health interventions.[8] The aetiology of AECOPD is multifactorial. Respiratory tract infections are recognised as the predominant cause, with bacterial infections accounting for 50–70% of cases.[9]

A major challenge in the management of AECOPD is the rising prevalence of antimicrobial resistance (AMR) among respiratory pathogens. Indiscriminate use of antibiotics, self-medication, incomplete treatment courses, and inadequate infection control measures have accelerated the development of resistance.[10] Resistance to aminopenicillins, macrolides, cephalosporins, and fluoroquinolones has been widely reported in respiratory isolates across India and other countries.[11] The emergence of extended-spectrum beta-lactamase (ESBL)-producing *Klebsiella pneumoniae* and multidrug-resistant *Pseudomonas aeruginosa* further complicates treatment, often necessitating the use of carbapenems and other reserve drugs.[12] This creates not only therapeutic dilemmas for clinicians but also increases healthcare costs and worsens patient outcomes.

In the Indian context, COPD represents a particularly pressing health issue. With an estimated prevalence of 4–10% among adults over 40 years, India accounts for nearly one-third of the global COPD burden.[13] Risk factors are widespread, including a high prevalence of smoking, widespread use of biomass fuels in rural households, vehicular and industrial pollution in urban areas, and occupational exposures in industries such as mining and construction.[14] Kerala, the state where this study was conducted, mirrors these national trends. While literacy and healthcare accessibility are relatively better compared to other Indian states, COPD remains highly prevalent due to continued tobacco use, occupational hazards, and an ageing population.

Despite the high prevalence of COPD and the clinical importance of exacerbations, there remains a relative lack of region-specific data on the bacteriological spectrum and resistance patterns of pathogens associated with AECOPD in Kerala. Most existing studies have been conducted in North India, and the bacterial ecology often varies across regions due to differences in risk factors, antibiotic prescribing practices, and environmental exposures. Local surveillance studies are therefore critical for developing evidence-based treatment strategies and hospital-specific antibiotic policies.

Materials and Methods

Study design & setting: A prospective observational study was conducted after ethical approval (Certificate No. NCP/IEC/46/01/2024) from the Institutional Ethics Committee.

Sample size calculation

The sample size is calculated using the formula:

$$n = \frac{4pq}{d^2}$$

The expected proportion (p) was adjusted to 37% based on the existing literature. The value of q was derived from the expected proportion and was calculated to be 63%. The precision (d) was adjusted to 10%. Hence, the calculation was as follows:

$$n = \frac{4 \times 37 \times 63}{10^2} = 93$$

The number of patients required for this prospective observational study was determined to be 93 persons in number.[15]

Inclusion/Exclusion Criteria

Major inclusion criteria comprised patients aged >40 years diagnosed with AECOPD. The diagnosis was done as per GOLD criteria. These patients must

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express high sputum volume and purulence with dyspnoea. However, patients affected with bronchiectasis,tuberculosis, lung cancer, or immunocompromised states must be excluded.

Form preparation

An informed consent form in the local language (Malayalam) was prepared to enrol the patient into the study. The patient was also provided with a patient information sheet describing the study's nature. Furthermore, the patient data form was prepared to include the demographic data, vitals (SpO_2, temperature, WBC count, erythrocyte sedimentation rate, C-reactive protein), microbiological profile on sensitivity, and antibiotic treatment regimens.

Translation process

The questionnaire was translated to Malayalam using standard translation protocols. The content of the questionnaire was reviewed for local interpretations, and necessary changes were made after consulting with instrument authors. The instructions and items were translated into Malayalam by the language translator. The questionnaire was back-translated into English, and any discrepancies presented were reconciled by the content expert. The question was face-validated by subject experts.

Data analysis

Descriptive statistics were used to summarise demographic, clinical, microbiological, and resistance data using a data analysis and statistical software (Jamovi 2.5.3). Microsoft Excel was also employed to produce certain graphical illustrations of obtained results.

Results

Demographic distribution

A total of 93 patients with AECOPD were enrolled in this study. The mean age of the study population was calculated to be 64.5±9.2 years. The demographic distribution, clinical characteristics, bacteriological profiles, and antibiotic resistance patterns are described below.

Age was not a significant factor ($p>0.05$) contributing to the onset of COPD. However, there was a linear relationship between age and COPD with excellent linearity ($R^2=0.9144$).

The smoking was a critical factor for AECOPD, with 60% (n=56) of patients being smokers. However, the pack years were less than 5.9 years for more than half of the smoking population (n=30; 53.57%).

Clinical data

Out of the total study population (n=93), most of the patients exhibited no major comorbidity along with AECOPD (n=39; 41.3%). Hypertension was the major comorbidity associated with the AECOPD (n=35; 37.63%). Dyspnoea was the most common symptom since all the study population experienced the symptom (n=93; 100%). Wheezing was the least common symptom within the study population because only half the population expressed the experience (n=51; 55%). The clinical data of the study population are shown in table 2.

Table 1.Demographic characteristics of AECOPD patients.

Study Characteristic	Population	Proportion (%)
Gender		
Male	70	75.27
Female	23	24.73
Age		
Age group 40–50	15	16.1
Age group 51–60	28	30.1
Age group 61–70	32	34.4
Age group 71–80	18	19.3

Table 2.Clinical features of AECOPD patients

Study Characteristic	Population	Proportion (%)
Clinical symptoms		
Dyspnea	93	100
Cough	84	90.32
Purulent sputum	65	70
Wheezing	51	55

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Morbidity		
Diabetes mellitus	12	12.9
Hypertension	35	37.63
Dyslipidemia	7	7.52
Others	11	11.82

Bacteriological profiling

Interestingly, no single patient was affected with a multi-pathogenic infection. Gram-negative bacteria were the causative microbes responsible for COPD, affecting more than two-thirds of the study population (n=80; 86.02%).

Pneumoniae strains were the most commonly affecting bacterial strains in COPD. *Streptococcus pneumoniae* was the only gram-positive bacteria affecting more than 10% of the study population (n=13; 13.98%). *Klebsiella pneumoniae* was the gram-negative organism affecting the study population.

The highly incident bacterial species in the study population, *Klebsiella pneumoniae,* was resistant to different drugs in many patients. On the other hand, the most sensitive bacterial species were the *Enterobacter spp.*, which were sensitive to 2 of 3 combination therapies and 7 of 9 monotherapies. Interestingly, *Escherichia coli* expressed either high resistance or high sensitivity to the selected drugs.

Penicillin was the chief drug category to which this bacterial strain was highly resistant. Cephalosporins and aminoglycosides were other bacterial-resistant antibiotic drug classes. It is important to note that amikacin was a common drug which was found highly resistant in COPD patients, irrespective of causative microbial organisms. Some drugs, like ceftriaxone and ciprofloxacin, revealed a mild resistance in selected microorganisms. Gentamicin also expressed moderate resistance to gram-negative bacterial species except *E. coli*. In terms of drug classes, cephalosporins exhibited resistance in every microorganism under Figure 1. Aminoglycosides were considered the second most resistant drug class in gram-negative bacteria except *E. coli* and *Enterobacter spp.*, which expressed complete sensitivity.

In combination therapies, piperacillin and tazobactam expressed mild to moderate resistance in selected microorganisms except *E. coli* and *Enterobacter sps*. Cefaperazone and sulbactam combination therapy exhibited mild resistance in two gram-negative bacterial species (*K. pneumoniae:* 8.34%, n=3 of 36; *Acinetobacter baumannii:* 18.19%, n=2 of 11).

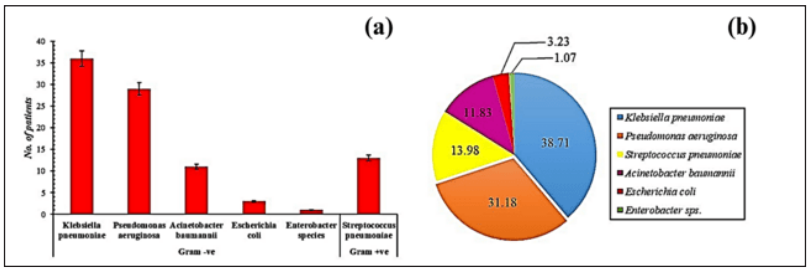

Figure 1.Graphical illustration representing Bacteriological profile of study population (n=93).

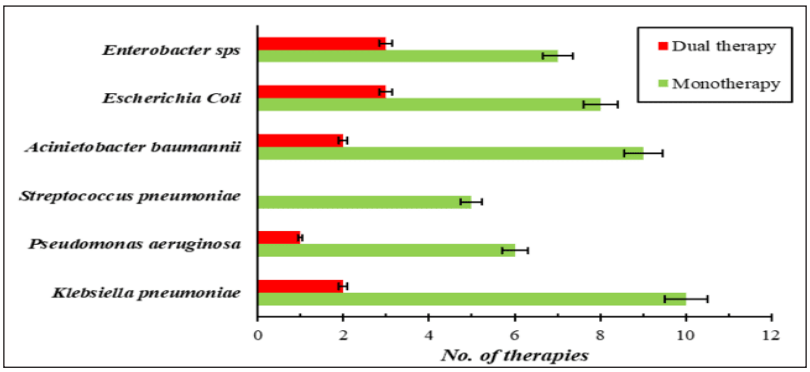

Figure 2.Graphical illustration representing sensitivity to different therapies against different microorganisms.

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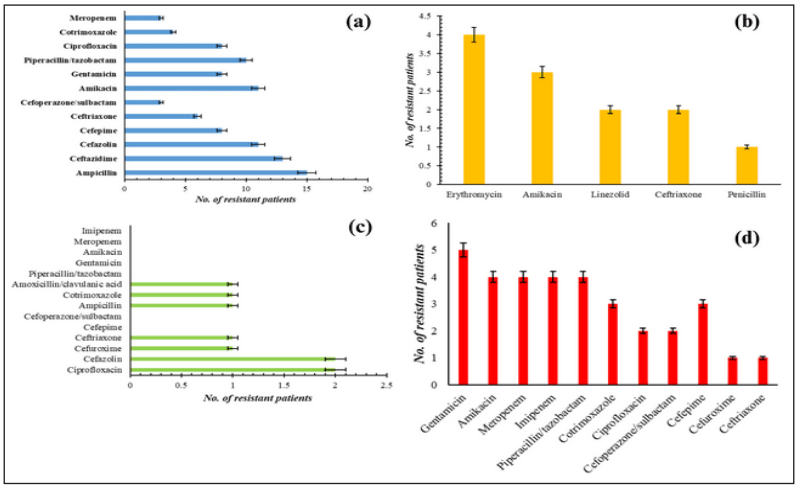

Figure 3 .Graphical representation of antibiotic resistance in patients affected with (a) *Klebisella pneumoniae* (b) *Streptococcus pneumoniae* (c) *Pseudomonas aeruginosa* (d) *Acinetobacter baumannii*

Prescribing patterns in AECOPD

Clarithromycin (n=40; 43.01%) was the commonly prescribed monotherapy for COPD. The most commonly prescribed combination therapy was cefoperazone and sulbactam (n=38; 40.86%). Ampicillin was the least common drug prescribed for COPD, prescribed to only 1 patient of the total study population, contributing 1.07%.

Nebulised formoterol + budesonide was the non-antibiotic medication used in the treatment of COPD widely (n=77; 82.79%). Nebulisers were widely used for the study population in which two combination drugs (formoterol & budesonide and levosalbutamol & ipratropium bromide) and one single drug (glycopyrrolate) were employed.

The most common change in prescription pattern was observed for *Acinetobacter baumanii*. The dual therapy of Tazobactam & Piperacillin was changed to Ciprofloxacin. The other changes in prescription therapy are tabulated in table 4.

Table 3.Prescribing patterns of antibiotics in geriatric patients affected with COPD.

Antibiotics	Patients	Proportion (%)
Clarithromycin	40	43.01
Cefoperazone +sulbactam	38	40.86
Tazobactam + piperacillin	32	34.40
Ciprofloxacin	20	21.50
Gentamicin	18	19.35
Meropenem	16	17.20
Amikacin	16	17.20
Ceftriaxone + sulbactam	11	11.82
Linezolid	8	8.60
Cefepime + tazobactam	5	5.37
Azithromycin	5	5.37
Cefixime + clavulanic acid	3	3.22
Cefotaxime + clavulanic acid	3	3.22
Ceftazidime+ avibactam	3	3.22
Amoxicillin + clavulanic acid	2	2.15
Levofloxacin	2	2.15
Ampicillin	1	1.07

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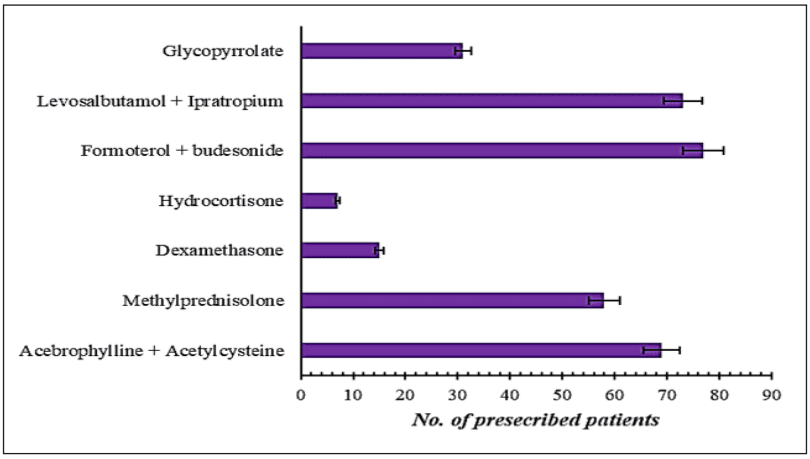

Figure 4.Prescription patterns of adjuvant therapies for geriatric patients affected with COPD.

Table 4.Prescription pattern trends after microbial culture test in geriatric COPD patients.

Organism	Prescribed antibiotic		No. of Patients
	Before culture test	After culture test	
Klebsiella pneumoniae	Cefoperazone + Sulbactam, gentamicin	Meropenem	1
	Cefoperazone + sulbactam, Gentamicin	Ampicillin	1
Pseudomonas aeruginosa	Amikacin	Tazobactam + piperacillin	1
	Linezolid Ceftazidime	Gentamicin, amikacin	1
	Meropenem, Ceftazidime	Amikacin	1
	Gentamicin Amikacin	Piperacillin + tazobactam	1
E. coli	Ceftriaxone + sulbactam	Gentamicin, Piperacillin + tazobactam	1
Acinetobacter baumanii	Tazobactam + piperacillin	Ciprofloxacin	4

Discussion

The men have a higher prevalence of COPD than women at a global level. This is due to the higher smoking rate of men than women.[16,17] However, the women are under-represented in prevalence, emphasising the need for better representation and awareness of females in COPD. In contradiction to *Sopriano et al.*, prevalence comparison between men and women is misleading since there is a lesser population of women than men in many research studies.[18] Hormonal response and smaller airways to smoke are major factors leading to higher incidence and prevalence of COPD in women.[19] Age is a crucial factor for an increase in the incidence and prevalence of COPD. The onset and prevalence. Spirometry is a feasible technique for diagnosis of COPD, which is age-independent in nature.[20,21] The main reason for the age-dependent increase in the onset of COPD is due to frailty. Frailty is a state of risk leading to detrimental effects on health and wellbeing.[22]

Smoking is a significant social habit which not only causes but also worsens the stage of COPD. The intensity of smoking is calculated in pack years. The persons with long pack years tend to experience more episodes of exacerbations than non-smokers, ultimately extending the prevalence of COPD.[23] Because the onset of COPD is high in even youngsters and tends to escalate with higher intensity non-linearly with an increase in age under smoking.[24] The non-smokers affected with COPD (40%) staying equivalent to smokers with COPD is due to passive smoking. This is a condition in which the smoke, fine dust and hazardous airborne chemicals are inhaled involuntarily during the process of respiration.[25] The risk exposure eventually damages the airway and pulmonary

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lobes through exacerbation-induced inflammation. Passive smoking also induces false spirometric test results. This is a crucial factor for the lack of linearity of increase in COPD for the patients beyond 70 years of age observed in this prospective study.[20,26]

Hypertension and diabetes mellitus were the most common comorbidity associated with COPD. Inflammatory markers increase significantly and cause COPD-based symptoms like laryngitis and dyspnoea.[27] Many subjects were affected with COPD even without a single comorbidity. However, this feature is extremely rare since the patients affected with COPD tend to develop some form of comorbidity. Adequate physical activity can reduce the development of a comorbidity along with COPD. Because it reduces the score on the frailty scale, thereby, minimising the risk of stress.[22,28]

Dyspnoea is the primary clinical symptom of COPD, which is caused by constriction of the airway. This leads to insufficient oxygen to the brain causing exacerbations and a dyspnoeic state.[29] Eventually, there is a need for categorising the grade of dyspnoea through proper clinical evaluation to rationalise the treatment of the symptom and, subsequently, COPD.[30] Fever is also a significant symptom other than cough. This is caused as a result of an immunocompromised state and inflammation in the lungs.[31] Bacteria are the main cause of COPD, acting as a communicable disease through purulent sputum. Exacerbated COPD with bacterial infections cause spread from one individual to another severely based on the pathogenicity of the microorganism.[32]

Gram-negative bacteria were the chief type of bacteria involved in COPD. The higher virulence and invasiveness under COPD of Gram-negative bacteria than Gram-positive bacteria lie in the type of molecules employed for the auto-inducer mechanism of quorum sensing. Because the gram negative bacteria use smaller molecules than Gram -positive bacterial species.[33] *Klebsiella pneumoniae* is generally the widely present microorganism in COPD patients. The virulence and pathogenicity of the microbe lie in the binding with mucin subtypes like MUC5.[34] *Streptococcus pneumoniae* is the only gram -positive bacterium observed in COPD due to its colonising ability in the respiratory tract, utilising the immunologically weakened state of the respiratory tract.[35] By the transformation into a capsule, it evades the mild immunological responses and prevents phagocytosis by immunological cells. It also prevents getting removed through mucus discharge by the mechanism of electrostatic repulsion.[36]

Pneumoniae strains were resistant to different classes of antibiotics due to the mechanism of acquiring genetic alteration to secrete enzymes responsible for breaking down the complex structure of antibiotics to simpler, non-therapeutic chemical structures. Certain enzymes, like β-lactamase, are rendering the standard antibiotics of choice (e.g., penicillin, cephalosporin) devoid of therapeutic activity.[37] This enzyme location in the microorganism distinguishes the gram-negative and gram-positive ones. The presence of the β-lactamase enzyme in the periplasmic membrane allows high concentrations within the microorganism. This makes it more virulent than the gram-positive pneumonia strains. As a result, there is a remarkable difference between *Klebsiella pneumoniae* and S*treptococcus pneumoniae.*[38] *Escherichia coli* revealed an interesting all-or-nothing phenomenon compared to other microbes. This Gram-negative bacterium employs horizontal gene transfer, similar to *Klebsiella pneumoniae,* secreting enzymes like β-lactamase.[39] This phenomenon is achieved mainly by induction of arabinose transporters. As a result, it either develops complete resistance against a drug or drug class.[40]

The prescription pattern for COPD patients was well-aligned with recent literature. Cephalosporins and macrolides were the most frequently prescribed antibiotics.[41] Clarithromycin is a widely prescribed antibiotic in COPD and AECOPD conditions, even in geriatrics.[42] This is chiefly due to the multitherapeutic purpose of this macrolide. The anti-inflammatory effect of this drug reduces the exacerbation of COPD, while antibiotic activity prevents the growth of a broad spectrum of microbes.[43] Levofloxacin expresses promising antibacterial efficacy with bacteriological activity higher than clarithromycin.[44] Nevertheless, it is not prescribed in COPD of old-age patients. This is due to a shorter exacerbation-free state of levofloxacin than clarithromycin.[45] Besides, the ADR of levofloxacin includes aortic aneurysm, peripheral neuropathy and Achilles tendonitis, which is a high risk in geriatric patients.[46]

Conclusion

This study underscores the shifting bacteriological landscape of AECOPD, with gram-negative organisms, particularly *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*, emerging as dominant pathogens and exhibiting worrisome resistance to commonly prescribed antibiotics. The high prevalence of resistance to aminoglycosides and cephalosporins, coupled with the selective sensitivity to reserve drugs, highlights an urgent need for culture-guided therapy rather than empirical prescribing. Beyond their immediate clinical implications, these findings serve as a wake-up call to strengthen antibiotic stewardship, implement routine microbiological surveillance, and tailor region-specific treatment guidelines. Unless addressed proactively, the dual burden of COPD and antibiotic resistance threatens to transform routine exacerbations into life-threatening crises, especially in vulnerable populations. By bridging clinical vigilance with rational antibiotic use, healthcare systems can not only improve

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patient outcomes but also slow the inexorable march of antimicrobial resistance.

Author Contribution

R P T: Methodology; Resources; V S N: Data analysis; Review & Editing-Manuscript preparation; Visualization. M C R: Conceptualization; Data Analysis. S G: Writing original draft-Manuscript preparation; Data Curation. K V: Conceptualization; Methodology; Data Interpretation.

Conflict of Interest: None

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