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Original Article

Compliance of Aerosol Therapy with Evidence-based Guideline and Cost Incurred in Adult Critically-ill Patients: A Prospective Observational Study

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ABSTRACT

OBJECTIVE: Aerosol therapy is widely used in intensive care units (ICUs) for managing respiratory conditions. However, non-adherence to evidence-based guidelines can compromise outcomes and increase healthcare costs. This study evaluated the compliance of aerosol therapy with the "Indian Guidelines on Nebulization Therapy" and the cost incurred in critically ill patients.

MATERIAL AND METHODS: A prospective observational study was conducted in 307 adult patients across the ICUs of a tertiary care hospital during a six-month study period. Analysis was performed using the chi-square test and the Wilcoxon rank-sum test in RStudio (version 4-4.3, 2024). Multivariate logistic regression identified independent predictors of compliance.

RESULTS: Of the 307 ICU patients analyzed, 64.5% were male, with an average age of 57±16 years. Jet nebulizers were used in 91.5% of cases. Bronchodilators (47.13%) and corticosteroids (35%) were widely used classes of drugs. Compliance of drug therapy with evidence-based guidelines varied significantly by duration of ICU stay ($P = 0.0062$) and by ICU category ($P = 0.0005$). Drug compliance was higher in critical care and neurology ICUs [odds ratio (OR): 6.500, $P = 0.0001$; OR: 4.574, $P = 0.005$]. Administration compliance was significantly associated with the diagnosis category ($P = 0.00186$) and was higher among patients with non-respiratory diagnoses (OR: 4.96, $P = 0.0068$). Adherence to guidelines for drug therapy significantly lowered costs ($P = 0.0103$).

CONCLUSION: Targeted interventions, protocol standardization, and staff training are needed to enhance compliance, optimize patient care, and control aerosol-related expenditures. Clinically, these findings highlight that adherence to evidence-based aerosol therapy not only enhances patient outcomes but also reduces ICU expenditure, thereby supporting integration into routine clinical practice.

KEYWORDS: Aerosol, critically ill patients, ICU, nebulizers, compliance, nebulization, cost

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INTRODUCTION

Aerosol therapy plays a crucial role in the management of respiratory conditions, particularly among critically ill patients who require immediate intervention. The prevalence of aerosol therapy use in India has been reported as 72.48%.[1]

The administration of aerosolized medications enables direct delivery to the lungs, thereby ensuring rapid therapeutic response, increased bioavailability at the target site, minimized systemic side effects, and reduced risk of toxicity.[2,3] It is routinely used for both mechanically ventilated and non-ventilated patients presenting with diseases such as asthma, chronic obstructive pulmonary disease (COPD), acute respiratory distress syndrome, pneumonia, and cystic fibrosis. Frequently administered medications, used as monotherapy or in combination, include bronchodilators, corticosteroids, mucolytics, and antibiotics.[1,4,5]

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The clinical efficacy of aerosol therapy depends on numerous factors, for example, characteristics of aerosolized particles, the patient's respiratory physiology, and management of the device.[2,5,6] An extensive range of aerosol delivery devices is used in hospital settings, including jet, vibrating mesh, and ultrasonic nebulizers, each with its advantages and disadvantages.[2,7]

Despite its therapeutic benefits, aerosol therapy is accompanied by several limitations, including variability in drug deposition due to device type, patient condition, and administration technique. Its effectiveness is further limited in the intensive care unit (ICU) environment due to increased risk of nosocomial infections due to device contamination,[8] lack of standardized protocols, and inconsistency in clinical practice.[9,10] Additionally, the limited availability of aerosol formulations and the high cost of advanced nebulization devices hinder their widespread use, particularly in resource-limited settings such as India.[7,11,12]

Non-compliance with established guidelines further reduces the effectiveness of aerosol therapy. Issues such as reduced drug efficacy, increased incidence of adverse effects, variability in delivery techniques, inadequate training of healthcare personnel, and poor maintenance of devices are commonly observed in clinical practice.[9,10,13] Financial barriers also play a significant role. In developing countries such as India, ICU-related expenses, including costs associated with aerosol therapy, ventilator use, and equipment maintenance, are often borne directly by patients and their families. This economic burden, compounded by inefficient drug delivery and deviations from recommended protocols, frequently results in premature discontinuation of therapy and suboptimal clinical outcomes.[8,9,14]

Effective utilization of aerosol therapy in ICUs requires a structured evaluation of current practices, particularly regarding guideline adherence and cost-effectiveness. Inconsistent practices and financial constraints often undermine its potential benefits, particularly in resource-limited healthcare settings.[11,12]

The "Indian Guidelines on Nebulization Therapy" provide a structured guide for the use of aerosol therapy in clinical settings, such as ICUs. However, compliance with this guideline and the associated costs incurred in Indian ICUs remain unclear.[8,10] This study aims to determine the proportion of aerosol therapy sessions in adult ICU patients that complied with the "Indian Guidelines on Nebulization Therapy" with respect to (a) drug therapy (indication, drug selection, dose/frequency, incompatible combinations, and duration) and (b) administration practices (device selection and placement, carrier gas, and device hygiene).

Main Points

- Jet nebulizers were the most commonly used aerosol delivery devices in critically-ill patients.
- Compliance of drug therapy with evidence-based guidelines varied significantly across intensive care unit (ICU) categories and duration of ICU stay.
- Non-respiratory patients demonstrated higher administration compliance as compared with respiratory groups.
- Drug regimen adherence was associated with a significant reduction in mean cost incurred.

MATERIAL AND METHODS

Study Design and Ethics

A prospective, exploratory (descriptive) observational study was conducted among 307 patients in the ICU and high-dependency unit of Bharati Hospital and Research Centre, Pune, and was approved by the Bharati Vidyapeeth (Deemed to be University) Medical College Ethics Committee (approval ID: BVDUMC/IEC/91/24-25, date 28/09/2024). The study was conducted over a period of six months (October 2024-March 2025). This study was not registered with CTRI. The authors acknowledge that registration is recommended for observational studies in clinical practice and will register future audits of a similar nature and encourage readers to take this into consideration when interpreting the results. All procedures were conducted in accordance with the ethical standards of the institutional research committee and the principles outlined in the Declaration of Helsinki (2024 revision). A waiver of written informed consent for this observational study was approved by the Ethics Committee, as data collection used routine clinical records and did not require changes to patient care.

Sample Size

For the primary outcome, the sample size was calculated based on the proportion of aerosol therapy sessions expected to be compliant with guideline recommendations. Based on published estimates of aerosol therapy guideline adherence and utilization in India (expected compliance ≈72.48% from [1]) using a two-sided 95% confidence level (Z = 1.96) and a desired absolute precision of 5%, the required sample size was: $n = (Z^2 \times p \times (1-p)) / d^2 = (1.96^2 \times 0.7248 \times 0.2752) / 0.05^2 \approx 307$).

Study Criteria

The study included patients aged more than 18 years receiving aerosol therapy for ≥24 hours during their ICU stay. All patients older than 85 years and those receiving aerosol therapy for more than 2 months were excluded from the study. Additionally, patients using inhalation devices, such as dry powder inhalers and pressurized metered-dose inhalers, as well as those receiving nebulization therapy with normal saline alone were not included. A structured proforma was designed, consisting of three sections (information related to aerosol drug therapy, compliance and cost) and validated by four expert panelists, in adherence to the evidence-based guideline of the "Indian Guidelines on Nebulization Therapy".

Diagnostic Characterization

The study classified patients into three broad diagnostic categories: respiratory, respiratory with comorbidities, and non-respiratory because this structure reflects how cases are typically organized and managed in the ICU. Individual disease labels, such as COPD, pneumonia, myocardial infarction, or sepsis, had very small numbers of patients in several groups, which would not allow for statistically meaningful comparisons and would violate chi-square assumptions. Using the three broader categories ensured adequate sample distribution, maintained

statistical validity, and allowed a more reliable evaluation of compliance patterns.

Operational Definitions and Timing

Aerosol Therapy Session: Any discrete episode of administration of an inhaled medication via a nebulizer or other inhalation device, documented in the patient's chart.

Drug Therapy Compliance: A session was considered compliant with drug therapy if all of the following criteria were met: (a) the indication for therapy matched guideline indications; (b) the drug class selection was appropriate for the indication; (c) the dosing frequency was in accordance with guideline recommendations; (d) no guideline-listed incompatible drug combinations were present; and (e) the duration was appropriate for the indication (Supplementary Table 1).

Administration Compliance: A session was considered compliant if device selection, device placement (e.g., endotracheal tube or venturi mask), carrier gas (oxygen, air, or ventilator setting), and device hygiene (documented cleaning/disinfection) adhered to the components recommended in the "Indian Guidelines on Nebulization Therapy" Supplementary Table 2.

Time Points Assessed: Data were recorded systematically for each aerosol therapy session using information present in the patient's drug chart and respiratory sheet during the patient's ICU stay.

Statistical Analysis

All data were compiled and cleaned in Microsoft Excel. Analysis was performed using RStudio software (version 4-4.3, 2024). Average age was presented as mean ± standard deviation. Categorical variables were presented as counts (n) and percentages (%). Associations between categorical variables (e.g., device placements) and compliance status (evaluated as per the guideline) were assessed using the chi-square test. To identify independent predictors of compliance, multivariate logistic regression models were used because they are well suited for binary outcomes. Covariates were selected based on clinical relevance and included ventilation type, age category, ICU categorization, length of ICU stay, and primary diagnosis. Results were expressed as odds ratios (ORs) with 95% confidence intervals (CIs).

Cost Incurred Assessment

The costs incurred in the study included direct medical costs attributable to aerosol therapy during the ICU stay, such as aerosol medication, device costs, respiratory therapist fees, nebulizer costs, and oxygen costs. Indirect (overhead) costs (e.g., ICU bed charges) were not included. The Wilcoxon rank-sum test was used to compare costs between compliant and non-compliant groups. A P value <0.05 was considered significant. In addition, a simple linear regression model was applied using ICU stay (in days) as the independent variable and total cost as the outcome, with model fit reported using R^2.

RESULTS

Patient Characteristics and Clinical Outcomes

A total of 307 patients admitted to the ICU between October 2024 and March 2025 were included in the study. The cohort had a male predominance, with 198 (64.5%) males and 109 (35.5%) females, and a mean age of 57±16 years. Of the total study population, 140 patients (45.6%) were discharged, 83 (27.03%) were transferred to the general ward, and 34 (11.07%) left against medical advice. The observed in-hospital mortality

Table 1. Demographic and clinical characteristics of the study population

	All patients receiving aerosol therapy (n = 307)	Patients receiving invasive aerosol therapy (n = 99)	Patients receiving non-invasive aerosol therapy (n = 174)	Patients receiving both invasive and non-invasive aerosol therapy (n = 34)
Age (years)	57±16			
Male/female	198 (64.5%)/109 (35.5%)	66 (66.67%)/33 (33.33%)	108 (62.1%)/66 (37.9%)	24 (70.6%)/10 (29.4%)
Categorization of ICU				
Critical care medicine	143 (46.6%)	61 (61.6%)	61 (35.1%)	21 (61.8%)
Neurological	47 (15.3%)	7 (7.1%)	35 (20.1%)	5 (14.7%)
Cardiovascular	25 (8.14%)	9 (9.1%)	12 (6.8%)	4 (11.8%)
Surgical	17 (5.53%)	6 (6.1%)	10 (5.7%)	1 (2.9%)
Non-speciality	75 (24.43 %)	16 (16.1%)	56 (32.2%)	3 (8.8%)
Classification of study population based on primary diagnosis				
Respiratory	41 (13.3%)	5 (5.1%)	32 (18.4%)	4 (11.8%)
Respiratory with co-morbidities	139 (45.3%)	43 (43.4%)	77 (44.3%)	19 (55.8%)
Non-respiratory	127 (41.4%)	51 (51.5%)	65 (37.3%)	11 (32.4%)

Values are presented as mean ± standard deviation or n (%), as appropriate
ICU: intensive care unit

rate was 14%, whereas 2.3% of patients were transferred to deluxe care units for continued treatment. Regarding ventilation type, 99 (32.23%) received aerosol therapy via invasive ventilation, 174 (56.7%) via non-invasive ventilation (NIV), and 34 (11.07%) transitioned between these two modalities during their ICU stay. The details of ICU categorization and primary diagnoses are summarized in Table 1.

Drugs and Devices Used for Aerosol Therapy

Jet nebulizers were the most widely used devices, accounting for 91.5% of cases, whereas vibrating mesh nebulizers (VMNs) accounted for 8.5%. Ultrasonic nebulizers were not employed in this study.

Among the 575 aerosol therapy sessions analyzed, 543/575 (94.43%) involved single-agent therapy, and the remaining 32/575 (5.56%) were administered in combination. Among single-agent treatments, the majority [47.13% (271/575)] were bronchodilators, followed by corticosteroids [35% (201/575)]. In terms of regimen complexity, 36.2% of patients received monotherapy, 47.6% received dual-drug therapy, and 11.4% received a regimen consisting of three aerosolized medications. A small subset (4.8%) received more than four aerosolized medications. The distribution of medication classes is shown in Figure 1.

Indications for Aerosol Therapy

Aerosol therapy was most frequently prescribed for respiratory conditions, accounting for 58.63% (n = 180) of the cohort, with pneumonia and COPD being the leading indications. The remaining patients received aerosol therapy for neurological, cardiac, or post-surgical indications (see Table 1).

Device Placements for Aerosol Therapy

Device placement varied significantly across the types of ventilation used. For jet nebulizers, invasive ventilation predominantly used endotracheal tube placement, while NIV was almost exclusively managed with Venturi masks. Patients who received both modalities commonly received a combination of a Venturi mask and an endotracheal tube. Similar patterns were observed in patients using VMNs. These findings, presented in Table 2, indicate a significant association between the type of ventilation and device placement for aerosol delivery.

Administration of Aerosol Therapy

Oxygen was the primary carrier medium, with the highest prevalence observed in the NIV group (77.32%). Flowmeter-based oxygen administration was used in 15.3% of cases, whereas ventilator-based delivery was limited to patients receiving invasive or combined ventilation. The diversity of administration methods highlighted the central role of oxygen in facilitating effective aerosol drug delivery. The distribution of administration methods is illustrated in Figure 2.

Compliance of Aerosol Therapy with Evidence-based Guideline

Compliance with evidence-based guidelines was assessed in two domains: drug therapy and administration (Tables 3 and 4).

The compliance with drug therapy was evaluated in terms of frequency, combination, and duration of treatment.

Drug therapy compliance varied significantly according to ICU categorization (P = 0.0005), suggesting that specific units of care may affect adherence. Furthermore, ICU stays affected drug compliance (P = 0.0062), indicating an influence on treatment adherence. Other variables, such as age group and diagnosis, were not associated with substantial differences in drug compliance. Drug administration compliance was largely uniform across all clinical subgroups, with no significant associations identified for most subgroups; however, a significant association was noted between diagnosis category and compliance (P = 0.00186).

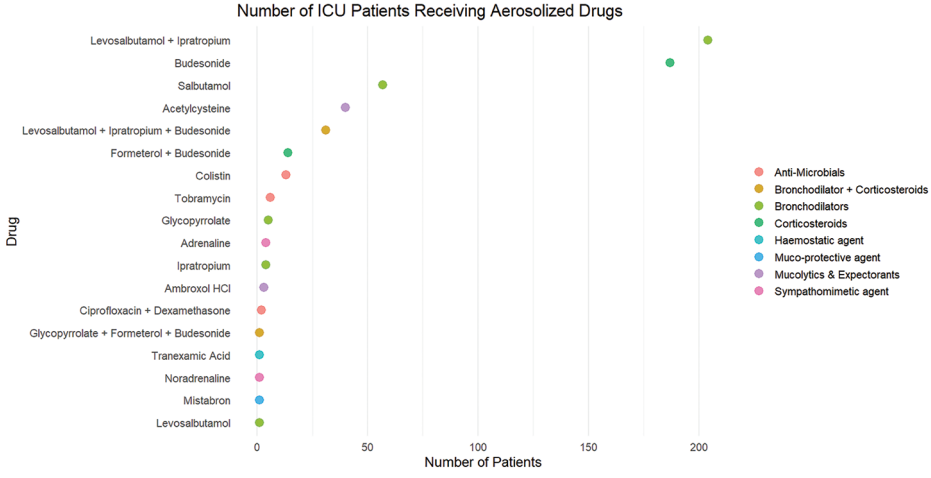

Figure 1. Drugs used as aerosol therapy in the study population. Dot plot depicting the number of ICU patients receiving aerosolized drugs, categorized by drug class. Each dot represents a drug; drug categories are color-coded. Frequencies are plotted on the x-axis

ICU: intensive care unit

Table 2. Device placements for aerosol therapy in the study population

Type of aerosol delivery device	Device placements	Invasive	Non-invasive	Both	*P* value
Jet nebulizer	Endotracheal tube	33/99 (33.33%)	0/174 (0%)	2/34 (5.9%)	***P* < 0.01**
	Nasal prongs	4/99 (4.04%)	0/174 (0%)	1/34 (2.94%)	0.14
	Venturi mask	22/99 (22.22%)	173/174 (99.4%)	5/34 (14.7%)	***P* < 0.01**
	Venturi mask + endotracheal tube	20/99 (20.20%)	0/174 (0%)	20/34 (58.82%)	***P* < 0.01**
	Nasal prongs + venturi mask	0/99 (0%)	0/174 (0%)	1/34 (2.94%)	1.00
Vibrating mesh nebulizer	Endotracheal tube	13/99 (13.13%)	0/174 (0%)	1/34 (2.94%)	***P* < 0.01**
	Nasal prongs	0/99 (0%)	0/174 (0%)	0/34 (0%)	-
	Venturi mask	6/99 (6.06%)	1/174 (0.6%)	0/34 (0%)	**0.02**
	Venturi mask + endotracheal tube	1/99 (1.01%)	0/174 (0%)	4/34 (11.76%)	0.14
	Nasal prongs + venturi mask	0/99 (0%)	0/174 (0%)	0/34 (0%)	-

Data are presented as the number of patients (percentage within group). *P* values were calculated using the chi-square test. *P* value of <0.05 was considered significant

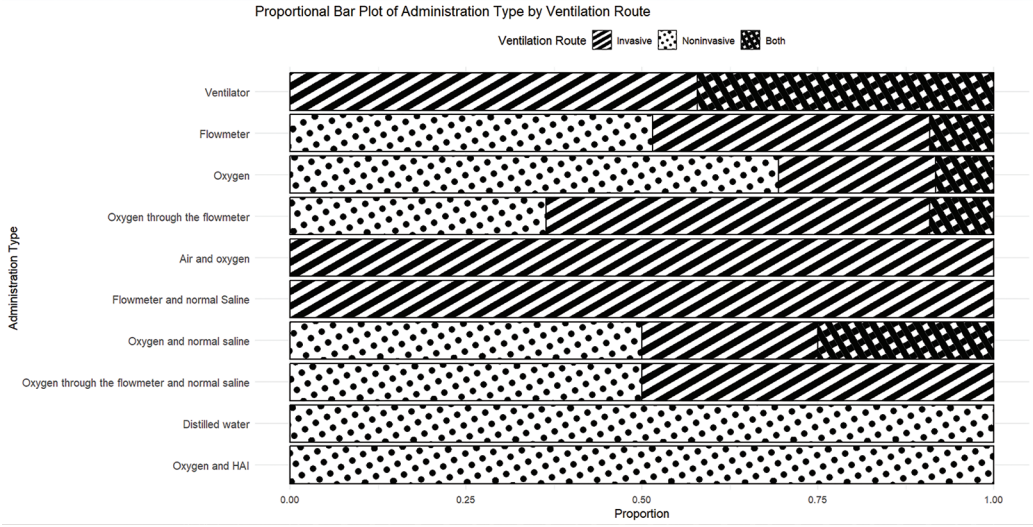

Figure 2. Patterned proportional bar chart representing types of aerosol therapy administration by ventilation route (invasive, non-invasive, both). Bars represent the proportion of each administration method used across invasive, non-invasive, and combined ventilation routes. Patterns differentiate the ventilation modes

HAI, hyperoxic anoxia

These findings highlight that, while drug administration practices were largely consistent, variations in medication adherence were influenced by incompatible drug combinations, prolonged therapy duration, and improper drug regimens.

Multivariate Analysis for Predictors of Compliance with Evidence-based Guideline

Multivariate logistic regression analysis identified several significant predictors of both drug and administration compliance, as illustrated in Figures 3a and 3b. For drug therapy, patients admitted to critical care medicine had higher odds of compliance than those in cardiology (OR: 6.50; 95% CI: 2.60–16.25; *P* = 0.0001), and patients in neurology ICUs also demonstrated increased compliance (OR: 4.57; 95% CI: 1.57–13.32; *P* = 0.005). In contrast, patients in cardiology ICUs had lower odds of compliance compared with both surgical (OR: 0.15; 95% CI: 0.03–0.83; *P* = 0.02) and non-speciality ICUs (OR: 0.13; 95% CI: 0.04–0.36; *P* = 0.0001). Shorter ICU stays were associated with higher compliance (OR: 2.38; 95% CI: 0.97–5.85, *P* = 0.05).

With respect to administration compliance, most comparisons did not reveal notable relationships. However, a significant association between diagnosis and compliance was observed: patients with non-respiratory conditions had significantly higher odds of compliance with the evidence-based guideline compared with those with respiratory illness and co-morbidities (OR: 4.959; 95% CI: 1.399–17.57; *P* = 0.007).

Cost Incurred Due to Aerosol Therapy

Among patients compliant with drug therapy protocols, the mean cost incurred was significantly lower (*P* = 0.01). Linear regression showed that ICU stay duration explained a moderate proportion of cost variation (R^2 = 0.56), with an estimated increase of ₹3495.5 per additional ICU day. These findings underscore the economic burden of prolonged hospitalization

Table 3. Drug compliance in terms of frequency, combination and duration of therapy with evidence-based guideline among different clinical variables in the study population

Compliance category	Clinical variable	Sub group	Compliant (n)	Non-compliant (n)	*P* value
Drug compliance	Invasive/non-invasive	Invasive (n = 99)	79/99 (79.8%)	20/99 (20.2%)	0.78
		Non-invasive (n = 174)	148/174 (85.1%)	26/174 (14.9%)	
		Both (n = 34)	27/34 (79.4%)	7/34 (20.6%)	
	ICU categorization	Critical care medicine (n = 143)	123/143 (86%)	20/143 (14%)	***P*** = 0.01
		Neurological (n = 47)	38/47 (80.9%)	9/47 (19.1%)	
		Cardiology (n = 25)	12/25 (48%)	13/25 (52%)	
		Surgery (n = 17)	15/17 (88.2%)	2/17 (11.8%)	
		Non-speciality (n = 75)	66/75 (88%)	9/75 (12%)	
	Days in ICU	<5 days (n = 65)	57/65 (87.7%)	8/65 (12.3%)	***P*** = 0.01
		6–10 days (n = 129)	106/129 (82.2%)	23/129 (17.8%)	
		>10 days (n =113)	91/113 (80.5%)	22/113 (19.5%)	
	Age	<30 (n = 16)	13/16 (81.3%)	3/16 (18.7%)	0.36
		30–44 (n = 46)	37/46 (80.4%)	9/46 (19.6%)	
		45–59 (n = 82)	67/82 (81.7%)	15/82 (18.3%)	
		60-74 (n = 101)	89/101 (88.1%)	12/101 (11.9%)	
		>75 (n = 62)	48/62 (77.4%)	14/62 (22.6%)	
	Diagnosis	Respiratory (n = 41)	35/41 (85.4%)	6/41 (14.6%)	0.42
		Non-respiratory (n = 127)	101/127 (79.5%)	26/127 (20.5%)	
		Respiratory with co-morbidities (n = 139)	118/139 (84.9%)	21/139 (15.1%)	

Compliance patterns for aerosol therapy in ICU patients are represented for drug therapy. The table presents the number of patients categorized as compliant or non-compliant for drug use. Comparisons are made across ventilation type, ICU categorization, ICU stay duration, aerosol mode, age and diagnosis. Statistically significant results are highlighted with corresponding *P* values

ICU: intensive care unit

and highlight the potential financial benefits of improving compliance. A detailed summary of cost data is presented as a grouped box plot in Figure 4.

DISCUSSION

This study provides a detailed evaluation of aerosol therapy utilization, compliance, and associated costs in critically ill patients admitted during the study period. The findings underscore the complexity of delivering standardized aerosol treatment in high-acuity settings and reveal important gaps in adherence despite well-established recommendations.

Among the 307 patients studied, demographic patterns and clinical outcomes were comparable to national data, reflecting the typical profile of critically ill patients in Indian ICUs. These consistencies reaffirm that the study cohort represents real-world practice and aligns with previously published literature on ICU severity and outcomes.[1,7,9]

Bronchodilators emerged as the most frequently administered drug class (47.13%), consistent with previous findings emphasizing their essential role in managing obstructive airway diseases.[8,11] Respiratory illnesses constituted the majority of indications for aerosol therapy. These findings mirror those reported in multiple Indian and international studies that identify respiratory infections and airway obstruction as the predominant drivers of nebulization in ICU settings.[1,3] This study supports the notion that aerosol therapy is primarily reserved for such conditions, while highlighting the importance of ongoing evaluation of compliance, cost-effectiveness, and staff training.[11,12]

The research also assessed adherence to the "Indian Guidelines on Nebulization Therapy",[15] which are divided into two key areas: medication regimen (drug frequency, incompatible combinations & duration of therapy) and administration procedures. While some elements of the treatment were consistent with the guidelines, there were notable discrepancies in several areas, highlighting a disconnect between theoretical recommendations and practical implementation.

The study highlighted issues with drug regimens, including extended treatment periods and the use of incompatible agents. These practices are frequently influenced by the prescriber's preferences and by a lack of awareness of guidelines.[1] Such deviations can result in reduced therapeutic effectiveness, increased adverse drug reactions, and prolonged ICU stays. To improve the rational use of aerosol therapy, it is essential to systematically incorporate guidelines into clinical practice.

Irregularities in dosing frequency were observed: some patients received excessive aerosol treatment, thereby increasing their risk of adverse events; others were undertreated,

Table 4. Administration compliance in terms of delivery of aerosol drugs (oxygen or air-driven)with evidence-based guideline among different clinical variables in the study population

Compliance category	Clinical variable	Sub group	Compliance (n)	Non-compliance (n)	*P* value
Administration compliance	Invasive/non-invasive	Invasive (n = 99)	95/99 (96%)	4/99 (4%)	0.71
		Non-invasive (n = 174)	158/174 (90.8%)	16/174 (9.2%)	
		Both (n = 34)	31/34 (91.2%)	3/34 (8.8%)	
	ICU categorization	Critical care medicine (n = 143)	136/143 (95.1%)	7/143 (4.9%)	0.20
		Neurological (n = 47)	42/47 (89.4%)	5/47 (10.6%)	
		Cardiology (n = 25)	25/25 (100%)	0/25 (0%)	
		Surgery (n = 17)	14/17 (82.4%)	3/17 (17.6%)	
		Non-speciality (n = 75)	67/75 (89.3%)	8/75 (10.7%)	
	Days in ICU	<5 days (n = 65)	62/65 (95.4%)	3/65 (4.6%)	0.71
		6–10 days (n = 129)	118/129 (91.5%)	11/129 (8.5%)	
		>10 days (n = 113)	104/113 (92%)	9/113 (8%)	
	Age	<30 (n = 16)	15/16 (93.8%)	1/16 (6.2%)	0.61
		30–44 (n = 46)	44/46 (95.7%)	2/46 (4.3%)	
		45–59 (n = 82)	76/82 (92.7%)	6/82 (7.3%)	
		60–74 (n = 101)	92/101 (91.1%)	9/101 (8.9%)	
		>75 (n = 62)	57/62 (91.9%)	5/62 (8.1%)	
	Diagnosis	Respiratory (n = 41)	38/41 (92.7%)	3/41 (7.3%)	**P = 0.02**
		Non-respiratory (n = 127)	122/127 (96.1%)	5/127 (3.9%)	
		Respiratory with co-morbidities (n = 139)	124/139 (89.2%)	15/139 (10.8%)	

Compliance patterns for aerosol therapy in ICU patients are represented for administration. The table presents the number of patients categorized as compliant or non-compliant for administration. Comparisons are made across ventilation type, ICU categorization, ICU stay duration, aerosol mode, age and diagnosis. Statistically significant results are highlighted with corresponding *P* values

ICU: intensive care unit

raising concerns about therapeutic insufficiency and clinical deterioration.[7,14] These patterns emphasized the need for standardized scheduling and electronic administration records to minimize human errors and optimize clinical decisions.

Regarding device selection, the study confirmed that jet nebulizers predominated, reflecting their affordability and widespread availability. VMNs, though used less frequently, demonstrate superior drug delivery efficiency and reduced medication loss, consistent with published evidence from Western settings.[6,16]

An important clinical observation was that non-respiratory patients demonstrated higher compliance with administration. This may be due to simpler therapeutic protocols, fewer aerosol sessions, and reduced disease complexity, which allow guideline-recommended administration to be implemented more consistently than in patients with respiratory illnesses.

Maintenance and hygiene practices showed positive trends, with high adherence to cleaning protocols and disinfection standards outlined by national guidelines. This contrasted with earlier reports documenting poor compliance with device hygiene and elevated risks of nosocomial infections.[17] Effective sterilization and maintenance practices contribute to improved clinical outcomes and patient safety.

The cost assessment of aerosol therapy revealed that multiple factors contributed to the overall expense in the ICU. Non-compliance with treatment protocols, particularly with respect to device selection, dosing, and the use of incompatible combinations, was associated with higher therapy costs.[11,18] Inappropriate device choices, especially frequent reliance on jet nebulizers, led to inefficient drug utilization and higher cumulative costs despite their initially lower unit price.[6,16] Adoption of VMNs in Indian ICUs, while limited due to cost, could offer savings in the long-term and improved therapeutic outcomes.

Frequent bronchodilator use, although clinically justified, contributed to increased pharmaceutical costs and indicated potential overuse or inappropriate dosing.[9] Studies suggest that implementing a national-level standardized aerosol protocol could reduce ICU expenditure by as much as 25–40%.[9,12]

This study adds a meaningful real-world perspective by demonstrating that following guideline-based aerosol therapy in critically ill patients can help maintain therapeutic effectiveness while reducing unnecessary costs. Optimized drug regimen (frequency and duration of therapy) and appropriate device selection, both of which can enhance drug delivery efficiency and minimise wastage, are likely to contribute to these benefits. However, the findings acknowledge that strict adherence may not always be feasible in resource-limited ICUs, where variations in practice may justify deviations from guidelines. This highlights the importance of balancing protocol adherence with individualized treatment.

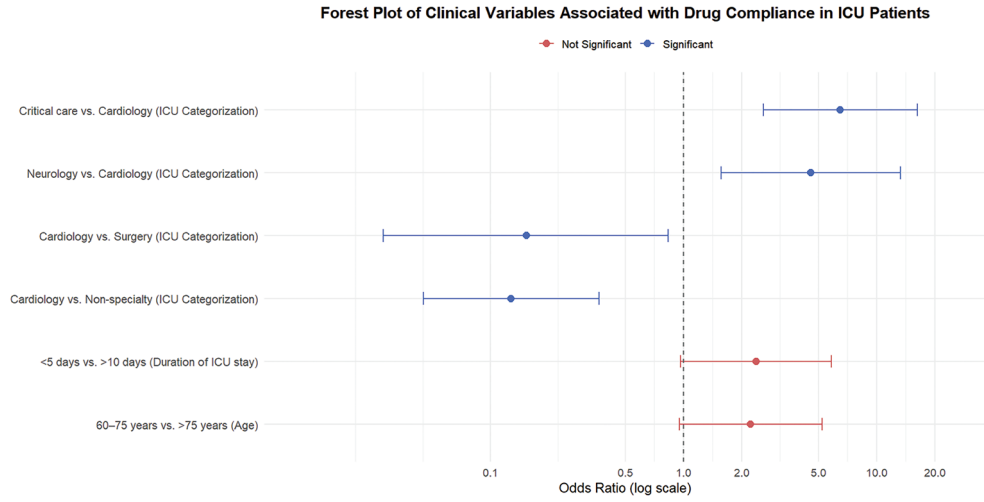

Figure 3a. Forest plot of clinical predictors of drug therapy compliance to aerosol therapy in ICU patients. It depicts the forest plot of odds ratios for drug therapy across various clinical comparisons. Statistically significant comparisons are shown in blue, with 95% confidence intervals represented by horizontal lines

ICU: intensive care unit

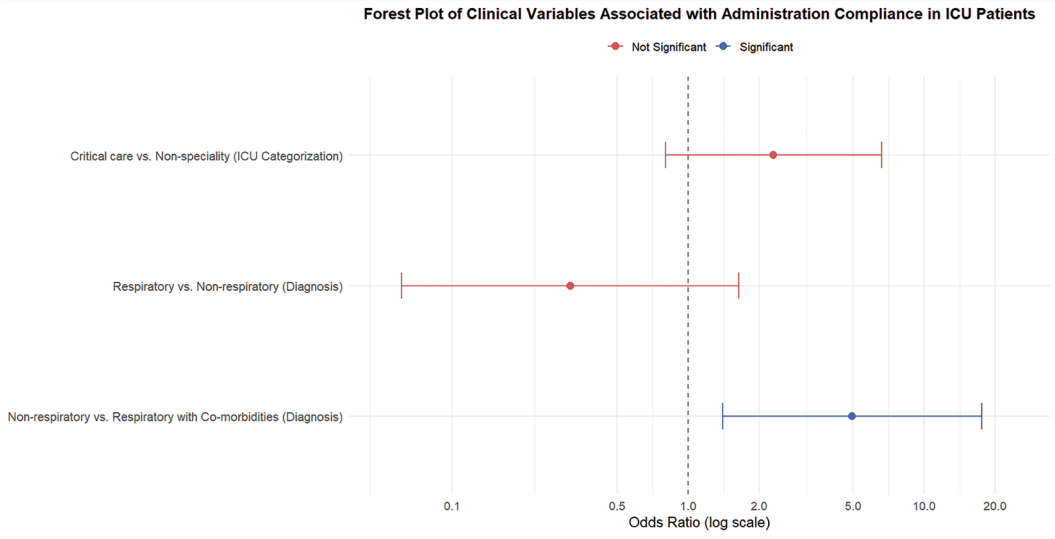

Figure 3b. Forest plot of clinical predictors of administration compliance to aerosol therapy in ICU patients. It depicts the forest plot of odds ratios for administration across various clinical comparisons. Statistically significant comparisons are shown in blue, with 95% confidence intervals represented by horizontal lines

ICU: intensive care unit

Future research should include multicentre studies conducted across diverse settings and regions to ensure external validity. Also, incorporating physician perspectives through qualitative or mixed-methods research could provide valuable insights into decision-making practices and challenges in guideline adherence.

Clinical Significance

Ensuring compliance with evidence-based guidelines for aerosol therapy in the ICU setting promotes uniformity in prescribing, administration, and overall patient care. This not only enhances therapeutic effectiveness and patient safety, but also minimizes unnecessary expenditure. Regular monitoring, periodic staff training, and cost-awareness strategies should be integrated into the hospital's ICU protocols to increase compliance and cost efficiency.

Study Limitations

The study has several limitations which must be acknowledged. Although data collection was prospective, the study was conducted in a single tertiary care teaching hospital, which limits the generalizability of its results to other healthcare settings with different infrastructure and resource availability. The relatively short duration of the study, i.e., 6 months, limited the ability to assess long-term trends in compliance and cost-effectiveness; a longer follow-up period could provide more insight into sustained adherence to guidelines. Validated severity scores (e.g., APACHE II/SOFA)

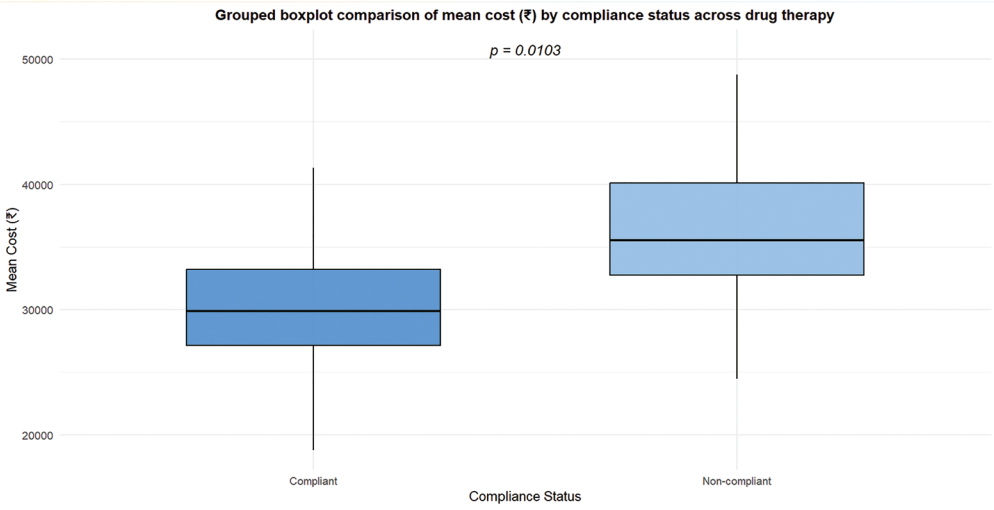

Figure 4. Grouped boxplot comparison of mean cost (₹) by compliance status across drug therapy. It shows a boxplot comparison of mean aerosol therapy costs between compliant and non-compliant cases across the drug therapy. Costs (₹) are represented for compliant and non-compliant groups

were not available for all patients, and adjustment for illness severity could not be undertaken because these scores are not routinely recorded in the hospital's workflow. This limits the study's ability to adjust for baseline severity, and the absence of a standardized severity assessment may have influenced the observed associations among compliance, duration of ICU stay, and overall cost. The study of costs incurred only included direct medical costs and excluded broader system or societal costs; integrating a formal health-economic evaluation would strengthen the study's conclusion. The study did not take into account the variability of clinical decision-making because physician preferences, experience level, awareness, workload, and institutional constraints were not assessed. These factors can act as barriers and affect the compliance pattern to it. Lastly, the study was not registered in CTRI, which is considered a methodological limitation with respect to clinical research transparency.

CONCLUSION

This single-centre study identified significant non-adherence to the "Indian Guidelines on Nebulization Therapy" among critically ill patients, particularly in the choice of drug regimen and its duration; this non-adherence was associated with increased healthcare expenditure and poorer therapeutic outcomes. Compliance with drug therapy was associated with lower direct costs of aerosol therapy. Non-compliance resulted in increased medication wastage, prolonged therapy, and extended ICU stays, which, in total, increased expenditures. The findings of this study underscore the imperative need for standardized protocols, comprehensive training, enforced compliance audits, and an enhanced focus on adherence. Reinforcing hospital policies and fostering interdisciplinary synergy among healthcare providers, including pharmacists and respiratory therapists can enhance the quality and cost-effectiveness of aerosol therapy in ICUs, ensuring judicious resource allocation and superior patient outcomes.

Ethics

Ethics Committee Approval: The Bharati Vidyapeeth (Deemed to be University) Medical College Ethics Committee (approval ID: BVDUMC/IEC/91/24-25, date 28/09/2024).

Informed Consent: A waiver of written informed consent for this observational study was approved by the Ethics Committee, as data collection used routine clinical records and did not require changes to patient care.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.L.R., J.S., S.K., A.R.V., S.A., R.P., K.K.P., Concept: A.L.R., J.S., S.K., Design: A.L.R., J.S., Data Collection or Processing: A.L.R., A.R.V., S.A., R.P., K.K.P., Analysis or Interpretation: A.L.R., A.R.V., S.A., R.P., Literature Search: A.L.R., A.R.V., S.A., R.P., K.K.P., Writing: A.L.R., J.S., S.K., A.R.V., S.A., R.P., K.K.P.,

Conflict of Interest: No conflict of interest was declared by the authors.

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