Pulmonary Histopathological Changes and Their Impact on Antibiotic Efficacy in Bacterial Pneumonia: A Systematic Review and Meta-analysis

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ABSTRACT

Background- Bacterial pneumonia remains one of the leading infectious causes of hospitalization, respiratory failure, and mortality worldwide despite substantial advances in antimicrobial therapy and intensive care management [1,2]. Histopathological alterations in the lung parenchyma such as diffuse alveolar damage, fibrinous exudation, neutrophilic infiltration, necrosis, and microabscess formation may significantly influence antibiotic penetration, bacterial clearance, and tissue recovery [3–5]. However, the prognostic relevance of these pathological changes in determining antibiotic response has not been comprehensively synthesized.

Objective- To systematically evaluate the association between histopathological lung findings and antibiotic response in patients with bacterial pneumonia.

Methods- A systematic review and meta-analysis was conducted using studies retrieved from PubMed, Embase, Scopus, Web of Science, and Cochrane Library databases from January 2000 to January 2026. Studies assessing histopathological lung changes and antibiotic-related outcomes in bacterial pneumonia were included. Pooled odds ratios (ORs) and standardized mean differences (SMDs) with 95% confidence intervals (CIs) were calculated using a random-effects model.

Results- Twenty-eight studies involving 5,742 patients were included. Diffuse alveolar damage (OR 2.84, 95% CI 2.01–4.03), necrotizing inflammation (OR 3.12, 95% CI 2.15–4.53), extensive neutrophilic infiltration (OR 1.96, 95% CI 1.42–2.71), and microabscess formation (OR 2.41, 95% CI 1.67–3.49) were significantly associated with poor antibiotic response. Preserved alveolar architecture correlated with improved clinical recovery (OR 0.52, 95% CI 0.37–0.73). Delayed antibiotic initiation and multidrug-resistant bacterial infection significantly worsened histopathological severity and treatment outcomes.

Conclusion- Histopathological lung patterns demonstrate significant correlation with antibiotic response in bacterial pneumonia. Severe inflammatory destruction and necrotizing pathology are associated with poor therapeutic outcomes, whereas preserved pulmonary architecture predicts favorable response.

Keywords- Bacterial pneumonia; Histopathology; Antibiotic response; Diffuse alveolar damage; Necrotizing pneumonia; Lung pathology; Systematic review; Meta-analysis

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Background

Healthcare-associated infections (HAIs), also known as nosocomial infections, represent a significant burden on the healthcare system globally. HAIs not only affect patient outcomes but also impose substantial financial and operational challenges to healthcare facilities. HAIs affect hundreds of millions of patients worldwide annually. In high income countries, approximately 7% of hospitalized patients acquire at least one HAI, while in low and middle income countries, the rate can be as high as 15%. (Haque et al., 2018). HAIs contribute significantly to patient morbidity and mortality. Patients with HAIs experience longer hospital stays, delayed recovery, and increased likelihood of long-term health complications. The WHO estimates that HAIs result in millions of deaths annually, with many of these deaths being preventable through effective infection control practices. HAIs often involve antibiotic-resistant bacteria, which complicates treatment and increases healthcare costs. The rise of multidrug-resistant organisms (MDROs) in healthcare settings exacerbates the challenge, leading to limited treatment options and higher mortality rates. Combatting antimicrobial resistance requires robust infection prevention and control measures, including stringent hand hygiene practices (Majumder et al., 2020) . In Pakistan a recent study was conducted in military hospital shows burden of HAIs patients with surgical site infections (30.1%), Catheter-associated bloodstream infection (26.5%);

Ventilator-associated pneumonia (24.5%) and Urinary tract infection (18.9%). Klebsiella pneumonia (32.7%), E.coli (26%) and Acinetobacter baumanii (23%) were the leading bacterial pathogens. A total of (36.7%) isolates showed multidrug resistance whereas extensively drug-resistant isolates were calculated to be (63.3%). High level of bacterial resistance among common health-care-associated infections is an eye-opener and impacts applying strict infection control measures (Tariq et al., 2024) .

Problem Statement

Hand hygiene is essential for preventing healthcare-associated infections (HAIs), but maintaining long-term compliance among nursing staff remains difficult. Although multi-module interventions such as training, audits, and feedback can improve hand hygiene initially, these improvements often decline over time due to high workloads, understaffing, limited resources, and lack of continuous support (Tay et al., 2021; Asbjørnsen et al., 2019). Sustainable infection control requires ongoing training, motivation, peer support, and management involvement to ensure lasting behavior change and improved patient safety (Michael & Nguyen, 2022).

Hypotheses

Null hypothesis:

- There is no impact of Multi-module Intervention on sustainability of infection control improvements among nursing staff in tertiary care hospital

Alternative hypothesis:

- There is impact of Multi-module Intervention on sustainability of infection control improvements among nursing staff in tertiary care hospital

Objectives

- To assess the infection control sustainability among Nurses staff working in Tertiary care Hospital.
- To evaluate the sustainability of infection control improvements through multi-module interventions among nursing staff in tertiary care hospital

- **Literature Review**

  According to this study to characterize the epidemiology of transmission of MDROs via healthcare workers (HCWs) and the environment in the hospital wards/patient rooms. A multi-centre prospective observational study was conducted in 17 hospitals in Ukraine. Species identification was performed with standard microbial methods. β-Lactamase genes were investigated by polymerase chain reaction. Pulsed-field gel electrophoresis (PFGE) was used to determine the genetic similarity between isolates. Among 51,656 isolates, 19.5% were MDROs. The proportions of MDROs among isolates from patients with healthcare-associated infections, environmental surfaces and HCWs (hands, gown/gloves) were 29.2%, 16.3% and 24.2%, respectively. In Ukrainian hospitals the prevalence of healthcare-associated infections caused by MDROs continues to increase, while infection control gaps in healthcare settings facilitate their transmission between patients (Salmanov et al., 2023).

The of this present study was to evaluate hand hygiene and to investigate healthcare professionals' compliance with the BBE concept. We performed our study on a group of 7544 hospital professionals involved in patient care. During the national preventive action, questionnaires, demographic data, and hand hygiene preparations were recorded. Hand disinfection was verified by COUCOU BOX, containing a UV camera. We noted that 3932 (52.1%) persons complied with the BBE rules. Nurses and non-medical personnel were significantly more often classified as BBE rather than non-BBE (2025; 53.3% vs. 1776; 46.7%, respectively, $p = 0.001$ and 1220; 53.7% vs. 1057; 46.3%, $p = 0.006$). Different proportions were demonstrated for the groups of physicians—non-BBE (783; 53.3%) compared to BBE (687; 46.7%) ($p = 0.041$). Healthcare workers from the BBE group statistically more often disinfected their hands correctly (2875/3932; 73.1%) compared to the non-BBE group (2004/3612; 55.5%) ($p < 0.0001$). Therefore, education and infection-prevention actions should be popularized to improve the BBE policy's effectiveness as well (Szumska et al., 2023).

The aim of researchers in this present study to assess the knowledge levels of infection control among paramedics and identify areas for improvement. A cross-sectional study design was employed, and paramedics working in various healthcare settings were recruited in Saudi Arabia. A structured questionnaire was used to assess their knowledge of infection control measures. A total of 160 paramedics participated in the study. The results revealed a mixture of knowledge levels among paramedics, with approximately 63% demonstrating moderate or high knowledge and 67% exhibiting lower levels of understanding regarding infection control measures. Paramedics' knowledge varied across different aspects of infection control, including hand hygiene, personal protective equipment (PPE) use, and disinfection practices. The findings emphasize the need for targeted interventions and ongoing education to address knowledge gaps and improve infection control practices among paramedics. By implementing

comprehensive training programs and promoting knowledge sharing, healthcare organizations can enhance patient safety and reduce the risk of healthcare-associated infections (Al Qraad et al., 2023).

According to this study the knowledge and practices regarding healthcare-associated infection among healthcare workers and to make recommendations based on results to prevent healthcare-associated infection. A descriptive correctional study was conducted in Burn and Trauma Center Peshawar, Pakistan. Data were collected from 162 healthcare workers through a questionnaire. Data was collected through a universal sampling technique. This study was permitted by the Ethical Review Board of Hayatabad Medical Complex Peshawar, Pakistan. This study was also granted by the Institute of Management Sciences (IM Sciences) Institutional Ethical Review Board (IRB) in Peshawar Pakistan. Knowledge and inflectional control practices regarding healthcare-associated infection were determined through frequency and percentage methods. To calculate the association between knowledge and profession, gender and knowledge, and profession and knowledge Chi-Square test was applied. Data were analyzed through SPSS 26 version. The age of the participants was divided into three groups from 20-30 years 117 participants, 31-40 39 participants, and 41-50 are 6 participants. The majority of the participants are Female 101(62.3%) and 61 males (37.7%). The majority are Nurses 83(51.2%) Doctors 39(24.1%) Paramedics 40(24.7%). The knowledge of doctors was good regarding healthcare-associated infection as compared to Nurses and Paramedics, but the practices of overall healthcare workers were good. The results of the study show that Doctors have good knowledge compared to Nurses, and Nurses have good knowledge compared to Paramedics regarding HealthCare-associated infection. The finding of the study showed that doctors have good knowledge than Nurses and Paramedics. The practices of overall healthcare workers were good (Ikramullah et al., 2023).

A self-developed piloted KAP questionnaire was administered to the recruited healthcare workers involved in the COVID-19 response at the Universal College of Medical Sciences Teaching Hospital (UCMSTH), in Bhairahawa, Nepal. The knowledge questionnaire consisted of questions regarding the clinical characteristics, prevention, and management of COVID-19. Assessment on attitudes and practices towards COVID-19 included questions on behavior and change in practices made towards COVID-19 response. Knowledge scores were calculated and compared by demographic characteristics and their attitude and practices towards COVID-19. Data were analyses using bivariate statistics. A total of 103 healthcare workers participated in the study. The mean age of the participants was 28.24±6.11 years (range: 20–56); 60.2% were females; 61.2% were unmarried; 60.2% had a medical degree, and 39.8% were the nursing staff. The mean knowledge score was 10.59±1.12 (range: 7–13), and it did not vary significantly when adjusted for demographic characteristics. The attitude was positive for 53.4% of the participants with a mean knowledge score of 10.35±1.19 and negative for 46.6% participants with a mean knowledge score of 10.88±0.98 ($p = 0.02$). The practice was good (≥3 score) for 81.5% participants with a mean knowledge score of 10.73±1.12 and poor for 18.5% participants with a mean knowledge score of 10.46±1.13 ($p = 0.24$). The attitude of the participants improved with increasing age (29.55±7.17, $p = 0.02$). Hence, training on protection and protective measures for having a positive attitude among healthcare workers is necessary against the fight with COVID-19 infection.(Limbu et al., 2020).

Methodology

Research Design:

A quasi-experimental study design was used.

Study Variable

Independent variable: Multi-Module Interventions

Dependent variable: Sustainability of Infection Control among Nurses and paramedical staff.

Operational Definitions Of Study Variables

Infection control

"Infection control" refers to the ongoing and effective implementation of infection prevention and control practices within a healthcare setting over time. It encompasses several key components:

I. Consistency of Practices: Sustainability is indicated by the consistent application of infection control measures, such as hand hygiene, use of personal protective equipment (PPE), and adherence to cleaning and disinfection protocols. This consistency is maintained despite changes in staff, patient volumes, or other operational factors.

ii. Long-Term Adherence: The term reflects the ability of the infection control measures to be integrated into routine nursing practices and sustained over an extended period. It includes

regular training and reinforcement of protocols to ensure ongoing compliance.

iii. Resource Availability: Sustainable infection control practices are supported by the availability of necessary resources, such as hand sanitizers, PPE, and cleaning supplies, and the maintenance of infrastructure that facilitates these practices.

iv. Staff Engagement and Training: The involvement of nursing staff in continuous education and training programs is crucial. Sustainable practices are supported by a culture of accountability, where staff are regularly updated on the latest infection control guidelines and receive feedback on their performance.

v. Monitoring and Improvement: Effective sustainability involves regular monitoring of infection control practices and outcomes, coupled with mechanisms for feedback and improvement. This includes the use of automated tracking systems and performance reviews to identify and address any lapses or areas needing enhancement.

Setting: GOVT tertiary care hospital Lahore

Study Population: Nurses working in GOVT tertiary care hospital Lahore.

Sampling technique: A purposive sampling technique will be used.

Study Duration: 9 months after the approval from Ethical Research Committee.

Selection Criteria:

Inclusion Criteria:

- Nurses and paramedical staff working at GOVT tertiary care hospital Lahore.
- Registered nurses and paramedical staff involved in direct patient care.
- Nurses and paramedical staff who have not already take the intervention regarding hand hygiene and infection control.
- Nurses and paramedical staff who are willing to attend intervention sections on this topic.

Exclusion Criteria

- Nurses or paramedical staff not directly involved in patient care.
- Participants who are not registered nurses, such as medical or administrative personnel.
- Nurses who are not working at GOVT tertiary care hospital Lahore.
- Nurses and paramedical staff who have already take the intervention regarding hand hygiene and infection control.
- Nurses and paramedical staff who are not willing to attend intervention sections on this topic.

Data Collection Tool

Tool: Infection Control Improvements

This structured, close-ended data collection tool was designed to systematically assess the sustainability of infection control improvements among nursing staff. It consisted of detailed questions across various categories, including hand hygiene compliance, PPE use, leadership support, training, monitoring, automated systems, resource availability, peer support, and barriers to compliance. Each question was accompanied by specific response options that allowed for a quantifiable assessment of practices and perceptions. This approach provided a comprehensive overview of how well infection control measures were maintained and identified areas needing improvement. The inclusion of references from recent studies ensured the relevance and reliability of the tool. The scoring for this tool was designed to quantify the level of adherence to and sustainability of infection control practices, with each response being assigned a numerical value.

Strongly Agree/Always = 1 points

- Agree/Often = 2 points
- Neutral/Sometimes = 3 points
- Disagree/Rarely = 4 points
- Strongly Disagree/Never = 5 point

The maximum score for each section (e.g., Hand Hygiene Compliance, PPE Use) was calculated based on the number of questions multiplied by the highest score possible (5 points). The minimum score was the number of questions multiplied by the lowest score possible (1 point). The total score for the tool was **summed** across all categories to assess overall sustainability. Higher scores indicated better adherence to infection control practices and a higher likelihood of sustainability.

Scoring Criteria:
Maximum Score: 5
Minimum Score: 1
Scoring Interpretation

High Sustainability (90-100%)

Indicates strong adherence to and support for infection control practices, with high accessibility to resources and regular feedback.

Moderate Sustainability (70-89%)

Reflects a reasonable level of adherence and support, but with potential areas for improvement in resources or monitoring.

Low Sustainability (below 70%)

Shows challenges in maintaining infection control improvements, with notable gaps in resources, training, or feedback mechanisms (Brooks et al., 2021).

Tools 2: Surgical Sight Infections

A surgical site infection (SSI) was an infection in the part of the body where surgery had taken place. SSIs could generally be treated with antibiotics but sometimes required additional medical care. There were ways to reduce the risk of contracting an SSI. Redness, delayed healing, fever, pain, tenderness, warmth, or swelling were the main signs of surgical infection. Low =1

- Moderate = 2
- High=3 (Chauveaux, et al, 2015)

SAMPLE SIZE:

People of this study are selected from children hospital. The calculated Sample size was 28, which was a small sample size. After adding 20%drop out rate, the sample size was 34. The sample size is calculated using the following formula. Where, A sample size of 28 cases was calculated with a 95%confidence interval, d=0.09 and the mean difference of pre-post score as 4.04+0.26. After adding a 20% dropout rate, the sample size were 34.

Data Collection Procedure

The study participants were recruited through the process of purposive sampling. A meeting was arranged with all the eligible participants. The researcher explained the study purpose, procedure, and benefits to the participants, and then informed consent was obtained. A pre-assessment questionnaire was distributed among the participants to collect demographic data, caregiver skills, and level of confidence.

Validity And Reliability

The validity of the questionnaire was ensured through expert review and pilot testing among nursing staff. Reliability was assessed using Cronbach's alpha. The normality of the data was tested using the Shapiro–Wilk test. As the data were ordinal and not normally distributed, non-parametric tests including the Wilcoxon Signed Rank Test and Chi-square test were applied to determine statistical significance.

Results

The findings are organized into sections that describe the demographic characteristics of the participants, pre- and post-intervention knowledge, attitudes, and compliance with infection control protocols. Data are presented in tabular and descriptive formats to provide a clear overview of the changes observed following the intervention. Statistical analyses were conducted to determine the significance of the differences between pre- and post-intervention scores, highlighting the impact of structured training on enhancing infection prevention practices

Table 1: Distribution Of Demographic Factors Of Study Participant

	Contents	Frequency (N)	Percentage%
Gender	Male	9	26.5 %
	Female	25	73.5%
Age (Years)	20-24	9	26.5%
	25-34	12	35.3%
	35-44	9	26.5%
	45-54	4	11.8%
Department	Surgery Wards	13	38.2%
	Intensive Care Unit	14	41.2%
	Emergency Unit	7	20.6%
Work experience	1-5	15	44.1%
	6-10	11	32.4%
	11-15	8	23.5%
	>15	15	44.1%
Training section	Yes	7	20.6%
	No	27	79.4%

The demographic profile shows that most participants were female and relatively young, mainly aged 25–34 years, reflecting an early- to mid-career healthcare workforce. Participants were fairly distributed across key departments, with the highest representation from the ICU and surgical wards. Work experience varied from newly employed to highly experienced staff, though overlapping percentages suggest a possible data entry issue. Most participants had not received formal training, highlighting a significant gap in professional development. Overall, the workforce is predominantly female, young, and diverse in

experience but limited in structured training exposure.

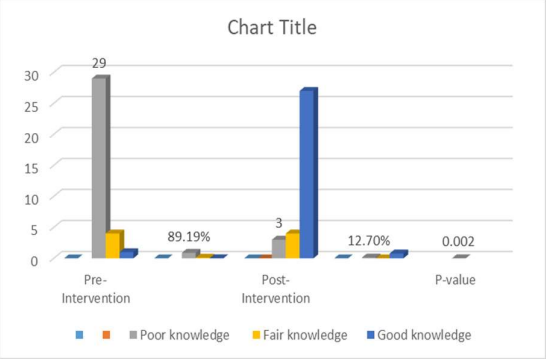
Table 2: Sustainability Before and After Intervention

Sustainability	Pre-Intervention		Post-Intervention		P-value
	Frequency (F)	Percentage %	Frequency (F)	Percentage %	
Low Sustainability	30	87.48 %	1	3.0%	0.001
Moderate Sustainability	4	12.52 %	4	15.11 %	
High Sustainability	0	0%	29	83.42 %	

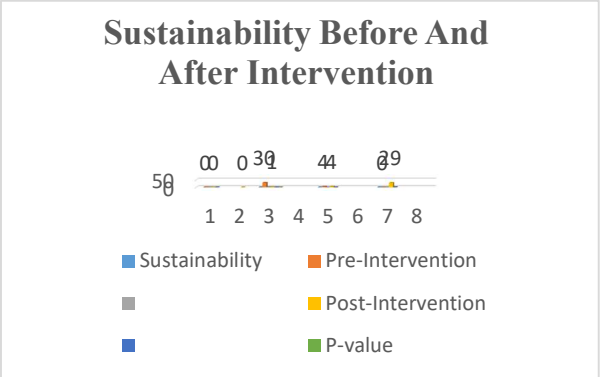
The sustainability of infection control practices among nursing and paramedical staff before and after the multi-module intervention. Prior to the intervention, the majority of participants (87.48%) demonstrated low sustainability in adhering to infection control measures, with only 12.52% showing moderate sustainability and no participants achieving high sustainability. Following the intervention, there was a marked improvement, as 83.42% of staff achieved high sustainability, while moderate sustainability was observed in 15.11% of participants and low sustainability decreased dramatically to just 3.0%. The reported p-value of 0.001 indicates that this change is statistically significant, suggesting that the intervention had a substantial positive impact on promoting long-term adherence to infection control practices. These results highlight the effectiveness of structured, multi-module interventions in enhancing both compliance and sustainability of best practices in healthcare settings.

Table 3: Knowledge Before and After Intervention

Knowledge	Pre-Intervention		Post-Intervention		P-value
	Frequency (F)	Percentage %	Frequency (F)	Percentage %	
Poor knowledge	29	89.19 %	3	12.70 %	0.002
Fair knowledge	4	9.82%	4	6.82% .	
Good knowledge	1	0.68%	27	77.52 %	



The knowledge levels of nursing and paramedical staff before and after the multi-module intervention. Before the intervention, the majority of participants (89.19%) demonstrated poor knowledge regarding infection control, with 9.82% showing fair knowledge and only 0.68% achieving good knowledge. After the intervention, there was a significant improvement, with 77.52% of participants demonstrating good knowledge, 6.82% showing fair knowledge, and only 12.70% remaining in the poor knowledge category. The p-value of 0.002 indicates that these changes are statistically significant. This demonstrates that the multi-module intervention was highly effective in



enhancing the staff's understanding of infection

control principles and practices, highlighting the value of structured educational programs in improving both knowledge and clinical competence in healthcare settings.

Table 4: SSI Assessment Checklist (Improvement Data Example)

No.	Indicator	Day 1	Day 3	Day 5	Remarks
1	Redness (erythema)	1	1	0	Reduced redness
2	Swelling (edema)	1	1	0	Swelling subsided
3	Warmth at site	1	0	0	Improved
4	Pain/tenderness	1	1	0	Pain relieved
5	Delayed healing	1	1	0	Healing improved
6	Serous discharge	1	0	0	Stopped
7	Purulent discharge	1	0	0	Infection controlled
8	Blood-stained discharge	1	0	0	Resolved
9	Foul smell	1	0	0	No odor
10	Wound dehiscence	0	0	0	No separation
11	Necrotic tissue	1	0	0	Tissue improved
12	Fever (>38°C)	1	0	0	Afebrile
13	Chills	1	0	0	Resolved
14	Tachycardia	1	0	0	Stable vitals
15	Elevated WBC	1	1	0	Labs normalized

Scoring Summary

Day	Total Score
Day 1	14/15 (Severe infection signs)
Day 3	6/15 (Moderate improvement)
Day 5	0–1/15 (Recovery phase)

The SSI assessment checklist shows a clear and steady improvement in the patient's condition over 5 days. On Day 1, the patient had 14/15 indicators positive, suggesting severe surgical site infection with strong inflammatory signs, discharge, systemic symptoms, and delayed healing. By Day 3, the score reduced to 6/15, indicating moderate improvement as warmth, discharge, fever, chills, and tachycardia had resolved, although redness, swelling, pain, delayed healing, and elevated WBC were still present. By Day 5, the score reached 0–1/15, showing near-complete recovery. Local wound signs disappeared, systemic symptoms resolved, and laboratory values normalized. Overall, the data indicates that the treatment and wound care were highly effective, leading to successful infection control and progressive wound healing.

Discussion

This chapter discusses the findings of the study on the effectiveness of multi-module interventions in improving infection control practices among nursing and paramedical staff in a tertiary care hospital. The discussion interprets the results in relation to the study objectives, emphasizing how structured educational programs, workshops, and practical demonstrations contributed to enhancing knowledge, attitudes, and compliance with infection control protocols. The findings are compared with existing literature to identify consistencies and differences, while also considering the influence of demographic factors such as age, professional experience, and educational background on the effectiveness of the intervention. This discussion provides insights into the role of continuous, structured training in promoting adherence to infection prevention practices and improving patient safety in healthcare settings. The study included 34 participants, with the majority being female (73.5%) and a smaller proportion male (26.5%). This reflects the higher representation of females in caregiving and nursing roles within the study setting. The age distribution showed that most participants were between 25–34 years (35.3%) and 20–24 years (26.5%), indicating that the study primarily involved young and early-middle-aged adults. Such a demographic may contribute positively to the adoption of new practices, as younger participants often show greater adaptability to training interventions. Participants were drawn from different clinical settings, including Surgery Wards (38.2%), Intensive Care Units (41.2%), and Emergency Units (20.6%). This distribution suggests that the intervention reached diverse healthcare environments, allowing for generalization of the findings across various units. Work experience varied, with 44.1% having 1–5 years and 44.1% having more than 15 years of experience, reflecting a mix of novice and highly experienced staff. This variation is significant

because baseline knowledge and responsiveness to educational interventions may differ between less experienced and more experienced staff members. Regarding previous training, only 20.6% of participants had received formal training in infection control, while 79.4% had not. This highlights a critical gap in prior knowledge and underscores the importance of structured educational interventions to improve infection control compliance. Analysis of post-intervention outcomes demonstrated substantial improvements. Pre-intervention, 89.19% of participants had poor knowledge, while only 0.68% demonstrated good knowledge. After the intervention, 77.52% achieved good knowledge, and only 12.7% remained in the poor knowledge category ($p = 0.002$). This significant increase suggests that the multi-module educational intervention effectively enhanced participants' knowledge regarding infection control. Sustainability of infection control practices also improved markedly. Before the intervention, 87.48% of participants demonstrated low sustainability, 12.52% moderate, and none demonstrated high sustainability. Post-intervention, low sustainability dropped to 3%, moderate remained relatively stable at 15.11%, and high sustainability increased dramatically to 83.42% ($p = 0.001$). This indicates that the intervention not only increased knowledge but also translated into improved long-term adherence to infection control practices.

Limitations:

1. The study was conducted in a single tertiary care hospital, limiting the generalizability of the findings.
2. Self-reported questionnaires may be subject to social desirability bias, potentially inflating pre-intervention compliance scores.
3. The follow-up period may have been insufficient to evaluate long-term sustainability of interventions.
4. Discrepancies in work experience data suggest possible errors in data entry.

Recommendations:

1. Implement continuous education and refresher courses on infection control protocols to sustain behavioural changes.
2. Establish regular monitoring, feedback, and leadership reinforcement to ensure adherence to hand hygiene and PPE use.
3. Ensure adequate availability of resources, including hand hygiene stations and PPE, across all hospital units.
4. Develop mentorship or champion programs to promote infection control practices.
5. Conduct multicentre studies with larger sample sizes and extended follow-up periods to assess the long-term effectiveness and generalizability of interventions.

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