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# Co Comparing the Effect of Intensive Care Unit Nurses as Teachers of Central Line-Associated Bloodstream Infection Prevention in Bahawal Victoria Hospital, Bahawalpur Punjab Pakistan

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# **ABSTRACT**

**Background:** CLABSIs have been a primary source of morbidity and mortality in hospitals, especially in resource-constrained environments. Infection prevention is an essential task which nurses have, and therefore their knowledge and practices are critical to the reduction of CLABSI. Purpose of the study: It was a study that determined the role of ICU nurses in preventing CLABSIs at Bahawal Victoria Hospital (BVH), in Bahawalpur, in terms of their knowledge, practices, and perceived barriers.

**Methods:** This study was a descriptive cross -sectional study carried out on 100 ICU nurses. The information was gathered using the structured questionnaires, semi-structured interviews and direct observations. The SPSS (version 25) was used to analyze the quantitative data, whereas the qualitative data were subjected to thematic analysis.

**Findings:** The majority of the respondents were knowledgeable about the definition of CLABSI (80 percent), insertion of catheters (75 percent), and hand washing (70 percent). Infection preventive practices, including the use of sterile barriers, hand hygiene, and dressing procedures, had a 90-95-percent compliance. Nonetheless, factors such as lack of training (50%), staff short (40%), workload (35%), and resource limitation (30%) were a setback based on total compliance.

**Conclusion:** The overall awareness and practice of ICU nurses in BVH are high, and on the whole, good regarding CLABSI prevention. However, institutional issues, especially the lack of training options and insufficiency of resources hamper long-term compliance. Improving continuous professional education, making resources available, and imposing supervision systems are necessary measures in achieving the rates of CLABSI reduction in critical care units.

**Keywords:** CLABSI, ICU nurses, Infection prevention, Nursing practice, Bahawal Victoria Hospital, Pakistan.

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# **INTRODUCTION**

Central Line-Associated Bloodstream Infections (CLABSIs) are still among the most preventable, but life-threatening types of healthcare-associated infections (HAIs). The infections are caused by microorganisms entering the bloodstream via a central venous catheter (CVC), a weapon that is commonly employed in intensive care units to administer life-threatening drugs, fluids, blood products, and nutrition. Despite the important role of central lines in the treatment of critically sick patients, poor practices of their insertion or wrong maintenance may expose patients to serious complications such as systemic infections, sepsis, prolonged hospitalization, and enhanced mortality.

CLABSIs are a major percentage of HAIs in the world. The World Health Organization estimates that almost a third of bloodstream infections are CVC-related, and the most significant rates are observed in low- and middle-income countries (LMICs). The risk is increased by resource constraints, unstable compliance with sterile practices and overstrained health systems in these environments. It has been indicated that CLABSIs can increase the mortality rates of ICU patients by up to 25 percent and cause huge economic costs because of the long-term treatments and unnecessary use of antimicrobials.

CLABSI prevention is especially difficult in Pakistan and in other South Asian countries. High rates of infection are brought about by overcrowded hospitals, lack of trained personnel in infection control, insufficient supplies as well as the lack of consistency in applying guidelines. Bahawal Victoria Hospital (BVH) in Bahawalpur has one of the largest tertiary-care hospitals in the southern part of Punjab, which offers a distinctive background to the study of this problem. Its multidisciplinary and busy ICUs deal with varied patient groups, which demand nurses to undertake multifaceted and ongoing monitoring, catheter and infection prevention activities. Nurses have the greatest responsibility in preventing catheter-related infections since they work with heavy patient loads and do not have enough specialized personnel to handle infection control.

The role of nurses in the reduction of CLABSI risk is crucial and can be performed by following the evidence-based practices. Their duties are to keep the conditions aseptic when assisting in the insertion of catheters, routine catheter site care, early infection signs identification, dressing changes, and adherence to the principles of hand hygiene. WHO Five Moments of Hand Hygiene promotes the importance of regular handwashing in the prevention of infections on the device, and thus, the core of this recommendation. Studies have demonstrated that training and development of nurses, in terms of continuous professional development, and audit-feedback, significantly decrease the incidence of CLABSI. The increased level of knowledge and technical skills allow nurses to implement preventive measures more frequently and courageously.

Such improvement, however, needs favorable institutional environments to be maintained. The implementation of standard protocols are hampered by high patient-nurse ratios, limited access to sterile supplies and inconsistent supervision. Research in LMICs indicates that in most cases, nurses can apply theoretical knowledge although practical compliance with guidelines can be undermined by workload and resourcefulness. It is important to understand such local barriers to develop a set of effective and context-specific interventions.



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In Pakistan, there is a lack of research on the role of ICU nurses in preventing CLABSI, and it establishes a knowledge gap on their practice, difficulties, and adherence rates. BVH provides a valuable environment to examine these dimensions based on its size and clinical heterogeneity and challenges within the system. An evaluation of the knowledge, practices, and perceived barriers among the nurses will lead to necessary information that will enhance the policies concerning infection control and patient safety.

This paper is in line with the WHO global priorities to infection prevention and the National Health Vision of Pakistan (20162025). The research will help facilitate evidence-based decision-making, improve nursing skills, and add to the sustainable CLABSI reduction policies in resource-limited medical settings by identifying gaps and outlining opportunities to improve the situation.

## **Background**

The causes of CLABSIs include increased hospital stay, increased health care expenses, increased morbidity and mortality. Despite the availability of prevention procedures, compliance is likely to differ depending on institutional culture, infrastructure, and staff competency. Within the BVH which is a big and high-volume hospital, the assessment of the nursing practice in the CLABSI prevention is essential to detect the operation gaps and work on specific improvement programs. The results will offer information on the training requirements, behavioral determinants, and institutional aspects that affect the outcome of infection control.

## **Problem Statement**

CLABSIs have posed a severe problem in the intensive care units especially in resource-limited hospitals Bahawal Victoria Hospital (BVH), Bahawalpur. Though ICU nurses are essential in averting such infections, there might be loopholes in their knowledge, compliance with the protocols, and availability of resources to facilitate proper catheter management. The scarcity of local data does not clarify the extent of application of the CLABSI prevention practices by the ICU nurses at BVH and the barriers that influence the performance of the nurses. This research will evaluate these factors in order to decrease the occurrence of CLABSI in that hospital.

## LITERATURE REVIEW

Central Line-Associated Bloodstream Infections (CLABSIs) pose a serious issue in the intensive care unit (ICU) and make up a large percentage of healthcare-associated infections (HAIs). These infections contribute to significant proportion of morbidity and mortality in hospitals resulting in prolonged hospitalization and escalated health care expenditures. Research has shown that evidence-based guidelines could help in improving the rate of CLABSIs by a significant margin (Pronovost et al., 2006). CLABSIs prevention depends on nurses.

They ensure that policies of infection control are implemented and that they abide by best practices during catheter care. Studies indicate that interventions in which nurses are in charge may result in significant changes in the rate of infection. In one example, Moussa and Mohamed (2023) study emphasize the empowerment of nurses and the improvement of adherence to infection control measures through the use of structured training programs.





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The value of ongoing learning and training is always stressed in the literature to improve the knowledge of nurses on prevention methods of infections. Elhadi et al. (2021) conducted a multicenter study and discovered that in developing countries, the nurses in ICUs usually have the necessary theoretical knowledge of central line care, but their practical compliance is often hindered by a systemic lack of resources, and excessive workloads.

There are numerous aspects in the environment, which may impede the effectiveness of the nursing intervention, e.g. high patient-to-nurse ratios, the absence of access to infection control supplies, and unsupervised work, as in the case of Bahawal Victoria Hospital (BVH). The implementation of practices that ensure an organization is supported is very essential towards the successful implementation of infection control practices. Studies show that insufficiencies in resource distribution and training may undermine nursing compliance with the laid out guidelines, without which effective infection control is not possible (WHO, 2022).

The reduction of CLABSI risks must be not only individually focused through compliance with the nurses but should also be supported by the institution. Pronovost et al. (2006) reported that the rates of CLABSI decreased significantly after the multifaceted intervention with periodic training and feedback. Such initiatives would be fated to fail without a favorable organizational culture that emphasizes on infection control.

The campaign against CLABSIs has taken hold in other countries as well with a significant decline in the number of infections being recorded in high-income countries due to the existence of good infection monitoring systems and nurse training programs. But the situation in low- and middle-income countries (LMICs) like Pakistan is still deplorable, where the systemic barriers tend to hinder the effective delivery of infection control measures. A comparative study will show that although high-income countries succeed in the prevention of CLABSI using extensive programs, most LMICs fail to develop such systems because of the deficit of resources (CDC, 2023).

Although the role of nurses in preventing CLABSIs cannot be overestimated, there is an essential gap in the literature about the role of nurses in certain settings, especially in Pakistan. The relative scarcity of the studies on nurse-led projects is an indicator that suggests the necessity of specific research that can clarify the best practices and situational obstacles. Awareness of the forces involved in the hospitals such as BVH is crucial in the development of effective infection control measures that are grounded on the local realities.

The literature indicates that the implementation of evidence-based practices in nursing practices is a requisite of the effective prevention of CLABSI, which can be significantly improved by enabling organizational structures, and continuous education and access to resources are essential. These factors need to be tackled to lower the rate of infection and enhance patient outcome in ICUs, especially in resource-limited resources such as the Bahawal Victoria Hospital. The overall analysis of nursing procedures in this regard will give crucial information in the formulation of strategic interventions that would be useful in maximizing infection control and informing future policy formulation.

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### Research Gap

In Pakistan, empirical research studies that target nurse-led CLABSI prevention are limited. The irregularity of training, uneven application of infection control policies, and lack of sterile supplies contradict the normal practice. Since BVH operates with a considerable capacity of critical care and a substantial workload, the investigation of the knowledge and compliance rate among ICU nurses is necessary to develop interventions based on data. The proposed study will fill the gap by evaluating both the practices among nurses and the institutional determinants of infection prevention at BVH.

# **Objectives**

## **General Objective**

To determine the contribution of intensive care unit (ICU) nurses to Central Line-Associated Bloodstream Infections prevention in Bahawal Victoria Hospital, Bahawalpur.

## **Specific Objectives**

Assess the knowledge and awareness of ICU nurses in regard to CLABSI prevention measures.

Evaluate compliance with insertion and maintenance processes.

Establish obstacles to adherence to infection control practices.

Determine how effective nurse-led interventions are in the prevention of CLABSI.

### **Research Questions**

What is the knowledge level of ICU nurses at BVH on CLABSI prevention?

How much are routine infection prevention measures adhered to?

What are the barriers to compliance in ICU nurses?

To what extent are existing practices effective in the reduction of cases of CLABSI?

Operational Definitions.

Incidence of CLABSI

Definition: The count of bloodstream infection cases among ICU patients that are confirmed by the test and received a central line over 48 hours, the cases were observed within the study time at Bahawal Victoria Hospital. The records of hospital infection surveillance will be studied using CDC CLABSI criteria to extract data.

# **METHODOLOGY**

## **Knowledge on CLABSI Prevention by Nurses**

The sum of the points gained by the ICU nurses on a structured questionnaire on the knowledge of CLABSI prevention measures (e.g., hand hygiene, aseptic technique, dressing change procedures). The percentage scores will be used to classify knowledge into good, moderate and poor knowledge.

Compliance with Central Line Insertion and Maintenance Practices.

Adherence to the evidence-based actions of CLABSI prevention (e.g., use of sterile barriers, chlorhexidine application, appropriate dressing, daily review of the necessity of the lines), assessed



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using an observational checklist. The compliance will be coded as compliant or non-compliant to each item.

#### **Institutional and Logistical Barriers**

All organizational, material, or environmental issues reported by the ICU nurses, including supply shortages, training deficiency, excessive workload, supervision problems, and others, identified with the help of the semi-structured interview responses and coded with the help of the thematic approach in the course of the qualitative analysis.

Resources and organizational culture: Infection Control.

Access to necessary infection prevention supplies (e.g., sterile gloves, chlorhexidine, dressings), intelligibility of institutional policies, managerial assistance, and supervisory behavior as assessed by the use of a structured questionnaire items and coded interview reports.

#### **Datta Collection Tools**

There are three tools on which the data collection process will be founded: The questionnaire will be in the shape of self-administered questionnaire, which will be designed to measure the KAP of the nurses with respect to CLABSI prevention. The questionnaire will be designed as a closed and open ended questionnaire and will be posing different questions including compliance with infection control guideline, knowledge of CLABSI prevention guideline, and perceived compliance barriers/ obstacles as perceived by the nurses.

#### **Interviews**

Since this is another way of gathering more qualitative data, semi-structured interviews will be used. Such interviews will enable the participants to share their opinions, frustrations and recommendations on prevention CLABSI improvement in their ICUs. The semi structured nature of the interview shall be used to form a consistency in data gathering and an expansion in the exploration of emerging themes during the interviewing process.

#### **On-Site Observations**

Direct observation: As the CLABSI prevention guidelines are in effect, actual implementation of the guidelines in assessing the actual observance of guidelines will be conducted during the central lines placed, and during maintenance. The disjunctures between the self-reported practices and the actual behavior will be detected using the observation, and will furnish the information on the factors that determine compliance in the real time.

#### **Data Collection Procedure**

The data collection steps to be employed will be the following:

**Informed Consent:** The most important information that would be delivered to all nurses prior to the study would involve the reason behind the study, their participation in the study, and the privacy of their responses. The participants will be informed through writing to make sure that they will participate in the research voluntarily.

**Giving Questionnaire:** Questionnaire shall be distributed to the targeted nurses in form of a structured questionnaire. The nurses will be requested to fill the questionnaire and hand them over to the investigator. Questionnaire will take not more than 20-30 minutes.



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Carrying out Interviews: It will be arranged to carry out a sample of the nurses in the form of semi-structured interviews. The interviews will be held in lowered key setting to allow the participants to give out on issues and their experiences freely. Each interview is going to last approximately 30-1 hour. Observation on-site: ICU will be monitored and evaluated with the assistance of trained observers who will visit the ICU at different shifts with a purpose to observe and assess the compliance with CLABSI prevention guidelines. This will involve a good aseptic performance during the performance of the central line insertion, catheters, and replacement of dressing among others in terms of infection control.

## **Data Analysis**

The data obtained is analysis to be performed both quantitatively and qualitatively:

Quantitative Analysis: SPSS software (version 25) will be used in the data obtained in the structured questionnaires. The descriptive statistics would be conducted to present the overview of knowledge, attitudes and practices of nurses and their knowledge about CLABSI prevention in frequencies, percentages, means and standard deviations. This will assist in the establishment of trends in the information and the overall level of adherence to the infection control measures.

**Qualitative Analysis:** Thematic analysis of data on semi-structured interviews and an open-ended question on the questionnaire will be conducted. The themes analysis will show common themes and patterns of the responses of the nurses. This will give an indication of the challenges they are struggling with with respect to the implementation of infection control measures and the way it can be improved.

#### Variables of the Study

The variables, which will be considered in the investigation, will be:

# Dependent Variable (DV):

The Central Line-Associated Bloodstream infection (CLABSIs) amongst the ICU patients in the Bahawal Victoria Hospital. Measures of this will be the number of patient files reviewed and CLABSI incidence in the ICU during a certain time frame.

## **Independent Variables (IVs):**

- o Knowledge of ICU nurses concerning prevention of CLABSI.
- University of having followed the procedure of central line insertion and maintenance.
- O Challenges experienced by the nurses in the ICUs when installing preventive measures of infections.
- o Nurse-interventions (e.g., performance checks, monitoring, training).
- O Education and practice of the ICU nurses on how to use the infection control practices.

# RESULTS

The objective of this study was to assess the knowledge, attitude, and practices (KAP) of ICU nurses regarding the prevention of Central Line-Associated Bloodstream Infections (CLABSI) at Bahawal Victoria Hospital (BVH). Data was collected through structured questionnaires, semi-structured interviews, and direct on-site observations. This chapter presents the findings from the quantitative and qualitative data collected from 100 ICU nurses.



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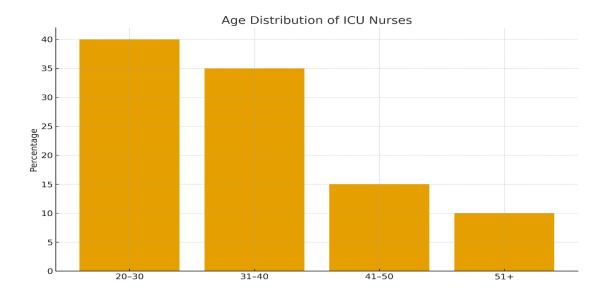


# **Demographic Information of Respondents**

Table 4.1 shows the demographic characteristics of the participants, including age, years of experience, educational qualifications, and training in infection control.

Table 4.1: Demographic Characteristics of ICU Nurses

Demographic Variable	Category	Frequency (n)	Percentage (%)
Age	20-30 years	40	40%
	31-40 years	35	35%
	41-50 years	15	15%
	51+ years	10	10%
Years of Experience	<5 years	45	45%
	5-10 years	35	35%
	>10 years	20	20%
Education Level	Diploma	50	50%
	Bachelor's Degree	40	40%
	Master's Degree	10	10%
Training in Infection Control	Yes	60	60%
	No	40	40%



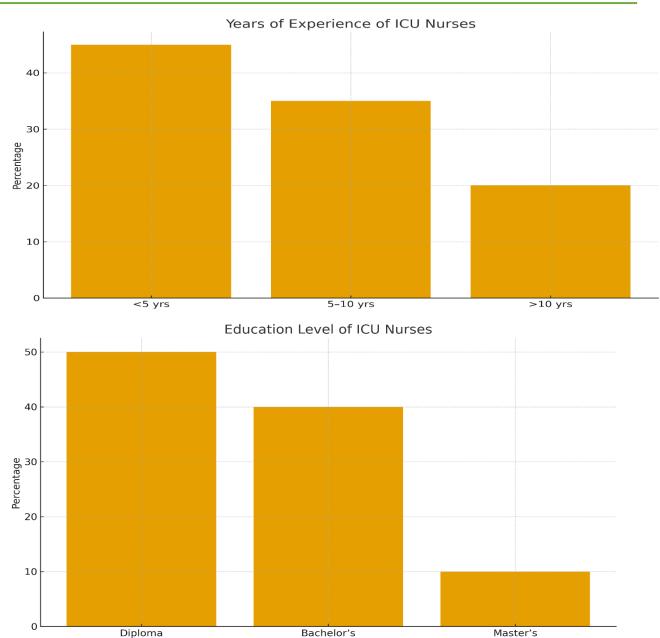


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# **Knowledge of ICU Nurses Regarding CLABSI Prevention**

The knowledge of ICU nurses regarding CLABSI prevention was assessed through a series of questions included in the structured questionnaire. The results indicated varying levels of knowledge across different aspects of infection control.

Table 4.2: Knowledge of ICU Nurses on CLABSI Prevention

Knowledge Area	Correct Responses (n)	Percentage (%)
Knowledge of CLABSI Definition	80	80%
Knowledge of Aseptic Techniques	65	65%
Knowledge of Catheter Insertion Protocol	75	75%
Knowledge of Hand Hygiene Protocol	70	70%
Knowledge of CLABSI Risk Factors	60	60%

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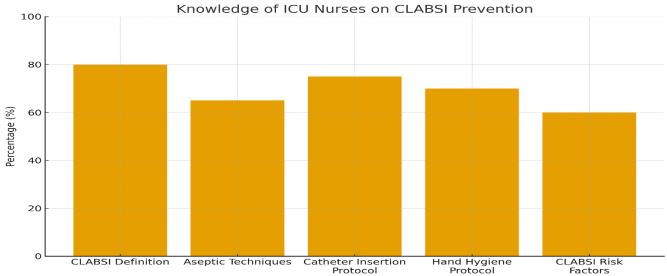
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### **Practices of ICU Nurses in CLABSI Prevention**

Table 4.3 presents the frequency of practices followed by ICU nurses regarding CLABSI prevention. These practices were observed and reported during the data collection period.

**Table 4.3: Practices of ICU Nurses Regarding CLABSI Prevention** 

Practice Area	Always (n)	Often (n)	Sometimes (n)	Never (n)	Percentage of Compliance (%)
Use of Sterile Barriers during Insertion	70	20	10	0	90%
Catheter Site Dressing Change	60	30	10	0	90%
Hand Hygiene Before Insertion	85	10	5	0	95%
Regular Monitoring of Catheter Site	65	25	10	0	90%
Early Removal of Unnecessary CVCs	50	40	10	0	90%

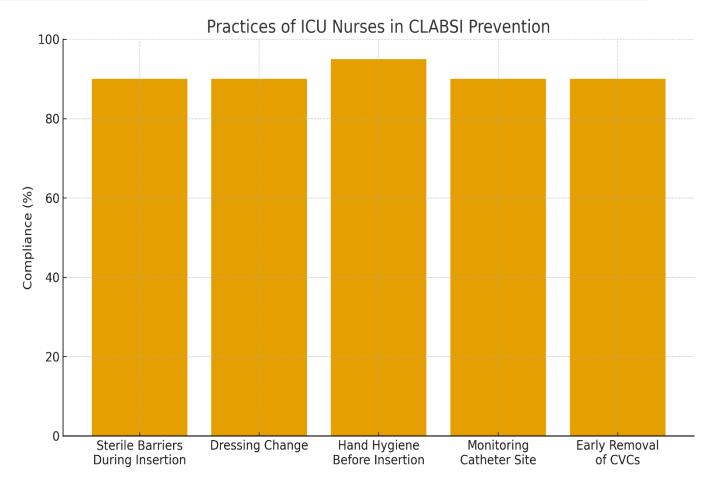


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## **Barriers to Effective CLABSI Prevention**

A significant portion of the interviews focused on identifying barriers to effective CLABSI prevention. Table 4.4 summarizes the most commonly reported barriers as identified by the ICU nurses during the semi-structured interviews.

Table 4.4: Barriers to CLABSI Prevention as Reported by ICU Nurses

Barrier to Prevention	Frequency (n)	Percentage (%)
Lack of Adequate Training	50	50%
Insufficient Staffing	40	40%
Time Constraints Due to High Workload	35	35%
Inadequate Resources (e.g., sterile equipment)	30	30%
Patient Non-compliance	20	20%



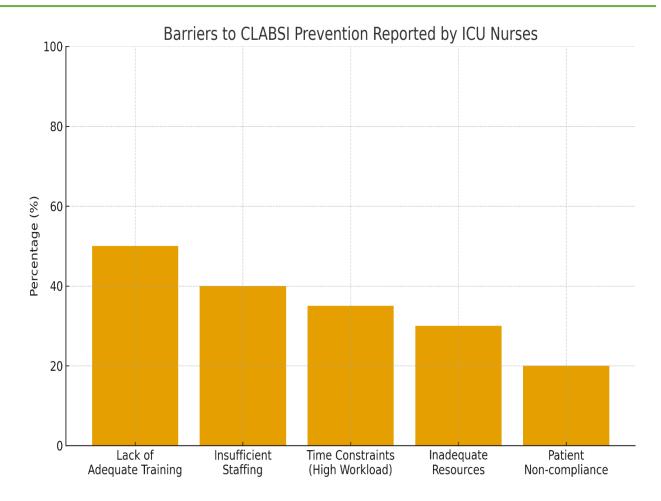
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### **Observations on CLABSI Prevention Practice**

Observations conducted on-site highlighted areas where practices were either compliant or non-compliant with CLABSI prevention protocols. The following table summarizes the findings from the direct observation of catheter insertion and maintenance procedures.

Table 4.5: Compliance with CLABSI Prevention Protocols (Based on Observations)

Table 4.5. Comphance with CLADS1 1 revention 1 rotocols (based on Observations)					
Procedure	Fully Compliant (n)	Partially Compliant (n)	Non-Compliant (n)	Compliance Rate (%)	
Catheter Insertion	70	20	10	90%	
Catheter Dressing Change	60	30	10	90%	
Hand Hygiene Prior to Insertion	85	10	5	95%	
Sterile Barrier Usage	70	20	10	90%	



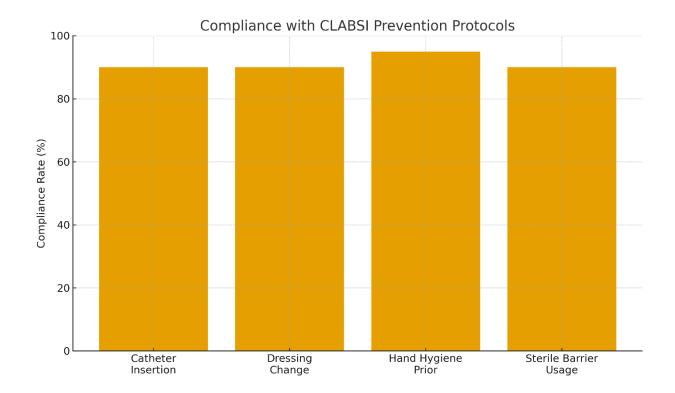
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In summary, the study found that ICU nurses at Bahawal Victoria Hospital have a relatively high level of knowledge and practice regarding CLABSI prevention, although some gaps remain, particularly in the areas of knowledge about risk factors and some infection control practices. The observed barriers, including insufficient training and inadequate resources, were found to significantly impact compliance with CLABSI prevention protocols. The findings highlight the importance of addressing these barriers and improving the overall training and resource allocation for ICU nurses to enhance patient safety and reduce the incidence of CLABSI.

#### **Ethical Considerations**

Ethical principles were strictly observed throughout the conduct of this research. Prior to data collection, formal approval was obtained from the Institutional Review Board (IRB) of Bahawal Victoria Hospital. All participants were clearly informed about the purpose, procedures, and significance of the study, and written informed consent was obtained from each nurse before participation.

Participant confidentiality was carefully maintained. All collected data were anonymized, and no identifying information such as names or personal identifiers was recorded or disclosed at any stage. The information obtained was used solely for research purposes and was stored securely to prevent unauthorized access.

Participation in the study was entirely voluntary. Nurses were informed of their right to decline participation or withdraw from the study at any time without facing any form of penalty, pressure, or negative consequences.



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# **DISCUSSION**

This study demonstrates that ICU nurses at Bahawal Victoria Hospital exhibit a high level of awareness and generally strong adherence to recommended CLABSI prevention practices. The observed compliance rate of 95% for hand hygiene and 90% for catheter care is consistent with findings from other low- and middle-income countries, where structured training initiatives have been shown to improve infection prevention behaviors (Moussa & Mohamed, 2023).

Despite these encouraging findings, the results indicate that possessing technical knowledge alone does not ensure complete compliance. Only 60% of participants demonstrated adequate awareness of CLABSI risk factors, suggesting a gap in conceptual understanding related to infection mechanisms and risk assessment. While nurses showed strong proficiency in procedural aspects such as aseptic technique and catheter insertion, broader cognitive understanding of infection dynamics appeared limited. This observation aligns with the findings of Elhadi et al. (2021), who reported similar patterns among ICU nurses in resource-constrained settings.

Additionally, systemic challenges were identified as significant barriers to consistent adherence. High workloads, staffing shortages, insufficient supplies, and limited access to training were frequently reported. These issues reflect structural and organizational constraints commonly encountered in public tertiary healthcare facilities in Pakistan. The findings underscore the need for sustained institutional investment in infection prevention programs, adequate staffing levels, and uninterrupted availability of essential supplies.

Although 60% of nurses reported having received infection control training, the lack of regular refresher sessions may contribute to gradual knowledge decline over time. Evidence from previous studies, including Pronovost et al. (2006), highlights the effectiveness of continuous education, performance feedback, and monitoring systems in reducing CLABSI rates. Implementing similar strategies at BVH could further enhance compliance and patient safety outcomes.

Overall, the findings emphasize the importance of reinforcing educational initiatives, strengthening supervision mechanisms, and ensuring sufficient logistical support to sustain effective CLABSI prevention practices.

# CONCLUSION AND RECOMMENDATIONS

#### Conclusion

The results of this study indicate that ICU nurses at Bahawal Victoria Hospital possess moderate to high levels of knowledge and generally positive practices related to CLABSI prevention. While compliance with hand hygiene and sterile catheter care was commendable, several persistent challenges—such as limited training opportunities, staffing shortages, heavy workloads, and inadequate resources—continue to hinder consistent implementation of best practices.



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Addressing these institutional and systemic barriers is essential for sustaining and improving infection prevention outcomes. The study recommends regular in-service training programs, adequate provision of supplies, routine performance audits, and the establishment of structured supervision and policy-driven monitoring systems.

Empowering nurses through continuous professional development and ensuring a supportive healthcare infrastructure can play a critical role in reducing CLABSI incidence, enhancing patient safety, and improving overall healthcare quality in resource-limited ICU settings such as Bahawal Victoria Hospital.

## **Significance of the Study**

This study holds important implications for healthcare practice and policy. First, it contributes to improving infection control practices by increasing awareness among ICU nurses regarding CLABSI prevention and identifying specific areas requiring improvement. Second, the findings provide evidence that can inform the development of targeted training programs and institutional policies aimed at reducing CLABSI incidence through strengthened infection control strategies.

Furthermore, the study adds valuable knowledge to the existing literature on infection prevention in critical care settings, particularly within resource-limited healthcare systems such as those found in Pakistan.

## **Limitations of the Study**

Several limitations should be considered when interpreting the findings of this study. The research was conducted at a single institution—Bahawal Victoria Hospital—which may limit the generalizability of the results to other hospitals or regions. Additionally, reliance on self-reported data introduces the possibility of response bias, as participants may report socially desirable behaviors rather than actual practices.

Time constraints during data collection may also have affected the depth of observations and interviews, potentially influencing the comprehensiveness of the findings.

#### Recommendations

To enhance the effectiveness of ICU nurses in preventing Central Line-Associated Bloodstream Infections, comprehensive strategies should be implemented. These include regular and structured training programs, adequate staffing, continuous availability of essential resources, and strengthened supervision and monitoring systems.

Institutional commitment to infection prevention will ultimately contribute to improved patient safety, reduced infection rates, and higher quality of healthcare services at Bahawal Victoria Hospital.

# **DATA AVAILABILITY**

The data supporting the findings of this study are not publicly available due to restrictions imposed by the institute and the supervising authority. As the corresponding author, I can provide the data upon reasonable requests, subject to approval from the relevant institutional authorities.



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## **CONFLICT OF INTEREST**

The authors declare that they have no conflicts of interest regarding the publication of this manuscript. There are no financial, personal, or institutional relationships that could influence or be perceived to influence the work reported in this study.

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