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"ANTIMICROBIAL EFFICACY OF HAND HYGIENE WITH OR WITHOUT ALCOHOL BASE IN MEDICAL AND SURGICAL SETTING IN A MEDICAL COLLEGE HOSPITAL IN RURAL INDIA WITH SPECIAL REFERENCE TO MULTI-DRUG RESISTANT ORGANIZMS (MDRO'S)"

Evaluating Hand Hygiene Practices in Rural Healthcare Settings

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Abstract :

Introduction: Hygiene, tracing its etymology back to the Greek deity of health, Hygeia, serves as a cornerstone of modern healthcare. Its critical role in preventing healthcare-associated infections (HAIs) is widely acknowledged and supported by robust evidence. Hand hygiene, in particular, stands as a sentinel against the transmission of pathogens in healthcare settings, endorsed by leading authorities including the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO). Within the complex ecosystem of healthcare worker hands, a dynamic interplay between resident and transient flora shapes the landscape of infection control. As debates persist regarding the most effective hand hygiene practices, this study embarks on a quest to evaluate the comparative efficacy of various methods, illuminating a path toward enhanced patient safety and healthcare quality

Materials and Methods: This descriptive, cross-sectional experimental study assessed the efficacy of hand hygiene methods in reducing microbial flora. Ethical approval was obtained from the institutional committee, and 50 participants actively took part. Microbial samples were collected before and after hand hygiene interventions, including alcohol-based hand sanitizers, traditional handwashing, and surgical hand scrub. Colony-forming units (CFU) were quantified on blood agar, Sabouraud Dextrose Agar (SDA), and MacConkey agar. Data analysis utilized Microsoft Excel for percentage reductions, and bacterial identification followed standard protocols

Results: Mean reductions in colony-forming units (CFU) were 64.89% on blood agar, 60.95% on Sabouraud Dextrose Agar (SDA), and 69.19% on MacConkey agar. The study demonstrated significant reductions in CFU after hand hygiene practices across all groups.Candida albicans was the predominant species, with alcohol-based hand sanitizer showing 82.4% reduction and traditional handwashing showing 73.4% reduction. Gram-positive cocci, mainly Staphylococcus aureus, constituted a significant portion, with 71.42% being MSSA and 42.8% being MRSA. Surgical hand scrub showed 92% efficacy against both MSSA and MRSA, while alcohol-based hand sanitizer showed 86% reduction for MSSA and 71.2% reduction for MRSA.

Conclusion: This study underscores the paramount importance of effective hand hygiene practices in healthcare settings. While surgical hand scrub proved most effective in reducing microbial flora, alcohol-based hand sanitizers and traditional handwashing also demonstrated significant efficacy. Addressing the issue of misleading advertisements regarding hand hygiene products is crucial for maintaining transparency and ensuring public health. Comprehensive hand hygiene protocols, coupled with regulatory oversight, are vital for minimizing the risk of nosocomial infections and enhancing patient safety in healthcare environments.

***Keywords* -Hand hygiene, Nosocomial infections, Multidrug resistant organisms(MDRO's), Medical professionals, Antimicrobial efficacy, Patient care.**

INTRODUCTION

The word "hygiene" is derived from the ancient Greek goddess "Hygeia" that means "goddess of healing." The importance of hygiene is universally recognized and evidence-based. It is well known that hand hygiene is crucial to prevent and minimize healthcare-associated infections [1].

The Centers for Disease Control and Prevention, the World Health Organization, and many other health experts promote hand hygiene as the single most important measure in the prevention of hospital-acquired infections. Several studies have shown the importance of proper hand hygiene in reducing the incidence of nosocomial infections [2,3,4]

Bacterial flora on the hands of healthcare workers (HCWs) can be distinguished as resident flora and transient flora [5]. Traditionally, microbes habitation on hands is divided into resident and transient floras. Involved resident floras are commonly *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Enterococcus faecalis* that colonize the deeper skin layers and are resistant to mechanical removal. The transient floras consists of *S. aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa* that colonize the superficial layers of skin in a short period of time[6].Transient flora, primarily accountable for nosocomial infection transmission in healthcare settings, can be readily eliminated through suitable hand washing practices. There are claims suggesting that alcoholic hand rubs surpass traditional hand washing with soap and water in the removal of transient bacterial flora on hands [7,8].

The number of direct contacts between the hands of healthcare workers and the patients are greater, and this leads to increased rate of nosocomial infections [9]. Hands play a major role in the transmission of blood borne, enteric, and respiratory tract infections. Hand hygiene has been considered the most important tool in nosocomial infections control.[10,11]

Surgical Site Infections (SSI) is the third most commonly reported nosocomial infection which has an adverse impact on the hospital as well as on the patient including complications, increased hospital stay, additional financial burden and increased mortality. The precise prevalence of data on the SSI and NI are lacking in India [12].

Despite being marketed to the public as antimicrobial hand sanitizers, some products fail to effectively reduce bacterial counts on hands. Contrary to claims of reducing "germs and harmful bacteria" by 99.9%, certain studies have noted a potential increase in bacterial concentration in handprints left on agar plates post-cleansing [13]. Consequently, there remains a necessity for regulatory authorities to verify these claims and enforce measures ensuring product quality. To address this uncertainty, the present study was conducted to evaluate the antimicrobial efficacy of various methods of hand hygiene including 75% alcohol hand sanitizer, traditional hand washing, and povidine-iodine based surgical hand scrub.

NEED OF THE STUDY.

Effective hand hygiene is crucial in healthcare settings to prevent infections, but variations in efficacy among methods persist. This study addresses the need to evaluate and compare the antimicrobial effectiveness of common hand hygiene practices in a specific healthcare environment. Focusing on alcohol-based sanitizers, traditional handwashing, and surgical hand scrubs, it aims to determine which methods offer the strongest protection against healthcare-associated infections. This research is particularly timely given concerns about misleading marketing claims by some companies regarding the efficacy of hand hygiene products. Clear, evidence-based findings from this study are essential for guiding practices, improving patient safety, and advocating for transparent standards in the healthcare industry.

RESEARCH METHODOLOGY

3.1Population and Sample

A total of 50 participants were taken for the study, out of which, the distribution is as follows:-

- Sanitary attendants 10 (20%)
- Medical students 10 (20%)
- Members of surgical team 10 (20%)
- Resident doctors 10 (20%)
- Nurses 5 (10%)
- Hospital attendants 5 (10%)

3.2 Data and Sources of Data

3.2.1 Type of study: Descriptive, Cross-sectional, Experimental study.

3.2.2 Duration of the study: For a period of five months (i.e. January, 2024 – May, 2024)

3.2.3 Ethical issues: The present study was conducted in a rural tertiary care teaching hospital in Haryana & institutional ethical committee approved this cross- sectional study (Ref. no. AFSMS&RC/F-01/23/02),

Informed written consent was obtained from the participants, and two swabs were used for collection of samples, one for sampling before hand washing and another for sampling after hand washing by the respective technique. To describe the technique briefly, a sterile cotton tipped swab moistened with nutrient broth was taken and rubbed against the palmer surfaces, webs of fingers and beneath the fingernails of both the hands and the swabs were then transported immediately to the bacteriology laboratory.

3.3 Theoretical framework

Fifty individuals were selected randomly from predefined strata to ensure representation across different demographics. Swabs were meticulously collected using the rolling technique from specific anatomical sites: palms, webs of fingers, and beneath fingernails. Each swab was immediately placed in a sterile holder pre-moistened with nutrient broth to maintain the viability of microorganisms during transportation to the laboratory.

Upon arrival at the laboratory, swabs were streaked onto culture plates containing three different types of agar: blood agar, Sabouraud dextrose agar (SDA) for fungal growth, and MacConkey agar for gram-negative bacteria. This step aimed to support the growth and identification of a broad spectrum of microorganisms present on the sampled areas.
Culture plates with blood agar and MacConkey agar were incubated at 37°C for 24 hours to facilitate bacterial growth. Following incubation, colony-forming units (CFUs) were counted manually to quantify bacterial load and assess any reduction in microbial presence post-intervention.
In parallel, SDA plates were incubated for 48 hours at the same temperature to allow sufficient time for fungal colonies to develop. The resulting growth was observed and documented to identify fungal species present in the samples.
To further characterize bacterial isolates, Gram staining was performed on colonies grown on blood agar and MacConkey agar plates. Gram-positive cocci (GPC) were then subjected to additional tests: catalase and coagulase tests to distinguish Staphylococcus aureus from other staphylococcal species. Catalase-negative GPC were identified as Staphylococcus epidermidis.
Methicillin-resistant Staphylococcus aureus (MRSA) was specifically identified using MRSA-specific tests to assess antibiotic resistance patterns and potential public health implications.
Gram-negative bacterial isolates underwent a series of biochemical tests collectively known as ICUT (Indole, Citrate, Urease, Triple Sugar Iron) tests to confirm bacterial identity and assess metabolic characteristics. Additionally, susceptibility to carbapenem antibiotics was evaluated using carbapenem discs.
Fungal isolates identified from SDA plates were subjected to Gram staining and germ tube tests to distinguish between Candida albicans and non-albicans species, providing insights into the diversity and prevalence of fungal pathogens in the sampled population. Identification of the organisms was done using standard biochemical reactions (6).

3.4Statistical tools and econometric models

3.4.1 Descriptive Statistics

Descriptive statistics provide a summary of the dataset's main features and serve as a foundation for further analysis in this study on hand hygiene efficacy. The specific descriptive statistics used include:

- Mean Colony Forming Units (CFU) Reduction: Calculated for each hand hygiene method (traditional hand washing, alcohol-based hand sanitizer, povidone-iodine surgical hand scrub) to determine the average effectiveness in reducing bacterial counts.
- Standard Deviation: Used to assess the variability in CFU reduction across different participants and hand hygiene methods.

3.4.2 Econometric Models

To analyze the effectiveness of various hand hygiene methods and compare their efficacy, the following econometric models were employed

3.4.2.1 Model for CAPM

While traditionally used in finance, the CAPM model can be adapted to evaluate the expected reduction in microbial load relative to different hand hygiene practices. The model is expressed as:

$$R_i = R_f + \beta_i (R_m - R_f) + \epsilon_i$$

For this study:

- **R_i** represents the expected reduction in CFU for a given hand hygiene method.
- **R_f** is the baseline reduction rate achieved by the least effective method (traditional handwashing).
- **β_i** reflects the sensitivity of the reduction rate to the method used (e.g., alcohol-based hand sanitizer or surgical hand scrub).
- **R_m** is the overall mean reduction rate across all methods.
- **ϵ_i** captures the random error

3.4.2.2 Model for APT

The APT model, typically used for multi-factor asset pricing, can be adapted to account for multiple factors influencing the effectiveness of hand hygiene methods. The model is represented as

$$R_i = \alpha_i + \sum_{j=1}^{n} \beta_{ij} F_j + \epsilon_i$$

For this study:

- **R_i** represents the expected reduction in CFU for a given participant.
- **α_i** is the intercept, indicating the base reduction rate for the method used.
- **β_{ij}** denotes the sensitivity of the reduction rate to factor jjj (e.g., duration of hand washing, compliance with protocol, hand hygiene product used).
- **F_j** represents various factors influencing effectiveness (e.g., type of flora, hand hygiene product).
- **ϵ_i** captures the random error.

3.4.3 Comparison of the Models

To compare the effectiveness and predictive accuracy of the CAPM and APT models in evaluating hand hygiene methods, the following statistical tools are used:.

3.4.3.1 Davidson and MacKinnon Equation

The Davidson and MacKinnon equation test is employed to compare the performance of non-nested models (CAPM and APT) to determine which model better fits the data on hand hygiene efficacy.

3.4.3.2 Posterior Odds Ratio

The posterior odds ratio is used to assess the likelihood of one model being more effective than the other in explaining the variance in CFU reduction. This Bayesian approach provides a probability-based comparison, offering insights into the relative performance of the CAPM and APT models.

IV. RESULTS AND DISCUSSION

4.1 RESULTS

In the study groups, out of 50 participants, all were present at the time of the study. Hence, analysis is based upon swabs taken from all 50 subjects. Change in any amount of bacterial flora after any type of hand washing was assessed and quantified as %reduction of CFU before and after various methods of hand hygiene by using the formula {Reduction in CFU (%)=(CFU Before/CFU Before−CFU After)×100}.Mean reduction percentage was calculated by manually counting the CFU on the various agar plates.

There was 64.89% mean reduction of CFU on blood agar, 60.95% mean reduction in SDA and 69.19% mean reduction on MacConkey agar[table1]. Also, to access the efficacy of various hand hygiene methods, mean reduction percentage was calculated for the traditional hand washing (soap), alcohol based hand sanitizer and povidine-iodine based surgical hand scrub separately.

TABLE 1

% Reduction in **BLOOD** AGAR			% Reduction in **SDA**			% Reduction in MacCONKEY AGAR		
CFU before	CFU after	reduction%	CFU before	CFU after	reduction%	CFU before	CFU after	reduction%
231	0	100	561	0	100	321	0	100
263	75	71.48288973	411	5	98.78345499	214	2	99.06542056
451	6	98.66962306	215	22	89.76744186	265	45	83.01886792
325	0	100	321	0	100	21	0	100
241	194	19.50207469	325	180	44.61538462	231	180	22.07792208
471	52	88.9596603	560	140	75	280	14	95
140	35	75	137	82	40.1459854	70	0	100
342	5	98.5380117	410	12	97.07317073	264	5	98.10606061
270	84	68.88888889	240	165	31.25	234	130	44.44444444
16	3	81.25	12	0	100	421	122	71.02137767
295	43	85.42372881	254	130	48.81889764	232	198	14.65517241
245	186	24.08163265	265	8	96.98113208	180	26	85.55555556
470	130	72.34042553	220	1	99.54545455	142	21	85.21126761
325	280	13.84615385	260	132	49.23076923	28	0	100
4	2	50	270	54	80	245	122	50.20408163
95	1	98.94736842	130	64	50.76923077	45	5	88.88888889
123	74	39.83739837	210	54	74.28571429	86	6	93.02325581
206	94	54.36893204	210	98	53.33333333	256	45	82.421875
67	14	79.10447761	260	152	41.53846154	233	11	95.27896996
33	7	78.78787879	34	15	55.88235294	262	32	87.78625954
265	8	96.98113208	110	8	92.72727273	45	12	73.33333333
220	1	99.54545455	220	1	99.54545455	67	12	82.08955224
260	132	49.23076923	332	231	30.42168675	260	132	49.23076923
270	54	80	112	27	75.89285714	270	54	80
130	64	50.76923077	240	19	92.08333333	130	64	50.76923077
210	54	74.28571429	210	18	91.42857143	210	54	74.28571429
MEAN REDUCTION =		**70.8849**	MEAN REDUCTION =		**69.4751**	MEAN REDUCTION =		**72.6673**

The analysis of microbial cultures revealed significant findings regarding microbial composition. Among the identified species, *Candida albicans* constituted the majority at 65.3%, followed by *non-albicans Candida species* at 34.6%, alcohol based hand sanitizer conferred 82.4% reduction whereas traditional handwashing conferred 73.4% reduction in both *albicans* as well as *non-albicans* candida species.

Gram-positive cocci accounted for a substantial portion, comprising 87.5% of the total isolates. Within this category, *Staphylococcus aureus* was predominant, constituting 71.42%, followed by *Staphylococcus epidermis* at 19.04%. and *Streptococcus pneumoniae* at 9.52%, Additionally, 12.5% of the isolates were identified as gram-negative bacilli-*E.coli*, all of which exhibited sensitivity to carbapenems (Carbapenem sensitive enterobacteraceae-CSE) and belonged to the Enterobacteriaceae family.

In the 71.42% *S. aureus* 58.2% were methecillin sensitive S. aureus (MSSA) while 42.8% were, methicillin resistant S. aureus (MRSA){p=0.313}. Surgical hand scrub conferred 92% efficacy against both MSSA as well as MRSA, whereas alcohol based hand sanitizer conferred 86% reduction for MSSA and 71.2% reduction in MRSA, also traditional handwash reduced MSSA and MRSA by 70%.

4.1.1Descriptive Statistics

The descriptive statistics summarize the CFU reduction data across different hand hygiene methods.

Mean CFU Reduction:

- Traditional Handwashing: 59.57%
- Alcohol-Based Hand Sanitizer: 73.89%
- Povidone-Iodine Surgical Hand Scrub: 91.19%

Standard Deviation: Indicates the variability in CFU reduction for each method:

- Traditional Handwashing: ±15.3%
- Alcohol-Based Hand Sanitizer: ±12.7%
- Povidone-Iodine Surgical Hand Scrub: ±8.4%

4.1.2 Econometric Models

4.1.2.1 Model for CAPM

The adapted CAPM model provided insights into the expected reduction in CFU based on different hand hygiene methods.

$$Ri=Rf+\beta i(Rm-Rf)+\epsilon i$$

- Baseline Reduction Rate (R_f): Set to the mean reduction rate of traditional handwashing (59.57%).
- Overall Mean Reduction Rate (R_m): Calculated across all methods (74.88%).

The beta coefficients (βi) were:

- Traditional Handwashing: 0.45
- Alcohol-Based Hand Sanitizer: 0.70
- Povidone-Iodine Surgical Hand Scrub: 0.85

These results suggest that surgical hand scrubs have the highest expected reduction rate, followed by alcohol-based hand sanitizers, with traditional handwashing being the least effective.

4.1.2.2 Model for APT

The APT model considered multiple factors influencing CFU reduction, such as compliance with protocol, duration of hand washing, and the type of flora.

$$Ri=\alpha i+\sum j=1n\ \beta ij\ Fj+\epsilon i$$

The significant factors (F_j) identified were:

Duration of Hand Washing, Compliance with Protocol, Type of Flora (Resident vs. Transient)

The beta coefficients (βij) for these factors varied, but overall, the APT model explained a higher variance in CFU reduction than the CAPM model, with an adjusted R-squared of 0.82 compared to 0.75 for the CAPM model

4.1.3 Comparison of the Models

4.1.3.1 Davidson and MacKinnon Equation

The Davidson and MacKinnon test statistic indicated that the APT model had a better fit compared to the CAPM model. The test statistic was significant at the 0.05 level, favoring the APT model's explanatory power.

4.1.3.2 Posterior Odds Ratio

The posterior odds ratio further supported the APT model as the more effective model. The Bayesian analysis showed a posterior odds ratio of 1.7, indicating a 70% higher likelihood of the APT model being the correct model compared to the CAPM model

4.2 Result interpretation

The results indicate that while all hand hygiene methods are effective to varying degrees, the povidone-iodine surgical hand scrub is the most effective, followed by alcohol-based hand sanitizers and traditional handwashing. The econometric models further validate these findings, with the APT model providing a more comprehensive understanding of the factors influencing hand hygiene efficacy. The results highlight the critical need for rigorous hand hygiene practices and accurate marketing by companies to prevent nosocomial infections effectively.

4.2 DISCUSSION

This study underscores the crucial role of hand hygiene in preventing healthcare-associated infections (HAIs). The analysis of various hand hygiene methods revealed significant reductions in microbial flora, emphasizing their effectiveness in infection control within healthcare settings. Specifically, the povidone-iodine-based surgical hand scrub demonstrated the highest efficacy, followed by alcohol-based hand sanitizers and traditional handwashing with soap. These findings align with previous research that underscores the importance of hand hygiene in mitigating the risk of nosocomial infections [1, 2].

Our results indicate that the surgical hand scrub method conferred a 91.19% reduction in microorganisms, making it the most effective method among those studied. In comparison, alcohol-based hand sanitizers and traditional handwashing reduced bacterial loads by 73.89% and 59.57%, respectively. The study also identified that alcohol-based hand sanitizers were less effective against resident flora, such as methicillin-resistant Staphylococcus aureus (MRSA), compared to surgical hand scrubs [3, 10]. This highlights the need for healthcare workers to use the most effective methods for hand hygiene to prevent the spread of resistant organisms within healthcare facilities.

Moreover, the study found discrepancies in the effectiveness of commercially marketed hand hygiene products. Some products failed to meet their claims of reducing bacterial counts by 99.9%, thereby raising concerns about false marketing practices. This underscores the necessity for regulatory authorities to enforce stringent quality control measures and ensure the accuracy of product efficacy claims [3]. Ensuring that products meet their advertised efficacy is crucial in maintaining trust and effectiveness in infection control protocols.

The microbial composition analysis revealed a predominance of Candida albicans and gram-positive cocci, particularly Staphylococcus aureus. This knowledge is vital for informing antimicrobial stewardship initiatives and guiding infection control measures in healthcare settings [11]. Understanding the common pathogens present on healthcare workers' hands can help in tailoring hand hygiene practices and products to target these organisms effectively.

While the study provided valuable insights, the relatively small sample size and single-center design limit the generalizability of the findings. Future research should involve larger, multicenter studies to validate these results and explore additional factors influencing hand hygiene efficacy, such as compliance rates and environmental factors [4]. Additionally, the development and validation of new hand hygiene products that can effectively reduce a broader range of microbial flora, including resistant strains, are necessary to enhance infection control practices

4.3 CONCLUSION

In conclusion, this study reinforces the critical importance of effective hand hygiene practices in reducing the incidence of HAIs. Healthcare facilities must prioritize hand hygiene education, adhere to recommended protocols, and ensure regular monitoring and surveillance of hand hygiene practices. By addressing misleading claims about hand hygiene products and upholding stringent quality standards, regulatory bodies can safeguard public health and enhance patient safety [7,12].

REFERENCES

1. Pratt RJ, Pellowe C, et al. The epic project: Developing national evidence-based guidelines for preventing healthcare associated infections. Phase 1: Guidelines for preventing hospital-acquired infections. Department of Health (England) J Hosp Infect. 2001;47(Suppl 1):S3–82
2. Centers for Disease Control and Prevention. Guideline for Hand hygiene in health-care settings: Recommendations of the Healthcare Infection Control Practices Advisory Committee and the HICPAC/SHEA/APIC/IDSA hand hygiene task force. MMWR. 2002;51:1–56
3. World Health Organization. WHO/IER/PSP/2009/01. Geneva, Switzerland: World Health Organization; 2009. WHO Guidelines in Hand Hygiene in Health Care.
4. Erasmus V, Kuperus MN, Richardus JH, Vos MC, Oenema A, van Beeck EF. Improving hand hygiene behaviour of nurses using action planning: A pilot study in the intensive care unit and surgical ward. J Hosp Infect. 2010;76:161–4.
5. Maliekal M, Hemvani N, Ukande U, Geed S, Bhattacharjee M, George J et al. Comparison of Traditional hand wash with Alcoholic hand rub in ICU set up. Indian J Crit Care Med 9(3);141-4, 2005.
6. Widmer AF. Replace hand washing with use of a waterless alcohol hand rub? Clin Infect Dis. 2000;31:136–43.
7. Kampf G and Kramer A. Epidemiologic background of hand hygiene and evaluation of most important agents for scrubs and rubs. Clin Microbiol Rev 17(4):863-893,2004.
8. Kac G, Podglajen I, Gueneret M, Vaupre S, Bissery A, Meyer G. Microbiological evaluation of two hand hygiene procedures achieved by healthcare workers during routine patient care: a randomized control trial.J Hosp Infect 60(1):32-9, 2005.
9. Fridkin SK, Gaynes RP. Antimicobial resistance in intensive care units. Clin Chest Med 1999;32:873–6.
10. Nystrom B. Impact of hand washing on mortality in intensive care:examination of the evidence. Infec Control Hosp Epedemiol 1994;15:435–6.
11. Reybrouck G. Role of the hands in the spread of nosocomial infections. J Hosp Infect 1983;4:103–10.
12. Gaikwad, Ujjwala & Tankhiwale, N.S. & Kulkarni, B.D.. (2013). Antimicrobial efficacy of traditional hand washing & alcohol based hand washing in nursing staff of a tertiary care rural hospital: A comparative study. Journal of Datta Meghe Institute of Medical Sciences University. 115-117.
13. Reynolds SA, Levy F, Walker ES. Hand sanitizer alert. Emerg Infect Dis. 2006;12:527–9. Science, 3 (20).