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ORIGINAL ARTICLE

Impact of an intervention on the hand hygiene compliance rates in paediatric surgical intensive care units in two tertiary care hospitals

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Abstract

Hand hygiene (HH) is comprehensively recognized to be the single most significant measure to prevent cross-transmission of microorganisms between patients. This study aimed to measure the HH compliance rates baseline, identify the barriers for HH non-compliance and to assess the impact of multidisciplinary intervention. An interventional study conducted from March 2017 to July 2017 in two surgical paediatric intensive care units (PICU) in two tertiary care hospitals. Root cause analysis (RCA) was used for identification of the barriers that affect HH compliance followed by an intervention that included HH training and education, video presentations in the hospital internal circuit, visual cues, using a code word for gentle verbal reminding and HH champions for follow up. Direct observation of HH was done before and after the intervention applying the WHO HH observation method. HH compliance rate was calculated by dividing the number of HH actions by the total number of opportunities. Chi-square ($\chi 2$) test was used to identify statistical significance. A total of 1735 HH opportunities were observed during all phases of the study. RCA identified skin dryness, forgetfulness and work intensity as the most common barriers for non-compliance. Significant improvement was observed among all groups in PICU A (+23%; p value <0.001); (+19% for nurses, +29 % for doctors, and +36% for others; p value <0.001), while significant improvement was reported among doctors (+28%; p value <0.001) in PICU B. Improvement in HH compliance is achievable by multidisciplinary intervention. Providing continuous intensified training and feedback is essential to maintain a high level of HH compliance.

Keywords: Hand hygiene, compliance, intensive care unit, root cause analysis, tertiary healthcare, Kuwait.

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Introduction

Hand hygiene (HH) is universally recognized to be the single most significant measure to prevent cross-transmission of microbes from one patient to another.[1] The transfer of microorganisms by the hands of healthcare workers (HCWs) has been recognized as a main factor in the transmission of healthcare associated infections.[2,3] HH is the cornerstone measure of prevention of healthcare associated infection and to ensure safe patient care. However, HCWs' compliance with good HH practice is low in most locations.[4] Obedience to HH is an important objective of the International Patient Safety Goals.[5]

In the management of patients in the intensive care unit (ICU) HH is particularly important. The provision of care includes rather frequent close contact between HCWs and patients. Meanwhile, colonization of the ICU staff is common, transmission of microbes through the hands of HCWs is widespread, and the prevalence of multi-drug resistant organisms in the ICU is high. Critically ill patients are particularly susceptible to hospital acquired infections as a consequence of their altered immune state and various invasive devices.[6,7]

Numerous strategies have been assessed in an attempt to improve rates of HH, including those focusing on infrastructure changes, education, visual reminders, or ongoing monitoring and feedback programs. While these individual components have proven effective, interventions that combine these strategies into multimodal HH campaigns appear to be the most successful in improving HH adherence by HCWs.[2,8,9]

The World Health Organization (WHO) has adopted an evidence based multimodal HH strategy as part of the First Global Patient Safety Challenge.[10] The WHO Multimodal HH Strategy has been employed comprehensively in high income, resource intensive countries; however there remain limited data on the impact of such programs in middle and resource-limited countries.[4,11,12] This study was carried out to measure the rates of HH compliance before and after an intervention and to identify the barriers for HH and to educate HCWs about HH in the two studied paediatric surgical ICUs. The study employed the WHO HH observation method.

Methodology

Study Design

A prospective intervention study was conducted in five phases over a period of five months (March – July 2017).

Setting

Two paediatric surgical intensive care units (PICUs) in two tertiary care hospitals, affiliated with the Ministry of Health, Kuwait; IbnSina Hospital (site A) and Chest Diseases Hospital (site B). These are the only PICUs in the State of Kuwait. Site A: 6-bed unit (4-bed bay with 1 hand washing station in addition to 2 cubicle isolation rooms each with a sink); site B: 7-bed unit (6-bed bay with 2 hand washing stations in addition to 1 cubicle isolation room with a sink). Infection control team delivers provision with daily rounds. The PICUs are headed by a consultant anaesthesiologist / intensivist, who are assisted by paediatric intensivists, a head nurse and the number of staff nurses necessary to maintain a nurse-to-patient ratio of one-to-one most of the time. In addition, doctors from the surgical departments perform daily rounds in the PICUs to assess their patients. Ethical approval for this study was provided by the Ministry of Health Joint Commission for Research.

Inclusion criteria

All HH opportunities relevant to the indicated WHO 5 moments of HH for all patients admitted to the PICUs in the selected facilities during the study period. HH compliance rates were calculated using the WHO form that measures HH compliance (%) as actions/ opportunities X100.

Exclusion criteria

- All HH opportunities coming during any lifesaving condition for all patients admitted to the PICUs in the selected facilities during the study period.
- All HH opportunities that occur whenever the HCWs were seen to be anxious.

Data collection

Data collection technique/tools: Observation of HH was done using the WHO observation form for inpatients. The study was conducted through the following phases:

1. *Pre-intervention Phase:* Direct HH observation of HCWs was conducted to measure baseline HH compliance rate for a period of 1 month and for at least 200 opportunities based on the defined WHO 5 moments of HH:
   1. before patient contact,
   2. before an aseptic technique,
   3. after exposure to blood/body fluids,
   4. after patient contact and
   5. after contact with patient surroundings.[13]

   HH action either by hand wash or handrub was counted and in cases where both hand wash and hand rub were done we counted only hand wash. In each study site, the observers were the infection control team which consisted of one infection control doctor and infection control nurses. The observations were conducted daily, for a period of 30-minutes during the morning rounds. The observations were completed during direct patient care with no more than two HCWs observed at one time. The team conducted the HH compliance surveillance unremarkably. The observed HCWs were not informed about the plan, or timing of the observation periods all through the study period.[13]

2. *Wash-out period for 1 month:* We calculated the HH compliance for each HCWs category. Root cause analysis (RCA) was used for identification of the barriers that affect the compliance of HH among different HCW categories. RCA is a structured method used to analyze many problems in healthcare settings.[14] We chose the cause effect analysis technique fishbone diagram since we wanted to capture the causal relationship between the cause and effect and to stratify the causes into meaningful grouping. The focus of investigation and analysis is to identify why the event occurred and not who made the error. Therefore, the first step is to identify the problem, and then to analyze it by asking why did it happen. The causes of non-compliance to HH were classified under five headings: people, environment, policies, procedures and materials.

   Brainstorming and staff interviews were used to identify the causes. HCWs were interviewed to identify the most common barriers from their point of view that can affect their compliance to HH. Based on the finding of the RCA, we tackled the modifiable barriers by introducing an intervention to improve HH compliance.

3. *Intervention Phase:* Rigorous HH training and education to all HCWs of the two surgical PICUs was undertaken. Discipline-specific education that put HH within the context of an employee's daily work and processes was provided. We held four classes in each study site, to ensure that all the HCWs in different shifts had equal opportunity to attend for training.

   There were video presentations in the hospital internal circuit, demonstrations, visual cues that reinforced HH messages and training, which included brochures, hangers, and posters. The visual reminders were changed periodically so that they continued to be effective.

   Availability of supplies for HH alcohol based hand rub, chlorhexidine and disposable towels was ensured. Dispensers for alcohol-based hand rub were installed inside the patient's zone area and at the PICUs' entrance, and dispensers were filled-in regularly.

   A new idea was generated; in every shift, one of the PICU staff leaders was responsible for reminding her/his colleagues and other HCWs to perform HH by a gentle verbal reminder using a code word to be repeated among HCWs to signal her/his colleagues that they missed an opportunity of HH and need to clean their hands.

   A HH champion team, responsible for daily following up of all the steps of the intervention, was created.

4. *Wash-out period was for 1 month*

5. *Post-intervention phase:* HH observation to measure the improvement in the HH compliance rates was done for a period of 1 month and for at least 200 opportunities, based on the defined WHO 5 moments. The same methodology conducted in the pre intervention phase was implemented during the post intervention phase to ensure consistency.

Statistical analysis

Data were analyzed using a statistical software package IBM SPSS version 18 (SPSS Inc. Released 2009. PASW Statistics for Windows, Version 18.0. Chicago: SPSS Inc.). HH compliance rates were calculated by dividing the total number of actual performed HH actions, either hand wash or hand rub, by the total number of opportunities and multiplying the result by 100 and expressed as percentage.[13] Frequency tables were done with 95% confidence intervals. Rates are stratified by HCWs categories (doctors, nurses & others) in pre intervention and post intervention phases. Comparison between the two phases in each PICU was done using Chi-square (χ^2) test, and the differences were deemed statistically significant if p value was less than 0.05.

Results

A total of 1735 HH opportunities were observed in the two study units from the participating hospitals during all phases of the study. In both locations, the majority of opportunities were for the nursing staff, followed by doctors, then other categories. Data of RCA from the two sites revealed 10 different causes for HH non-compliance. We categorized the data into five groups to identify the specific interventions that are needed to improve compliance. The total number of HCWs interviewed were 88: 18 (20.5%) indicated that the hand rub has a strong smell and causes skin dryness; 18 (20.5%) forgot to do HH; 14 (15.9%) indicated that because of heavy work load or patient intensity they missed HH; 10 (11.4%) reported lack of time; 8 (9.1%) mentioned that they did not do HH due to shortage of paper towel; 8 (9.1%) did not see importance of doing HH and were not adherent to HH due to poor knowledge. The cause of non-compliance attributable to inconvenient locations of hand rub dispensers was reported by 77.9%. These barriers are displayed in fthe ish bone diagram shown in Figure 1.

Overall baseline compliance was higher in site B (76.1%) in comparison to site A (62.2%). Moreover the highest compliance rate among HCWs category was observed among nurses in both sites (68.2% in site A, versus 85.4% in site B). All HCWs in both sites displayed improvement in their compliance rate. The overall compliance rate improved significantly in site A (+23.5%, p<0.001), however in site B it increased only by 3.2%, which was not statistically significant (p= 0.23). There was a statistically significant improvement in HH compliance after the interventions for all HCWs in site A: for the nurses χ^2 = 20.1, p<0.001; doctors

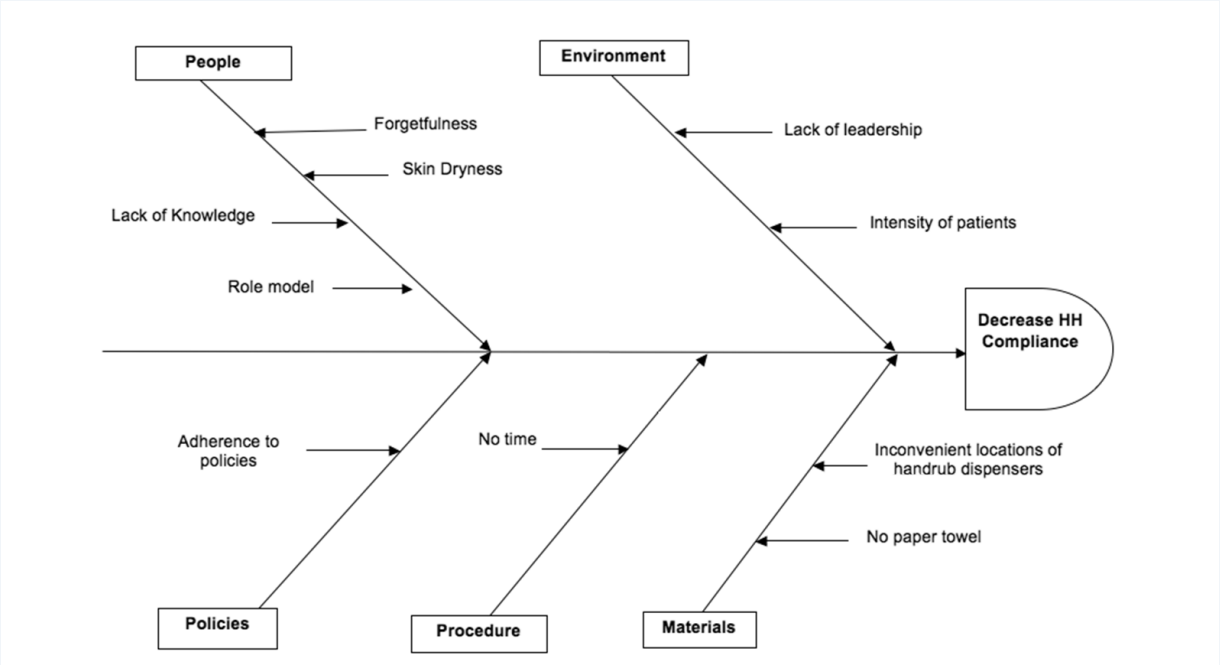

Figure 1. Root cause analysis fish bone diagram for hand hygiene barriers among healthcare workers in surgical PICU in the two study hospitals

Table I. Pre and post intervention hand hygiene compliance rates among healthcare workers in surgical PICU in the two study hospitals

		Pre-intervention		Post-intervention				
Surgical PICU location	Healthcare worker category	No. of HH opportunities	Hand Hygiene Compliance %	No. of HH opportunities	Hand Hygiene Compliance %	OR	95%C I	P value
Site A	Nurses	233	68.24	179	87.15	0.256	0.189-0.531	<0.001
	Doctors	103	51.46	77	80.52	0.317	0.129-0.508	<0.001
	Other	32	53.13	37	89.19	0.137	0.089-0.479	<0.001
	All	368	62.22	293	85.67	0.276	0.187-0.407	<0.001
Site B	Nurses	294	85.4	486	86.41	0.337	0.606-0.679	0.68
	Doctors	51	27.4	140	52.92	0.917	0.168-0.679	0.001
	Other	40	70	63	82.51	0.494	0.193-1.261	0.068
	All	385	76.1	689	79.25	0.834	0.619-1.124	0.23

χ^2 = 16.1, p<0.001; and the other category χ^2 = 11.2, p<0.001. Alternatively there was only a marginal increase in the overall rate of compliance in site B at the baseline versus post-intervention (76.1% vs. 79.3%; $p > 0.05$) while doctors showed statistically significant improvement at the post intervention phase (χ^2 = 9.7, p=0.001), data shown in Table I.

Discussion

Improving HH compliance is one of our main goals, especially during the care of critically ill patients. The current study demonstrated an overall baseline HH compliance of 69.1%, in contrast to a previous study conducted in an adult medical/ surgical ICU of a Kuwaiti teaching hospital that found the overall HH compliance was 43%.[15] Multiple studies also demonstrated the adherence of HCWs to HH was below 50%.[16-19] Moreover, Pittet and his colleagues found that compliance was higher among nurses than physicians and suggested that targeted educational programs may be useful.[19]

Several investigators conducted multimodal interventions and concluded that HH audits, routine feedback, education, visual cues and provision of alcohol-based hand rubs were successful in improving HH compliance.[12,20,21] The present study demonstrated improvement of overall HH compliance after implementation of a multidisciplinary HH intervention, from 69.1% to 81%. Several studies have been undertaken to improve HH compliance using diversity of interventions such as HCWs education, more sinks and availability of alcohol based hand rub as well as patient education.[4,21-23]

Bischoff *et al.* measured the effect of training, education and feedback on the rate of HH compliance among HCWs before and after patient contact and showed an improvement in HH from 10% to 23% before patient contact and from 22% to 48% after patient contact.[20] Another study was conducted in a teaching hospital ICU and demonstrated improvement in HH from 43% to 69% after HH campaign program.[15] Similar to our conclusions, HH compliance rate improved from 37.8% to 75.9% after an intervention study conducted in China.[24] Also the result of a cluster randomized controlled trial of a behaviourally designed feedback intervention in 60 hospital wards in England stated that HH intervention produced significant constant improvements in HH compliance.[25]

Improvement in HH compliance by HCWs has been difficult to achieve and varies due to diverse work environments, task requirements, HH best practice guidelines, education campaigns and auditing methods.[26] WHO reported that despite the different interventional methods used to improve HH compliance an increase in compliance rate is usually observed, however a sustainable improvement after implementation was rarely reported.[10]

As demonstrated by the present study, nurses demonstrated higher HH compliance when compared to doctors and others. This observation is concordant with the findings from a cross sectional study that identified a much higher compliance among nurses (71.9%) than for doctors (14.3%).[17] It was announced that doctors (as compared to nurses), high-intensity patient care, inadequate time and lack of institutional priority were some of the barriers that lead to poor HH compliance.[18,19,27] A successful intervention should be flexible enough and must focus on the different individual factors and interactions within the targeted group and setting.[28,29]

Different studies concluded that HH compliance rate varied inversely with the number of indications for HH, number of patients, the number of patient beds per room and working shifts.[16,30] This is in agreement with the current study in which lack of time and high patients' intensity were causes of HCWs non-compliance.

Skin irritation and dryness from frequent washing, availability of hand washing solutions, inconvenience or time constraints, and limited awareness of, or partial agreement with, HH guidelines were stated in multiple studies as important barriers to doctors' ultimate HH compliance.[31-34] Our investigation identified inconvenient locations of hand rub dispensers and poor role modelling were factors that hindered adherence to HH, which is similar to other researchers' findings that expressed the inconvenient location of hand rub dispensers was one of the consistent causes for poor HH compliance. In addition to these factors, poor role modelling in ICU was contributing to low rates of HH among intensivists.[35,36]

Limitations

We could not evaluate which of the specific interventions had the greatest effect on improving HH because multiple interventions were applied at the same time. Finally, even though we have good improvements in HH compliance, we did not relate this improvement to healthcare associated infection outcomes in the study hospitals.

Conclusion

Hand hygiene compliance remains an infection prevention and control priority. Although improvement in HH compliance is a complex challenge, it is achievable by multidisciplinary intervention. Providing continuous intensified education, training, reminding and feedback is essential to maintain a high level of HH compliance.

Altering human behaviour, HH role models, and providing suitable work environment, materials and infrastructure are essential to attain a high level of hand hygiene compliance. A high level of HH is every HCW's responsibility and should always be engaged in all healthcare facilities.

References

1. Larson EL. APIC guideline for hand washing and hand antisepsis in healthcare settings. *Am J Infect Control* 1995; **23(4):** 251-269. https://doi.org/10.1016/0196-6553(95)90070-5
2. Pittet D, Allegranzi B, Sax H, *et al*. Evidence-based model for hand transmission during patient care and the role of improved practices. *Infect Dis* 2006; **6:** 641-652. https://doi.org/10.1016/S1473-3099(06)70600-4
3. Larson E. A causal link between hand washing and risk of infection. Examination of the evidence. *Infect Control Hosp Epidemiol* 1988; **9:** 28-36. https://doi.org/10.2307/30144131
4. Allegranzi B, Sax H, Bengaly L, *et al*. Successful implementation of the World Health Organization hand hygiene improvement strategy in a referral hospital in Mali, Africa. *Infect Control Hosp Epidemiol* 2010; **31 Suppl 2:** 133-141. https://doi.org/10.1086/649796
5. Soule BM, Memish Z, Malani PN. Best Practices in Infection Prevention and Control. An International Perspective, 2nd edn. Ilinois, Joint Commission International 2012; 19-33.
6. Gold H. Vancomycin resistant enterococci: mechanism and clinical observation. *Clin Infect Dis* 2001; **33:** 210-219. https://doi.org/10.1086/321815
7. Albert RK, Condie F. Hand washing patterns in medical intensive care units. *N Engl J Med* 1981; **24:** 1465-1466. https://doi.org/10.1056/NEJM198106113042404
8. Rosenthal VD, Pawar M, Leblebicioglu H, *et al*. Impact of the International Nosocomial Infection Control Consortium (INICC) multidimensional hand hygiene approach over 13 years in 51 cities of 19 limited-resource countries from Latin America, Asia, the Middle East, and Europe. *Infect Control Hosp Epidemiol* 2013; **34:** 415–423. https://doi.org/10.1086/669860

9. Allegranzi B, Pittet D. Role of hand hygiene in healthcare-associated infection prevention. *J Hosp Infect* 2009; **73:** 305–315. https://doi.org/10.1016/j.jhin.2009.04.019
10. World Health Organization. WHO guidelines for hand hygiene in healthcare. First Global Patient Safety Challenge, Clean Care is Safer Care, Geneva, World Health Organization 2009; 99-124.
11. Grayson ML, Jarvie LJ, Martin R, *et al*. Significant reductions in methicillin-resistant *Staphylococcus aureus* bacteremia and clinical isolates associated with a multisite, hand hygiene culture-change program and subsequent successful statewide roll-out. *Med J Aust* 2008; **188:** 633–640.
12. Pittet D, Hugonnet S, Harbarth S, *et al*. Effectiveness of a hospital-wide program to improve compliance with hand hygiene. Infection control programme. *Lancet* 2000; **356:** 1307–1312. https://doi.org/10.1016/S0140-6736(00)02814-2
13. World Health Organization. SAVE LIVES: Clean your hands. Hand hygiene technical reference to be used by health-care workers, trainers and observers of hand hygiene practices, Geneva, World Health Organization 2009; 17-26.
14. Wilson PF, Dell LD, Anderson GF. Root Cause Analysis: A Tool for Total Quality Management, Wisconsin: ASQ Quality Press 1993; 8–17.
15. Salama MF, Jamal WY, Al Moussa HA, Al-Abdulghani KA, Rotimi VO. The effect of hand hygiene compliance on hospital-acquired infections in an ICU setting in a Kuwaiti teaching hospital. *J Infect Public Health* 2013; **6:** 27-34. https://doi.org/10.1016/j.jiph.2012.09.014
16. Kuzu N, Ozer F, Aydemir S, Yalcin AN, Zencir M. Compliance with hand hygiene and glove use in university affiliated hospital. *Infect Control Hosp Epidemiol* 2005; **26(3):** 312-315. https://doi.org/10.1086/502545
17. Patarakul K, Tan-Khum A, Kanha S, Padungpean D, Jaichaiyapum O. Cross-sectional survey of hand-hygiene compliance and attitudes of healthcare workers and visitors in the intensive care units at King Chulalongkorn Memorial Hospital. *J Med Assoc Thai* 2005; **88 Suppl 4:** S287-293.
18. Pittet D. Improving adherence to hand hygiene practices: a multidisciplinary approach. *Emerg Infect Dis* 2001; **7:** 234-240. https://doi.org/10.3201/eid0702.010217
19. Pittet D, Mourouga P, Perneger TV. Compliance with hand washing in a teaching hospital. *Ann Intern Med* 1999; **130:** 126-130. https://doi.org/10.7326/0003-4819-130-2-199901190-00006
20. Bischoff WE, Reynolds TM, Sessler CN, Edmond MB, Wenzel RP. Handwashing compliance by healthcare workers: The impact of introducing an accessible, alcohol-based hand antiseptic. *Arch Intern Med* 2000; **160:** 1017–1021. https://doi.org/10.1001/archinte.160.7.1017
21. Hugonnet S, Perneger TV, Pittet D. Alcohol-based handrub improves compliance with hand hygiene in intensive care units. *Arch Intern Med* 2002; **162:** 1037-1043. https://doi.org/10.1001/archinte.162.9.1037
22. Lankford MG, Zembower TR, Trick WE, Hacek DM, Noskin GA, Peterson LR. Influence of role models and hospital design on hand hygiene of healthcare workers. *Emerg Infect Dis* 2003; **9:** 217–223. https://doi.org/10.3201/eid0902.020249
23. McGuckin M, Storr J, Longtin Y, Allegranzi B, Pittet D. Patient empowerment and multimodal hand hygiene promotion: A win-win strategy. *AM J Med Qual* 2011; **26:** 10-17. https://doi.org/10.1177/1062860610373138
24. Mu X, Xu Y, Yang T, *et al*. Improving hand hygiene compliance among healthcare workers: An intervention study in a hospital in Guizhou Province, China. *Braz J Infect Dis* 2016; **20(5):** 413–418. https://doi.org/10.1016/j.bjid.2016.04.009
25. Fuller C, Michie S, Savage J, *et al*. The Feedback Intervention Trial FIT-- improving hand hygiene compliance in UK healthcare workers: a stepped wedge cluster randomized controlled trial. *PLoS One* 2012; **7(10):** e41617. https://doi.org/10.1371/journal.pone.0041617
26. Chagpar A, Banez C, Lopez R, Cafazzo JA. Challenges of hand hygiene in healthcare: The development of a tool kit to create supportive processes and environments. *Healthc Q* 2010; **13 Spec No:** 59-66. https://doi.org/10.12927/hcq.2010.21968
27. Ashu SM, Smitha EG, John A. Efficacy of a multimodal intervention strategy in improving hand hygiene compliance in a tertiary level intensive care unit. *Indian J Crit Care Med* 2011; **15(1):** 6–15. https://doi.org/10.4103/0972-5229.78215
28. Kretzer EK, Larson EL. Behavioral interventions to improve infection control practices. *Am J Infect Control* 1998; **26:** 245-253. https://doi.org/10.1016/S0196-6553(98)80008-4
29. Pittet D. Improving compliance with hand hygiene in hospitals. *Infect Control Hosp Epidemiol* 2000; **21:** 381-386. https://doi.org/10.1086/501777
30. Arenas MD, Sánchez-Payá J, Barril G, *et al*. A multicentric survey of the practice of hand hygiene in haemodialysis units: factors affecting compliance. *Nephrol Dial Transplant* 2005; **20(6):** 1164-1171. https://doi.org/10.1093/ndt/gfh759
31. Pittet D. Compliance with hand disinfection and its impact on hospital acquired infection. *J Hosp Infect* 2001; **48 Suppl A:** S40-S46.
32. Boyce JM, Kelliher S, Vallande N. Skin irritation and dryness associated with two hand-hygiene regimens: soap-and-water hand washing versus hand antisepsis with an alcoholic hand gel. *Infect Control Hosp Epidemiol* 2000; **21(7):** 442-448. https://doi.org/10.1086/501785
33. Larson E, Kretzer EK. Compliance with handwashing and barrier precautions. *J Hosp Infect* 1995; **30:** 88-106. https://doi.org/10.1016/0195-6701(95)90010-1
34. Zimakoff J, Kjelberg AB, Larson SO, Holstein B. A multicenter questionnaire investigation of attitude towards hand hygiene. *Am J Infect Control* 1992; **20:** 58-64. https://doi.org/10.1016/S0196-6553(05)80002-1
35. Qushmaq IA, Heels-Ansdell D, Cook DJ, Loeb MB, Meade MO. Hand hygiene in the intensive care unit: prospective observations of clinical practice. *Pol Arch Med Wewn* 2008; **118(10):** 543-547.
36. Chassin MR, Mayer C, Nether K. Improving hand hygiene at eight hospitals in the United States by targeting specific causes of noncompliance. *Jt Comm J Qual Patient Saf* 2015; **41(1):** 4-12. https://doi.org/10.1016/S1553-7250(15)41002-5