Central Line–Associated Bloodstream Infections in Limited-Resources Countries: A Review of the Literature

Victor D. Rosenthal
Bernal Medical Center, Infection Control and Infectious Diseases Department, Buenos Aires, Argentina

q1 **Central line–associated bloodstream infections (CLABSIs) are considered a significant cause of mortality in hospitalized patients; however, the incidence of CLABSIs in limited-resources countries has not been explored analytically. Likewise, the appropriate interventions to prevent, control, and reduce CLABSIs have yet to be analyzed thoroughly. This review demonstrates that CLABSIs are associated with significant extra mortality, with an odds ratio ranging from 2.8 to 9.5. The results of 6 sequential prospective interventional studies showed that hand hygiene and educational programs were related to a significant reduction in CLABSI rates. CLABSI rates in limited-resources countries are higher than US National Healthcare Safety Network benchmark rates and have a significant impact on mortality. Studies showing successful interventions for a reduction in CLABSIs are few. Subsequently, it can be inferred that additional epidemiological studies need to be conducted to achieve an appreciation of the effects of CLABSIs and to develop more-definitive approaches for CLABSI prevention in the form of practical, low-cost, low-technology measures that are feasible to implement in limited-resources countries.**

Vascular access poses significant potential risks of iatrogenic complications in general but in particular of central line–associated bloodstream infections (CLABSIs). Almost 60% of all types of nosocomial bacteremia are originated by some form of vascular access [1]. For this reason, intensive care practices have increasingly focused on the development of reliable and safe vascular access procedures, which have often been underestimated. In studies conducted >10 years ago, it was determined that CLABSIs are related to excess attributable mortality [2] and that the impact of CLABSIs on patient outcomes was directly related to an increase in the length of stay and extra health care costs, amounting to US$30,000 per case [3].

In most cases, CLABSIs can be prevented. Thus, hospital policies and care procedures should be directed toward the adoption of preventive measures rather than merely the identification and treatment of CLABSIs. During the past 15 years, there have been major advances in understanding the epidemiology and pathogenesis of CLABSIs [4]. A recent study conducted in a developed country suggested that CLABSIs can be prevented by applying 5 measures—hand hygiene, using full barrier precautions during the insertion of central venous catheters, cleaning the skin with chlorhexidine, avoiding the femoral site if possible, and removing unnecessary catheters [5]. Because of resource constraints, it is unclear whether such methods can be effectively adopted to prevent CLABSIs in limited-resources countries; additionally, if all the preventions cannot be implemented, which are the most important remains to be seen. The situation of CLABSIs in low- and middle-income countries has not yet been analyzed systematically. The main objective of this review is to estimate the CLABSI rate, extra mortality, and the impact of interventions to significantly reduce the CLABSI rate at different types of intensive care units (ICUs) in low-income countries.

METHODS

Search strategy. Full text articles in English or Spanish published from January 1998 through September 2008 were retrieved from Medline and the Cochrane Library to analyze investigations related to CLABSIs in limited-resources countries (as determined by the World Bank). Articles included in the bibliographic references of key reviews were also searched. The reviewer did not use information presented as abstracts at meetings (such as the Infectious Diseases Society of America's annual q2
meeting, the Interscience Conference on Antimicrobial Agents

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Reprints or correspondence: Dr Bernal Medical Center, Infection Control and Infectious Diseases Dept, Lavalleja 305, Floor 9, Apr B, Buenos Aires, 1414, Argentina (victor_rosenthal@inicc.org).
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and Chemotherapy, the Society for Healthcare Epidemiology's International Conference on Healthcare-Associated Infections, or any other national or international scientific meeting presented worldwide during the same period).

A combination of Medical Subject Heading terms was applied: ("central line" or "central vascular catheter" or "central venous catheter" or "device associated" or "Intravascular device" or "hospital" or "nosocomial" or "health care acquired") and ("bacteremia" or "bloodstream infection") and ("developing countries" or "limited resources" or "low income" or q3 "each name of the 144 limited-resource countries as defined by the World Bank list and definition").

The World Bank classifies countries into 4 economic strata according to 2007 gross national income per capita. These q4 groups are as follows: low income, US$935 or less; lower middle income, US$936–US$3705; upper middle income, US$3706–US$11,455; and high income, US$11,456 or more [6]. Low-income and middle-income economies (categories 2, 3, and 4) q5 are sometimes referred to as developing economies, developing countries, lower-income countries, low-resources countries, or emerging countries. These economies represent 144 (68.8%) of 209 countries of the world and >75% of the world population. In this review of the literature, it was found that only 10 (6.9%) of 144 countries reported their CLABSI rates using standardized definitions and methods.

On the basis of the search strategy described above, articles that appeared to be potentially relevant were identified by the reviewer after reviewing titles and abstracts of articles. Full articles were obtained for those that appeared to be potentially relevant. The reviewer, after reading the full texts, independently assessed the eligibility of all studies identified using eligibility criteria based on the inclusion criteria outlined above.

Study identification. The reviewer included all studies from limited-resource countries that

Table 1. Analyzed Studies

Country and reference	Year	ICU(s) studied	Target population	Patients, no.
Argentina [30]	2004	Medical	Adult	2525
Argentina [31]	2003	Medical, surgical, coronary	Adult	840
Argentina [32]	2004	Medical, surgical, coronary	Adult	992
Argentina [33]	2003	Medical, surgical, coronary	Adult	184
Argentina [34]	2003	Medical-surgical	Adult	213
Argentina [35]	2004	Medical-surgical-cardiovascular	Adult	3319
Argentina [36]	1998	Neonatal	Neonatal	725
Brazil [37]	2003	Burn	Adult, pediatric	320
Brazil [38]	2005	Medical	Adult	22
Brazil [39]	2008	Medical-surgical	Adult	1031
Brazil [40]	2007	Neonatal	Neonatal	2286
Brazil [41]	2002	Neonatal	Neonatal	225
Brazil [42]	2004	Neonatal	Neonatal	4878
Brazil [43]	2003	Pediatric	Pediatric	515
Colombia [44]	2006	Medical-surgical-coronary, pediatric	Adult, pediatric	2172
Colombia [45]	2007	Neonatal	Neonatal	289
India [46]	2007	Medical-surgical-neurosurgical	Adult	10,835
Iran [47]	2003	Burn	Adult	106
Mexico [48]	2007	Medical, surgical, neurosurgical	Adult	110
Mexico [49]	2005	Medical, surgical-neurosurgical	Adult	470
Mexico [50]	2006	Medical-surgical-neurosurgical	Adult	1055
Peru [51]	2008	Medical-surgical	Adult, pediatric	1920
Thailand [13]	2004	Neonatal	Neonatal	129
Thailand [52]	2004	Neonatal	Neonatal	2029
Tunisia [53]	2007	Neonatal	Neonatal	647
Turkey [54]	2008	Cardiovascular-surgical-anesthesiology-reanimation-neurosurgical	Adult, pediatric	1387
Turkey [55]	2006	Medical-surgical	Adult	1985
Turkey [56]	2007	Medical-surgical	Adult, pediatric	3288
Turkey [57]	2007	Medical-surgical	Adult	241
Turkey [29]	2007	Medical-surgical	Adult	133

NOTE. ICU, intensive care unit.

Table 2. Central Line–Associated Bloodstream Infection (CLABSI) Rates

Country and reference	Year	ICU(s) studied	Total CLABSIs (LCBIs + CSEP), no.	CL days, no.	CLABSI rate (95% CI)[a]
Argentina [35]	2004	Coronary	23	1618	14.2 (9.0–21.2)
Argentina [30]	2004	Medical	13[b]	4770	2.7 (1.4–4.6)
Argentina [34]	2003	Medical-surgical	41	919	44.6 (32.2–60.0)
Argentina [35]	2004	Medical-surgical	135	4452	30.3 (25.4–35.7)
Brazil [37]	2003	Burn	230	6765	34.0 (29.8–35.5)
Brazil [39]	2008	Medical-surgical	86	9494	9.1 (7.2–11.1)
Brazil [40]	2007	Neonatal	215	69,491	3.1 (2.6–3.5)
Brazil [41]	2002	Neonatal	19	316	60.0 (36.5–92.3)
Brazil [42]	2004	Neonatal	37	8635	4.3 (3.0–5.9)
Brazil [43]	2003	Pediatric	24	2120	10.2 (7.2–16.7)
Colombia [44]	2006	Medical-surgical-coronary, pediatric	126	11,110	11.3 (9.4–13.4)
Colombia [45]	2007	Neonatal	23	1701	13.5 (8.5–20.2)
India [46]	2007	Medical-surgical-neurosurgical	292	36,857	7.9 (7.0–8.8)
Iran [47]	2003	Burn	30 [b]	1739	17.0 (11.6–24.5)
Mexico [50]	2006	Medical-surgical-neurosurgical	149	6450	23.1 (19.5–27.1)
Peru [51]	2008	Medical-surgical	50	6514	7.7 (5.7–10.1)
Thailand [52]	2004	Neonatal	15	5667	2.6 (1.4–4.3)
Tunisia [53]	2007	Neonatal	26	1847	14.8 (9.2–20.5)
Turkey [54]	2008	Anesthesiology-reanimation	3	721	4.1 (0.8–12.1)
Turkey [54]	2008	Surgical-cardiothoracic	1	608	1.6 (0–9.1)
Turkey [55]	2006	Medical-surgical	130	13,402	9.7 (8.1–11.5)
Turkey [56]	2007	Medical-surgical	400	22,782	17.6 (15.8–19.3)
Turkey [54]	2008	Neurosurgical	1	115	8.6 (0–47.4)

NOTE. CI, confidence interval; CL, central line; CSEP, clinical sepsis; ICU, intensive care unit; LCBI, laboratory-confirmed bloodstream infection.
[a] No. of CLABSIs per 1000 CL days.
[b] Studies that did not collect data on CSEP (only on LCBIs).

1. applied the definitions and methods of the US Centers for Disease Control and Prevention (CDC) National Nosocomial Infection Surveillance System or National Healthcare Safety Network (NHSN) [7–9];
2. analyzed adult, pediatric, and newborn patients who stayed in the ICU;
3. assessed clinical sepsis and/or laboratory-confirmed bloodstream infections and analyzed the number of CLABSIs;
4. were prospective cohort surveillance studies or case-control studies designed to identify the CLABSI rate and extra mortality; and
5. were randomized clinical trials or sequential studies evaluating the impact on the CLABSI rate.

Data abstraction and outcome measures. The reviewer extracted data from each included study by means of a predefined data-extraction form. Details on the study design, the aim of the study, the setting of the study, the study quality characteristics, the study period, the interventions used, outcome data, potential confounding factors, and results were extracted. The quality of included prospective cohort and case-control studies was assessed using checklists recommended by the Scottish Intercollegiate Guidelines Network.

Table 3. Central Line–Associated Bloodstream Infection (CLABSI) Extra Mortality

Country and reference	Year	Target population	ICU(s) studied	Patients with CLABSI, no.	Patients without DAI, no.	Mortality, %		OR (95% CI)
						CLABSI	Non-DAI	
Argentina [34]	2003	Adult	Medical, surgical	24	43	62.5	37.2	2.8 (1.0–7.8)
Argentina [34]	2003	Adult	Medical, surgical, coronary	142	142	54.2	29.6	2.8 (1.7–4.5)
Mexico [48]	2007	Adult	Medical, surgical, neurosurgical	55	55	41.8	21.8	2.5 (1.1–5.9)
Thailand [13]	2004	Neonatal	Neonatal	45	184	27.0	7.0	5.2 (2.1–12.5)
Tunisia [53]	2007	Neonatal	Neonatal	38	509	42.0	5.9	9.5 (4.6–19.7)

NOTE. CI, confidence interval; DAI, device-associated infection; ICU, intensive care unit; OR, odds ratio.

Table 4. Interventional Studies Aiming at Central Line–Associated Bloodstream Infection (CLABSI) Reduction in Developing Countries

Country and reference	Year	ICU(s) studied	Intervention	CLABSI rate[a] Before	CLABSI rate[a] After	Difference (95% CI)
Argentina [31]	2003	Medical, surgical, coronary	Hand hygiene, catheter care, education, performance feedback	45.9	11.1	34.8 (32.1–37.5)
Argentina [32]	2004	Medical, surgical, coronary	Closed infusion system	6.5	2.4	4.2 (3.8–4.6)
Brazil [38]	2005	Medical	Hand hygiene, education, performance feedback	20.0	11.0	9.0 (28.2–46.2)
Mexico [49]	2005	Medical, surgical	Hand hygiene, education, performance feedback	46.0	19.5	265 (22.4–30.6)
Turkey [57]	2007	Medical-surgical	Education, performance feedback	13.0	7.6	5.4 (3.3 –7.6)
Argentina [36]	1998	Neonatal	Hand hygiene, catheter care, aseptic technique	20.0	12.4	7.6 (6.6–8.6)

NOTE. CI, confidence interval; ICU, intensive care unit.
[a] No. of CLABSIs per 1000 central line days.

The reviewer originally aimed to perform meta-analyses in this review. However, on closer examination of the results of the primary studies, it was determined that any form of pooled statistical analyses was not possible.

Data analysis. EpiInfo software, version 6.04b (Epitable Calculator; CDC), was used for data analysis. Rates of CLABSIs were analyzed, and 95% confidence intervals (CIs) were calculated to compare the different rates between studies.

For CLABSIs, mortality odds ratios with 95% CIs were determined for all study outcomes. For the effect of educational interventions on CLABSI rates, differences among studies were analyzed, and 95% CIs were calculated to compare the different rates between studies.

RESULTS

On the basis of a review of the abstracts of the articles, 99 studies were initially identified as being potentially eligible for inclusion, but no systematic review was found at the Cochrane
q6 Library. After the full text of these 99 studies were reviewed, 49 were excluded for the following reasons: 38 because they
q7 showed only overall health care–associated infection rates, 10 because they showed only ventilator-associated pneumonia rates, and 1 because it showed only catheter-associated urinary tract infection rates.

After the remaining 50 studies showing only CLABSI rates were reviewed, 20 were further excluded: 6 studies were excluded because they expressed the CLABSI rate per the number of patients instead of the number of central line (CL) days [10–14]; 3 studies were excluded because they expressed the CLABSI rate per the number of bed days instead of the number of CL days [15–17]; 2 studies were excluded because they were pooled reports that included data also published independently [18, 19]; 3 descriptive studies were excluded because they did not provide the numerators and denominators necessary to conduct the present analysis [20–22]; 1 study was excluded because it did not provide the definition of the studied population [23]; 2 studies were excluded because they did not apply CDC definitions [24, 25]; 2 studies were excluded because they did not apply CDC definitions and did not provide the numerators and denominators necessary to conduct the present analysis [26, 27]; and 1 randomized study was excluded because it did not provide the numerators and denominators necessary to conduct the present analysis [28]. One randomized study was analyzed independently, because it was not an interventional sequential study, as were the remaining 6 studies [29]. q8

A summary of the characteristics of the 30 included studies q9
is shown in Table 1. q10

CLABSI rates. The CLABSI rate was reported in 14 studies for different types of adult and pediatric ICUs that applied the CDC NHSN definition (Table 2). The CLABSI rate was reported in 6 studies for neonatal ICUs (NICUs) that applied the CDC q11
NHSN definition (Table 2).

CLABSI extra mortality. CLABSI extra mortality was reported in 3 studies for different types of adult and pediatric ICUs (Table 3) and for 2 NICUs (Table 3) that applied the CDC NHSN definition.

Impact of interventions on CLABSI rates. Sequential in- q12
terventions were described in 5 studies conducted at adult and pediatric ICUs (Table 4) and at 1 NICU (Table 4) that applied the CDC NHSN definition. Osma et al [29] conducted a randomized controlled trial to evaluate the impact of central venous catheters impregnated with chlorhexidine and silver sulphadiazine on the rate of CLABSI in the ICU. The CLABSI rates were reported as 5.3 cases per 1000 CL days for the antiseptic catheter group and 1.6 cases 1000 CL days for the standard catheter group ($P = .452$).

DISCUSSION

This review reveals variability in the incidence of and the mortality resulting from CLABSIs in low-income countries. The

Figure 1. Low-resource intensive care units (ICUs) with outdated technology: (1) crowded ICU; (2) 3-way stopcock; (3) open glass intravenous container with air filter; (4) ICU with 42 beds and no sinks; (5) central line insertion with no maximal barriers; (6) open semirigid plastic intravenous container with inserted needle; (7) sinks at a neonatal ICU with no antiseptic soap; (8) wet cloth towel; (9) open burette intravenous container with air filter.

rate of CLABSIs in limited-resource countries ranged from 1.6 to 44.6 cases per 1000 CL days in adult and pediatric ICUs and from 2.6 to 60.0 cases per 1000 CL days in NICUs. Several factors can explain these diverse rates, including variability in infection control and critical care practices, differences in patient populations, and variability in the methods applied for data collection and in the definition of CLABSI. It should be noted, however, that these rates reflect the situation in limited-resource countries that apply surveillance programs, indicating that these hospitals have some form of organizational health care structure [58]. In comparison with those facilities that lack such health care structure, it may be expected that CLABSI rates are higher possibly as a result of the absence of adequate surveillance methods that would enable them to apply infection-control practices.

These results can be compared with CDC NHSN hospitals in the United States, which report a mean CLABSI rate of 1.5 cases per 1000 CL days (95% CI, 1.3–1.5) in medical-surgical q13
ICUs and of 2.9 cases per 1000 CL days (95% CI, 2.6–3.1) in NICUs [9]. When comparing CLABSI rates in medical-surgical ICUs of Argentina, Brazil, Peru, and Turkey or CLABSI rates in NICUs of Brazil, Colombia, Thailand, and Tunisia, it was noticed that the 95% CIs did not overlap with CDC NHSN q14
CLABSI rates, meaning that CLABSI rates in low-resources countries are significantly higher in both medical-surgical ICUs and NICUs. As noted, CLABSI rates in limited-resource countries reveal an evident difference compared with industrialized countries. The prima facie explanation may be based on the fact that limited-resource countries lack resources, appropriate medical supplies, and sufficient skilled manpower.

Several of the studies included in this review have identified some of the main factors related to high CLABSI rates in ICUs of limited-resource countries [18, 19]. In those few instances where infection-control programs are regulated, compliance

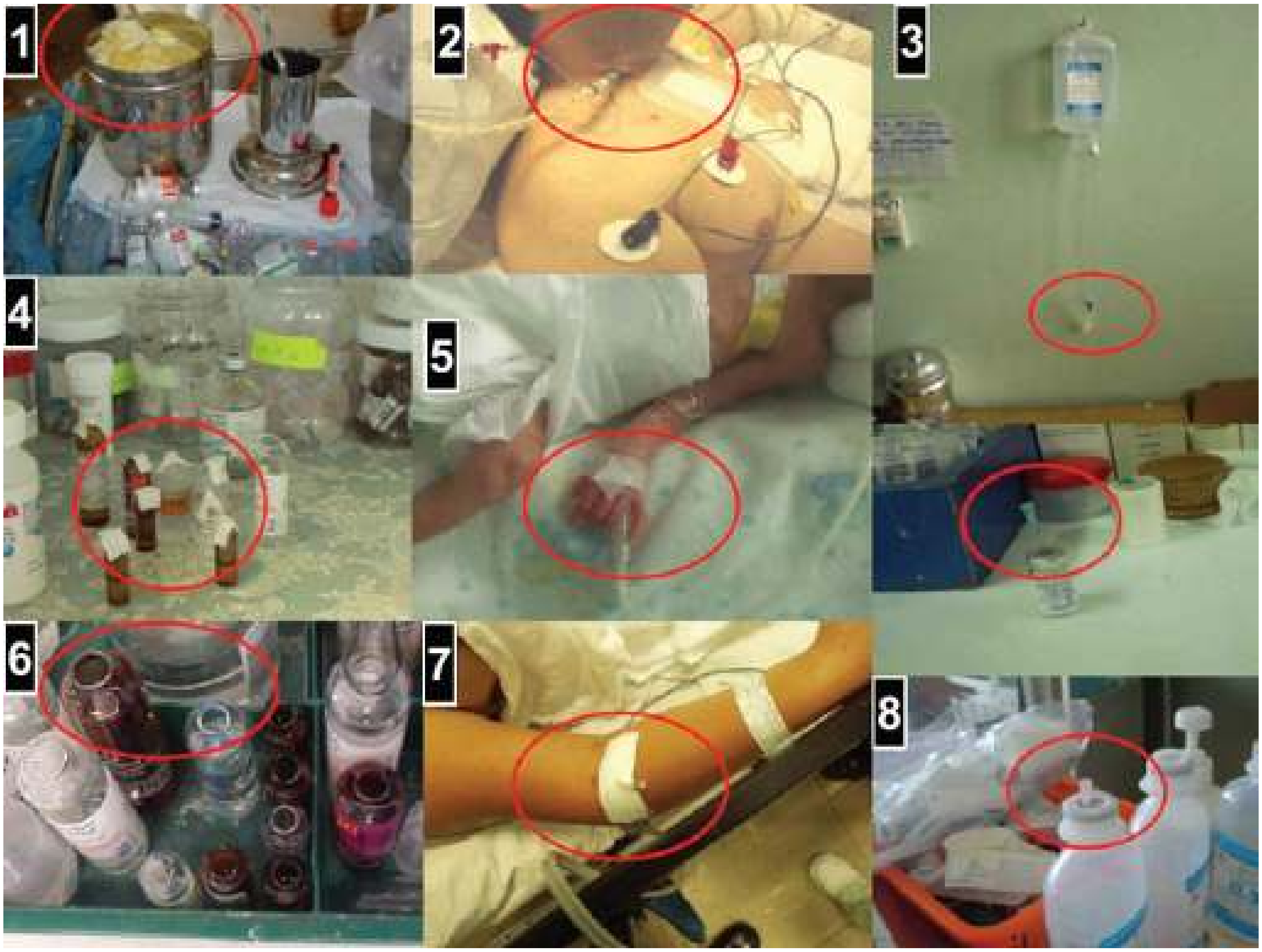

Figure 2. Low-resource intensive care units (ICUs) with outdated technology: (1) cotton balls already impregnated with a contaminated antiseptic; (2) central line in place with no dressing; (3) open semirigid intravenous container with administration set and 3-way stopcock for intravenous preparation; (4) one-use vials used multiple times and covered with contaminated tape; (5) peripheral line in a newborn with no sterile dressing; (6) one-use vials used multiple times; (7) peripheral line in an adult patient with no sterile dressing; (8) semirigid plastic container used for intravenous preparation.

with the rules is poor [58, 59]. In addition, infection-control surveillance and hospital accreditation are not mandatory at the national level, and compliance with hand hygiene measures is significantly variable in most hospitals [60]. The International Nosocomial Infection Control Consortium (INICC) (http://www.INICC.org) was established internationally in 2002 and is now prospectively collecting data from 29 low-resources countries to measure and reduce health care–associated infection rates in hospitals by focusing on education, feedback of outcome surveillance (infection rates), and process surveillance (compliance with infection-control measures) [58, 59]. INICC representatives have visited many different ICUs in several limited-resource countries and assessed their medical practices with the aim of achieving the mission and goals of the organization—training health care workers, measuring health care–
q15 associated infections by standardized methods and definitions based on those of the CDC NHSN, and reducing the frequency of these infections by applying evidence-based medicine [18, 19, 59]. The INICC team has provided health care workers with training in infection-control practices and surveillance methods. Among their most common observations were overcrowded ICUs, insufficient rooms for isolation, lack of sinks, and lack of medical supplies in general, including but not limited to alcohol hand rub, antiseptic soap, and paper towels (Figure 1). In addition, a lack of supplies for the wearing of maximal barriers during catheter insertion, a lack of chlorhexidine (and thus the use of povidone iodine), the use of vented intravenous containers instead of closed intravenous systems, and a lack of ready-to-use drugs (and the subsequent reliance on manual admixture for all drugs) were noted (Figure 1). Moreover, poor performance in infection-control practices—such as using cotton balls already impregnated with antiseptic contained in a contaminated container, not covering an insertion site with sterile dressing, storing drugs in already-open

single-use vials, reusing single-use vials, leaving needles inserted in multiple-use vials, taking fluids from a 1000-cc container for dilution of parenteral solutions, and using tacky mats (Figure 2)—were paramount. Finally, the difference in the nurse-to-patient ratio is also implicated as a major factor contributing to higher ICU CLABSI rates, as seen in the lower relationship between nurse staffing and patients in limited-resource countries compared with health care facilities in developed countries [61].

This being the reality of health care practices in several limited-resource countries, q16 it is unlikely that implementation of the 5 aforementioned measures (hand hygiene, using full barrier precautions during the insertion of central venous catheters, cleaning the skin with chlorhexidine, avoiding the femoral site q17 if possible, and removing unnecessary catheters) [5] would be sufficient to prevent CLABSIs in hospitals in countries with limited resources. The effectiveness of such measures in the United States—where they are applied on a supplementary basis together with the availability of alcohol hand rub, alcohol-based preparation of chlorhexidine, supplies for maximal barriers, nonvented systems, and sufficient skilled manpower—cannot q18 be duplicated in limited-resource countries [5]. Furthermore, the measures of Pronovost et al may not succeed in low-income countries as they have industrialized countries because regular use of antibiotics and catheters impregnated with antiseptics is not as affordable in low-income countries compared with industrialized countries.

This review demonstrates that CLABSIs are associated with significant extra mortality, with an odds ratio ranging from 2.8 to 9.5. Other studies have shown that mortality associated with CLABSI is higher in comparison with mortality in patients without CLABSI 62. Nevertheless, in some studies the difference between the mortality in patients with and those without CLABSI was not statistically significant [3].

According to this analysis of the 6 above-described sequential interventional studies conducted in limited-resource countries, unsophisticated, elementary infection-control measures may reduce the incidence of CLABSIs significantly, amounting to a reduction from 6.5–46.0 cases per 1000 CL days to 2.4–12.4 cases per 1000 CL days [31, 32, 38, 49, 57, 63]. However, this reduced rate is by no means comparable to the lower CLABSI rates identified in industrialized countries.

CONCLUSION

This review has evaluated the incidence of CLABSIs in countries with limited resources, where CLABSIs pose a threatening risk to patient safety, particularly because of their direct relationship with high mortality rates in ICUs and their impact on the scarce resources in limited-resources countries. The present review reflects that the prevention and control of CLABSIs in limited-resource countries needs to be widely and adequately addressed to reach the standard levels in developed countries. In other words, to make it feasible for hospitals in limited-resource countries to achieve the levels of quality and patient safety found in developed countries, public nationwide and global health care policies are needed to provide health care facilities with the necessary resources and support.

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