Effectiveness of a multidimensional approach for prevention of ventilator-associated pneumonia in 21 adult intensive-care units from 10 cities in India: findings of the International Nosocomial Infection Control Consortium (INICC)†

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SUMMARY

We report on the effect of the International Nosocomial Infection Control Consortium's (INICC) multidimensional approach for the reduction of ventilator-associated pneumonia (VAP) in adult patients hospitalized in 21 intensive-care units (ICUs), from 14 hospitals in 10 Indian cities. A quasi-experimental study was conducted, which was divided into baseline and intervention periods. During baseline, prospective surveillance of VAP was performed applying the Centers for Disease Control and Prevention/National Healthcare Safety Network definitions and INICC methods. During intervention, our approach in each ICU included a bundle of interventions, education, outcome and process surveillance, and feedback of VAP rates and performance. Crude stratified rates were calculated, and by using random-effects Poisson regression to allow for clustering by ICU, the incidence rate ratio for each time period compared with the 3-month baseline was determined. The VAP rate was 17·43/1000 mechanical ventilator days during baseline, and 10·81 for intervention, showing a 38% VAP rate reduction (relative risk 0·62, 95% confidence interval 0·5–0·78, $P = 0.0001$).

Key words: Developing countries, device associated infection, hand hygiene, infection control, ventilator-associated pneumonia.

INTRODUCTION

Ventilator-associated pneumonia (VAP) is widely considered to be the most serious device-associated infection (DAI) in the intensive-care unit (ICU) setting [1, 2]. According to studies from developed [3] and developing [1, 4] countries, the most important clinical consequences attributable to VAP are increased mortality rates, significant morbidity, and increased length of stay in hospital [4, 5]. From an economic perspective, VAP is also responsible for significant increases in healthcare costs, as reported in both developed and developing countries in Latin America [3, 4], but not yet in studies from India.

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The burden posed by VAP has not been systematically analysed at international level, particularly in limited-resource countries [1] where most hospitals do not implement basic infection control programmes, resulting in a general unawareness of the incidence of VAP [1]. As reported by the International Nosocomial Infection Control Consortium (INICC) in pooled studies [6–9], and in particular from India [10], the rates of VAP were found to be 3–5 times higher than reported from developed countries.

For analytical purposes, the World Bank classifies economies as low, middle, or high income. Since 1 July 2011 low-income is defined as an average income of US$1005 or less per year; lower-middle as US$1006–3975; upper-middle as US$3976–12275; and high-income above this figure. Low- and middle-income economies are commonly referred to as developing economies.

The influence of socioeconomic level over DAIs in developing countries has been assessed in two studies [11, 12]. The first, conducted in paediatric ICUs, showed that lower middle-income countries had higher VAP rates than upper middle-income countries [9·0 $vs.$ 0·5/1000 mechanical ventilator (MV) days] [11] and rates were highest in ICUs of academic hospitals compared to private or public hospitals (8·3 $vs.$ 3·5 VAP/1000 MV days) [11]. Similarly for neonatal ICU patients, the VAP rates in academic hospitals significantly exceeded those in private or public hospitals (13·2 $vs.$ 2·4 and 4·9 VAP/1000 MV days) [12]. Regrettably, there are no published studies from developing countries on this issue in adult ICUs.

It has been shown that the incidence of VAP in developed countries can be substantially reduced by more than 30% through basic but effective measures, such as systematic surveillance, hand hygiene (HH) compliance, semi-recumbent positioning, early removal of endotracheal tubes, maintenance of endotracheal cuff pressure and continuous subglottic suctioning [13]. By contrast, the importance of measuring patient infection risks and prevention practices remains greatly under-recognized in developing countries [1, 14] and specifically such programmes have not been evaluated in India, the second most populous country in the world, with a population of about 1·3 billion [1]. Launched in 2002 internationally [6–9], the INICC has supported hospitals in limited-resource countries in performing surveillance and reducing healthcare-associated infection rates. These hospitals contact INICC and receive forms and manuals with guidance to implement effective surveillance and infection control programmes. INICC also provides administrative and scientific support to upload, process, analyse and develop charts and tables with the collected data.

With the aim of reducing VAP rates in adult ICUs of INICC member hospitals in India, we implemented a novel multidimensional infection control programme that comprised six specific interventions: (i) a practice bundle, (ii) education, (iii) outcome surveillance, (iv) process surveillance, (v) feedback on DAI rates and (vi) feedback on the performance of infection control practices. The bundle integrated in this approach for VAP reduction is based on the guidelines published by the Society for Health Care Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA), which provide feasible and cost-effective infection control measures [13].

METHODS

Setting and study design

This quasi-experimental, prospective cohort study was conducted in 21 adult ICUs of 14 INICC member hospitals, in 10 cities in India. Each hospital has actively participated in the INICC surveillance programme for at least 1 year, each with an infection control team comprised of at least one medical doctor with formal education and background in infectious diseases, internal medicine, and/or hospital epidemiology, and infection control professionals (ICPs). The study period was 7 years and 3 months, from July 2004 to October 2011, and was divided into baseline and intervention periods. The Institutional Review Board (IRB) at each hospital approved the study protocol. Patient confidentiality was protected by codifying the recorded information, making it only identifiable to the infection control team.

Baseline period

The baseline period included only the performance of outcome and process surveillance and lasted for 3 months. This period allowed for monthly receipt of case report forms at INICC headquarters in Argentina from participating centres, validation, queries, computer analysis, and communication of results and feedback of performance to participants. The sample size of patients and duration of data collection during the baseline period was sufficient to

compare these parameters with the intervention period. From a statistical perspective, this was addressed by considering the changes in rates over time. The relatively short baseline period may impact the standard error of our estimates but this was not thought to bias the results as there were no systematic differences between the two groups. Finally, it was necessary to begin the intervention period as early as possible in order to achieve the desired results within the time-frame.

Intervention period

The intervention period started in the fourth month of participation. This was a cohort study, and for that reason, each ICU joined the INICC programme at different times. Thus, by the time the impact of the INICC intervention was analysed, we had ICUs with different lengths of participation in intervention periods with an average duration (±S.D.) of 23.33 ± 16.86 (range 6–76) months.

INICC multidimensional approach

The INICC multidimensional approach included the following practices: (1) bundle for VAP prevention, (2) education, (3) outcome surveillance, (4) process surveillance, (5) feedback on VAP rates, and (6) performance feedback of infection control practices [15].

Bundle for VAP prevention

The bundle included the following elements:

(1) Adherence to HH guidelines [13].
(2) Maintenance of patients in a semi-recumbent position (30–45° elevation of the head of the bed) [16].
(3) Performance of daily assessments of readiness to wean and use of weaning protocols [13].
(4) Performance of regular oral care with an antiseptic solution [17].
(5) Use of non-invasive ventilation whenever possible and minimization of the duration of ventilation [13].
(6) Preferable use of orotracheal instead of nasotracheal intubation [13].
(7) Maintenance of an endotracheal cuff pressure of at least 20 cm H_2O [18].
(8) Removal of the condensate from ventilator circuits [13] and keeping the ventilator circuit closed during condensate removal [13].
(9) Change of the ventilator circuit only when visibly soiled or malfunctioning [13].
(10) Avoidance of gastric overdistention [13].
(11) Avoidance of histamine receptor 2 (H_2) blocking agents and proton-pump inhibitors [13].
(12) Use of sterile water to rinse reusable respiratory equipment [13].
(13) We performed direct observation of HH compliance, duration of ventilation, and ventilation ratio use, using a structured observation tool at regularly scheduled intervals [15].

Education

The INICC chairman trained the principal and secondary investigators at most of the participating hospitals. In addition, investigators were provided with instruction manuals and training tools, and their updates, which describe how to perform surveillance and complete surveillance forms according to the guidelines published by the SHEA and the IDSA [13]. Investigators had regular email and telephone access to a support team at the INICC Central Office in Buenos Aires, Argentina, charged with responding to all queries within 24 h. The INICC chairman further reviewed all queries and responses.

INICC surveillance methods

The INICC surveillance programme included two components: outcome surveillance (DA HAI rates and their adverse effects, including mortality rates) and process surveillance (adherence to HH and other basic preventive infection control practices) [15]. Investigators were required to complete outcome and process surveillance forms at their ICUs, which were then sent for their monthly analysis to the INICC headquarters office in Buenos Aires.

Outcome surveillance

Outcome surveillance included rates of VAP/1000 MV days, microorganism profile and antimicrobial resistance, length of stay, and mortality rates in the participating ICUs. The definitions applied for surveillance were those developed by the U.S. Centers for Disease Control and Prevention for the National Health Safety Network (CDC NHSN) programme [19]. Additionally, INICC methods were adapted to the limited-resource setting of developing countries to take account of socioeconomic status [15]. The

Abdominal Surgery Impact Scale (ASIS) score was used instead of the APACHE II score due to budgetary limitations of participating ICUs [20].

Definitions

VAP was diagnosed in a mechanically ventilated patient when a chest radiograph showed new or progressive infiltrates, consolidation, cavitation, or pleural effusion. The patient also had to meet at least one of the following criteria: new onset of purulent sputum or change in character of sputum, organism cultured from blood, or isolation of an aetiological agent from a specimen obtained by tracheal aspirate, bronchial brushing or bronchoalveolar lavage, or biopsy [19].

Process surveillance

Process surveillance was designed to monitor compliance with easily measurable, key infection control measures and HH at each participating ICU. Due to budgetary limitations, only the following components of the bundle were monitored.

(1) HH compliance by HCWs was determined by monitoring practices by the hospital's ICP during randomly selected 1-h observation periods, three times a week. Although staff were aware of the monitoring, they did not have prior knowledge of the precise times of the observation periods [15]. ICPs were trained to monitor and record HH compliance through direct observation according to the 'Five Moments for Hand Hygiene' as recommended by the World Health Organization (WHO) which describes monitoring of HH: (1) before patient contact, (2) before an aseptic task, (3) after body fluid exposure risk, (4) after patient contact, and (5) after contact with patient surroundings [21] .

(2) Compliance with VAP preventive measures were recorded 5 days a week on a form that evaluated adherence to infection control procedures by HCWs and monitored (i) maintenance of patients in a semi-recumbent position (30–45° elevation of the head of the bed), (ii) compliance with nebulizer without turbidity; (iii) tubing without condensation, (iv) tubing without mucus, (v) absence of pharyngeal lake, and (vi) compliance with smooth enteric nourishment.

Feedback on VAP rates

The INICC Central Office team communicated monthly analysis reports (graphs, charts, etc.) to participating hospitals of outcome surveillance data on VAP rates, and microbiology profile. These data were posted in prominent locations in the ICU to increase awareness of patient outcomes and enable staff to focus on key issues and apply specific strategies to reduce DA HAI rates. The effectiveness of this approach had been demonstrated in previous INICC studies in limited-resource settings [22, 23]. Final reports on the surveillance and infection control interventions were similarly communicated to all staff.

Validation of reported ventilator-associated rates

Outcome surveillance forms for individual patients allowed validation of reported VAP rates as they included key clinical and microbiological criteria of infection. Internal validation of forms was performed by investigators at the participating centre to ensure relevant infection criteria were accurately recorded for each case. External validation at INICC headquarters, reviewed, and entered patient data on the reported infection into the INICC's database following discussion of queries with the submitting centre. Finally, consistency analyses of the database were performed to ensure matching of data entered and medical records.

Statistical methods

Patients' characteristics were compared using Fisher's exact test for dichotomous variables and unmatched Student's t test for continuous variables. Ninety-five percent confidence intervals (95% CI) were calculated using VCStat (Castiglia). Relative risk (RR) ratios with 95% CIs were calculated for comparisons of rates of VAP using Epi Info v. 6 (CDC, USA). P values <0·05 by two-sided tests were considered significant. Two types of analysis were conducted to evaluate the impact of interventions on VAP rates. First, the data of the baseline period were compared with the intervention period using RR, 95% CI and P value. Second, Poisson regression was used to analyse progressive VAP rate reduction data between baseline rates and 6-month follow-up intervention periods. For this comparison, we used as baseline data only those hospitals that contributed to follow-up in that period (i.e. excluding from the baseline those hospitals that had longer periods of follow-up). Poisson regression was also used to account for random effects of clustering of VAP rates within hospitals across time periods. These models were estimated

Table 1. *Characteristics of participating AICUs by speciality and type of hospital*

	AICUs *n* (%)	AICU patients *n* (%)
Type of AICU		
Cardiac medical	3 (14%)	5719
Cardiac surgical	2 (10%)	4300
Medical	3 (14%)	4343
Medical surgical	9 (42%)	25396
Surgical	2 (10%)	2944
Trauma	1 (5%)	1932
Ward	1 (5%)	2261
All AICUs	21 (100%)	46945
Type of hospital		
Academic teaching	4 (19%)	7421
Private community	13 (62%)	32001
Public	4 (18%)	7523
All hospitals	21 (100%)	46945

AICU, Adult intensive care unit.

using Stata v. 11.0 (StataCorp., USA). For this analysis we used incident rate ratio, 95% CIs, and *P* value.

RESULTS

During the study period, 46954 patients, hospitalized for 223320 days, in 21 adult ICUs (AICUs) from 10 cities in India were enrolled in the study, with a total of 65574 MV days (Tables 1 and 2). Age, gender, patients with thoracic surgery and immunocompromised patients were similar during both periods. ASIS mean score was lower during the intervention period. By contrast, MV use mean and MV duration mean were higher during the intervention period (Table 2). Surveillance showed that compliance with preventive measures improved significantly during the intervention period with improvements in HH of 5%, compliance with tubing without water by 36%, tubing without mucus by 22%, provision of smooth enteric nourishment by 100%, the presence of pharyngeal lake decreased by 22%. Maintenance of patients in a semi-recumbent position (30–45° elevation of the head of the bed) and compliance with nebulizer without turbidity were high during the baseline period and remained similar during the intervention period (Table 2).

During the baseline period, 4819 MV days, with a mean MV use of 0·27 was recorded. There were 84 VAPs and an incidence density of 17·43 VAP/1000 MV days. Merging all data of the intervention period, during the implementation of the multidimensional infection control programme, we recorded 60755 MV days, for a MV use mean of 0·30. There were 657 VAPs and an incidence density of 10·8 VAP/1000 MV days (RR 0·62, 95% CI 0·5–0·78, $P = 0·0001$). These results show a 38% VAP rate reduction (Table 2).

The random-effects Poisson regression showed that compared to baseline VAP rates for the 3 months before the intervention, VAP rates were reduced by 39% after 9 months of participation. This rate was further reduced by 13% during the second year, by 47% during the third year, by 67% during the fourth year and by 50% during the fifth and sixth years (Table 3).

Pseudomonas, Acinetobacter spp. and *Klebsiella* were the predominant microorganisms isolated during both sampling periods and accounted for >80% of all bacterial isolates. During the baseline period, only 2·4% of VAPs were detected without microbiological sampling and this rose to 18·6% in the intervention period.

DISCUSSION

A comparison of the baseline rate of VAP found in this study (17·43/1000 MV days) shows that it was almost tenfold higher than the USA 1·8 VAP rate/1000 MV days determined by the CDC NSHN [24], and more than twofold higher than the 6·8/1000 rate determined by KISS [25].

In comparison with VAP rates from other developing countries, our VAP baseline rate was lower than the first international INICC report published in 2006 (24·1 VAP/1000 MV days) [6], but similar to the second, third, and fourth INICC reports published in 2008 (19·5 VAP/1000 MV days) [7], 2010 (13·16 VAP/1000 MV days) [8], and 2012 (15·8 VAP/1000 MV days) [9]. Within the scope of other studies from India, the VAP rates were similar to the baseline rate reported here. A multicentre study in 12 ICUs of seven hospitals in 2007 found an overall rate of 10·46 VAP/1000 MV days [10], and similarly, in 2009, a rate of 15·87 VAP/1000 MV days in a tertiary-care hospital was reported [26].

Previous INCC studies have shown that implementation of the six-component multidimensional approach for VAP listed in the Methods section resulted in significant reductions in rates of VAP in Argentina (51·28 *vs.* 35·50 VAP/1000 MV days) [27], and in China, where a 79% cumulative VAP rate reduction was recorded [28]. Similarly high reductions

Table 2. *Patient characteristics, hand hygiene compliance, compliance with care bundle, device use, and VAP rates, in the baseline and intervention periods*

Patients' characteristics	Baseline period	Intervention period	RR	95% CI	P value
Study period by hospital in months, mean ± s.D. (range)	3	23·33 ± 16·86 (6–76)	—	—	—
Patients, *n*	3979	42966	—	—	—
Bed days, *n*	18154	205166			
MV days, *n*	4819	60755			
MV use, mean	0·27	0·30	1·12	1·08–1·15	0·0001
MV duration, mean ± s.D.	1·21 ± 3·1	1·42 ± 5·17	—	—	0·0001
Age, mean ± s.D.	54·78 ± 17·76	54·55 ± 18·28	—	—	0·455
ASIS score, mean ± s.D.	2·9 ± 1·2	2·6 ± 1·11	—	—	0·0001
Male	68% (2718)	66% (28421)	0·97	0·93–1·01	0·12
Female	32% (1260)	34% (14528)	—	—	—
Thoracic surgery, % (*n*)	1% (29)	1% (216)	0·7	0·47–1·02	0·061
Immune compromise, % (*n*)	1% (29)	1% (283)	0·91	0·62–1·33	0·6155
Hand hygiene compliance, % (*n/N*)	77·9% (2355/3023)	82% (29100/35521)	1·05	1·01–1·1	0·02
MV compliance with semi-recumbent position of the head (30–45°), % (*n/N*)	92·93% (552/594)	97·52% (8609/8828)	1·05	0·96–1·14	0·272
MV compliance water free tubing, % (*n/N*)	61·11% (363/594)	83·03% (7330/8828)	1·36	1·22–1·51	0·0001
MV compliance tubing without mucus, % (*n/N*)	70·88% (421/594)	86·63% (7648/8828)	1·22	1·11–1·35	0·0001
MV presence pharyngeal lake, % (*n/N*)	89·06% (529/594)	69·51% (6136/8828)	0·78	0·71–0·85	0·0001
MV compliance smooth enteric nourishment, % (*n/N*)	47·14% (280/594)	94·03% (8301/8828)	2·0	1·77–2·25	0·0001
VAP, *n*	84	657			
VAP rate/1000 MV days	17·43	10·81	0·62	0·5–0·78	0·0001

RR, Relative risk; CI, confidence interval; MV, mechanical ventilator; s.D., standard deviation; ASIS, average severity of illness score; VAP, ventilator-associated pneumonia.

Bed days are the total number of days that patients are in the intensive care unit during the selected time period.

MV days: the total number of days of exposure to mechanical ventilation by all of the patients in the selected population during the selected time period.

MV use ratios were calculated by dividing the total number of MV days by the total number of bed days.

Table 3. *VAP rates stratified by length of participation of ICU*

Months since joining INICC	No. of ICUs	MV days	VAP	Crude VAP rate per 1000 MV days	IRR accounting for clustering by ICU	P value
1–3 months (baseline)	21	4819	84	17·43	1	—
4–12 months	21	16809	195	11·6	0·61 (0·5–0·8)	0·0001
Second year	17	13709	226	16·5	0·87 (0·67–1·14)	0·324
Third year	12	11086	112	10·10	0·53 (0·4–0·72)	0·0001
Fourth year	8	13019	77	5·91	0·33 (0·0·27–0·46)	0·0001
Fifth–sixth years	2	6132	47	7·66	0·5 (0·322–0·73)	0·001

VAP, Ventilator-associated pneumonia; ICU, intensive care units; INICC, International Nosocomial Infection Control Consortium; MV, mechanical ventilator; IRR, incident rate ratio.

were found in pooled VAP rates in paediatric ICUs (31%) [29], neonatal ICUs (33%) [30] and AICUs (56%) [31] in limited-resource countries.

Patients' characteristics, such as age, gender, thoracic surgery and immunocompromised status, showed similar intrinsic risk in both study periods although the ASIS mean score was lower in the intervention period. By contrast, MV use mean and MV duration mean were higher during the intervention period indicating increased patient intrinsic risk.

The implementation of the multidimensional approach resulted in a significant improvement in

process surveillance rates, HH compliance and elements of the care bundle. The position of the head in semi-recumbent position and compliance with nebulizer without turbidity remained similarly high and similar, respectively, during the whole study period. According to the literature, HH, lack of turbidity with nebulizer and head position are some of the key elements to reduce the risk of VAP [32].

Regarding the microorganism profile, the predominance of *Klebsiella, Pseudomonas*, and *Acinetobacter* spp. as the most common pathogens associated with VAP has previously been noted in India [33], and increasingly associated with multidrug resistance in hospitalized patients, especially in ICUs [34].

This study has some limitations. The first is that our findings cannot be taken as representative of all AICU patients in Indian hospitals. However, it does demonstrate the value of a multidimensional approach for determination of VAP rates and their control of adverse effects in an AICU setting in a low-resource country. Second, we did not have the necessary resources to collect more data on process surveillance and measure compliance with all of the interventions examined and therefore we were unable to evaluate effects of specific interventions or other factors related to individual ICUs or hospitals. Additionally, due to budgetary limitations we were not able to analyse reduction in the time under MV, length of stay in ICU and hospital, mortality rate and costs. Finally, the setting of a 3-month baseline period may have been too short and might have overestimated the effect of interventions. However, we obtained a sufficient sample size during the baseline period with adequate confidence intervals for the baseline rates and this did not lead to a bias in the results obtained. In conclusion we have demonstrated a substantial reduction in VAP rates in the AICU setting in several Indian hospitals and confirm the effectiveness of this approach in low-resource settings. This was achieved despite higher patient intrinsic risk characteristics during the intervention period, through improved compliance with preventive measures and implementation of the multidimensional approach for VAP prevention trialled in infection control programmes in hospitals worldwide [35]. Through the INICC network, investigators are freely furnished with training and methodological tools to perform outcome and process surveillance, and to implement effective infection prevention models for VAP. We extend an invitation to other hospitals in the developing world to participate in this project.

APPENDIX: Remaining co-authors of this study, members of the International Nosocomial Infection Control Consortium from India

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DECLARATION OF INTEREST

None.

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