Surveillance of ventilator associated pneumonia in a network of indian hospitals using modified definitions: a pilot study

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Summary

Background Ventilator-associated pneumonia (VAP) is a major cause of morbidity and mortality in patients receiving mechanical ventilation in India. Surveillance of VAP is essential to implement data-based preventive measures. Implementation of ventilator-associated events (VAE) criteria for surveillance has major constraints for low resource settings, which can lead to significant underreporting. Surveillance of VAP using common protocols in a large network of hospitals would give meaningful estimates of the burden of VAP in low resource settings. This study leverages a previously established healthcare-associated infections (HAI) surveillance network to develop and test a modified VAP definition adjusted for Indian settings.

Methods In this observational pilot study, thirteen hospitals from the existing HAI surveillance network were selected for developing and testing a modified VAP definition between February 2021 and April 2023. The criteria used for diagnosing VAP were adapted from the CDC's Pediatric VAP definition and modified to cater to the needs of Indian hospitals. Designated nurses recorded each VAP event in a case report form (CRF) and also collected denominator data. The data was entered into an indigenously developed database for validation and analysis. At the time of data analysis, a questionnaire was sent to sites to get feedback on the performance of the modified VAP definitions.

Findings Out of 133,445 patient days and 40,533 ventilator days, 261 VAP events were recorded, with an overall VAP rate of 6.4 per 1000 ventilator days and a device utilization ratio (DUR) of 0.3. A total of 344 organisms were reported from the VAP events. Of these, *Acinetobacter* spp (29.6%, 102) was the most frequent, followed by *Klebsiella* spp (26.7%, 92). Isolates of *Acinetobacter* spp (98%) and Enterobacterales (85.5%) showed very high resistance against Carbapenem. Colistin resistance was observed in 6% of Enterobacterales and 3.2% of *Acinetobacter* spp.

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Interpretation Data from this pilot study needs to validated in the larger Indian HAI surveillance network so that it can help in wider implementation of this protocol in order to assess its applicability p VAP across India.

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Keywords: VAP; Surveillance; LMICs; Antimicrobial resistance; ICUs

Research in context

Evidence before this study

VAP surveillance has been stopped and replaced by VAE surveillance in most of the high-income countries. This is despite the fact that VAP has a high global incidence and high fatalities. In LMICs, surveillance of VAP is needed, since surveillance generates actionable data. VAE surveillance is not implementable in LMICs due to resource constraints and the complexity of VAE definitions.

Added value of this study

This study provides meaningful and implementable protocols for the surveillance of VAP in LMICs. The protocol can be implemented on a wider scale.

Implications of all the available evidence

The data generated can be used for developing preventive protocols for VAP that are resource-appropriate.

Introduction

Ventilator-associated pneumonia (VAP) is one of the most common, morbid, and fatal complications in patients receiving mechanical ventilation. It affects from 5 to 40% of patients receiving invasive mechanical ventilation for more than two days, the risk varying with the type of intensive care units (ICUs) and between high/lower-middle-income countries (LMICs).[1–3] LMICs in general report higher rates of VAP compared to hospitals in high-income countries (HICs). This may be an actual higher prevalence or due to other factors like differences in how definitions are applied or diagnostic/laboratory limitations.[4,5]

In 2013, Center for Disease Control's (CDC's) National Health Safety Network (NHSN) replaced the previous definition of pneumonia with its working group's classification of ventilator-associated events (VAE). This was done to cast a wider net using objectively defined criteria to capture all potentially preventable complications from the data available in the Electronic Medical Records (EMRs) in healthcare facilities.[6–8] However, even after ten years of coming out with these definitions, VAE surveillance has not been widely adopted beyond the United States. The reasons are uncertainty about possible overlaps between VAP and VAE criteria, with implications on clinical utility; poor concordance of surveillance definition of Ventilator-Associated Condition (VAC), Infection-related Ventilator-Associated Complication (IVAC), and Possible VAP (PVAP) with VAP-NHSN definitions and more active daily monitoring of ventilator settings.[9–11] VAE surveillance is often very difficult in low resource settings, where EMRs are not present in most institutions and there is a perpetual shortage of trained manpower.

VAP is often caused by highly resistant pathogens prevalent in the institutional ICUs, making treatment extremely challenging for Intensivists. The Indian Council of Medical Research (ICMR) reported a rising resistance to even last resort antimicrobials across different types of in-patient samples in 2023.[12] High rates of VAP, coupled with increasing antimicrobial resistance (AMR) in India require a network-level and reliable system for surveillance of VAP using definitions that are suitable, applicable, and sustainable in the local context.

Surveillance of healthcare-associated infections (HAIs) is important to generate country-specific and actionable data.[13] Establishing networks of hospitals performing surveillance using the same set of definitions is an invaluable tool for understanding the national burden and profile of HAIs. In low resource settings, there are limitations on human and financial resources for implementation of Infection Control Programs. Therefore, surveillance definitions need to be sensitive, and at the same time, not too labor or time intensive.

We have previously published our experience with establishing a network of hospitals in India performing surveillance for Bloodstream infections (BSIs) and Urinary tract infections (UTIs), using modified NHSN definitions tweaked for Indian ICUs.[14] This network and its definitions were established considering the laboratory diagnostic capabilities of institutions participating in ICMR's AMR surveillance network.[12,14]

We subsequently leveraged the capacity of this HAI surveillance network to pilot-test a definition for surveillance of VAP in 34 ICUs of 13 Indian hospitals.

This is the first collaborative attempt by All India Institute of Medical Sciences (AIIMS), New Delhi, and ICMR to develop and pilot an India-specific VAP surveillance algorithm across Indian hospitals. A network approach to HAI surveillance using uniform case definitions and surveillance methodology enables generation of high-quality data for action. In this pilot study, we present the details of establishing this surveillance and the data generated from participating hospitals.

Our main idea to pilot-test this definition for surveillance of VAP was driven by the necessity to include VAP in our HAI surveillance network (which had hitherto focused on BSI and UTI only), considering that VAP continues to be a major HAI in most countries, causing high fatality. Also, VAP is amenable to prevention and treatment by VAP prevention bundles or antimicrobials respectively. Therefore, surveillance of VAP in India will give more actionable inputs than surveillance of VAEs.

Methods

The ICMR has a robust AMR surveillance network involving tertiary care hospitals having quality-assured microbiology laboratories.[12] ICMR in collaboration with AIIMS, New Delhi, and National Centers for Disease Control (NCDC) created the first network of tertiary care hospitals using resource-appropriate standardized methods for BSI and UTI surveillance in line with the Ministry of Health and Family Welfare's National Action Plan (NAP) on AMR.[14]

We conducted this observational pilot study to develop and test a modified surveillance definition for VAP in a few hospitals of this network.

Surveillance setting

To initiate and test a VAP surveillance protocol, we selected 13 tertiary healthcare facilities that had robust Microbiology laboratory support and good coordination between the intensivists and microbiologists. Surveillance was carried out in 34 ICUs from these 13 hospitals across India. This study reports the data generated from these participating ICUs over an initial 27-month period (from February 2021 to April 2023). We also evaluated the response of sites towards the feasibility and perceived user-friendliness of the protocols. Suggestions of the participating hospitals to improve the definitions were also evaluated to understand if these definitions were suitable to roll them out to all sites participating in the Indian HAI surveillance network.

Methodology of surveillance of VAP

The modified VAP definitions used in this network were adapted from CDC's Pediatric VAP criteria and the diagnostic algorithms already being used in four participating hospitals. These definitions were used for patients who were on mechanical ventilators for more than 2 calendar days and were adopted from the PNEU 2&3 algorithms of CDC's NHSN guidelines.[15] We leveraged the Microbiology laboratory capacity of hospitals to include culture report as an essential criterion, along with respiratory, radiology, and clinical criteria, as shown in Box 1. A standard operating procedure (SOP) was made and distributed to all sites. All sites were trained on the protocol through a workshop. Re-trainings were given to staff online.

Box 1.
VAP surveillance definitions.

A. One or more serial chest imaging test results with at least *one* of the following
   - New and persistent or
   - Progressive and persistent Infiltrate
   - Consolidation
   - Cavitation

B. Signs and symptoms
   B.1 At least *one* of the following:
   - Fever (>38.0 °C or >100.4 °F)
   - Leukopenia (≤4000 WBC/mm3) or leukocytosis (≥12,000 WBC/mm3)
   - For adults ≥70 years old, altered mental status with no other recognized cause, And

   B.2 At least *one* of the following:
   - New onset of purulent sputum
   - change in character of sputum
   - Increased respiratory secretions
   - Increased suctioning requirements
   - New onset or worsening cough
   - Dyspnea
   - Tachypnea
   - Rales or bronchial breath sounds
   - Worsening gas exchange (for example: O2 desaturations [for example: PaO2/FiO2 ≤ 240], increased oxygen requirements, or increased ventilator demand)

C. Lab findings
   At least *one* of the following:
   - Organism identified from blood/or pleural fluid
   - Positive quantitative/semi-quantitative culture from BAL/endotracheal aspirate
   - ≥5% BAL-obtained cells contain intracellular bacteria on direct microscopic Gram's stain
   - Definitive diagnosis of fungal infection through histopathology/cultures; definitive diagnosis of Bordetella/Legionella/Mycoplasma/Chlamydia/Viral pneumonia through Molecular/serological tests

   For Immunocompromised patients, isolation of a matching *Candida* spp from blood and sputum/endotracheal aspirate/BAL will also be taken as positive laboratory confirmation.

For Diagnosis of VAP, the following algorithm will be used: At least one of each of the following components: A + B1 + B2 + C = VAP.

Case finding

Designated and trained nurses performed VAP surveillance in the selected ICUs. All patients who were

physically present in the ICUs were included in calculation of daily denominators of "Patient days". Similarly, all physically present patients who were on mechanical ventilators were counted from each ICU for calculation of "Ventilators days". Daily ICU rounds were taken by trained surveillance staff, and targeted surveillance was done for VAP. The surveillance staff evaluated all patients and sought out possible cases in the enrolled ICUs by screening a variety of patient data sources. These included admission, discharge/transfer records, X-rays, laboratory records, and patient charts, especially the history of the patients, physical exam notes, temperature charts, etc. Surveillance staff also reviewed the microbiology records each day to identify positive cultures for bronchoalveolar lavage (BAL) or endotracheal aspirates (ETA) and blood/pleural fluid samples. For each positive culture, surveillance staff along with the help of intensivists and ICU clinical staff collected additional clinical data to determine if the case definition for VAP was met. Chest X-ray findings were verified by the intensivists. Surveillance staff also screened the patient records for any report of atypical bacteria or viral pneumonia. All the data for a confirmed case of VAP was collected in a standardized case report form (CRF). These forms were submitted at the end of an event time frame (a 14-day period when the event of VAP was considered to be ongoing) after capturing the complete data.

Pathogen identification

The hospital Microbiology laboratories conducted microbial detection and identification using either conventional manual methods or automated systems.

Antimicrobial susceptibility testing

The participating hospitals tested antimicrobial susceptibility according to latest Clinical & Laboratory Standards Institute (CLSI) guidelines and their laboratory policies, which accorded with ICMR's established protocols.[12] Each hospital laboratory tested a large panel of antimicrobials for individual pathogens. For the sake of data analysis and presentation, we have included data of a limited number of sentinel antimicrobials like ceftriaxone (to represent third-generation cephalosporins); meropenem (to represent carbapenems); ciprofloxacin (to represent quinolone group of antimicrobials); and piperacillin-tazobactam to represent beta lactam-beta lactamase inhibitor combination.

Data entry and validation

A CRF was filled for each case of VAP by surveillance staff (a designated nurse). Ventilator and patient days were used for denominators (as for BSI/UTI Module[14]). A database was made for onsite data entry of the CRFs, denominator data, and for data analytics (https://vap.haisindia.com). All sites used their user ID and password for data entry. Data entered into the database was validated by a team of four people at the central AIIMS site. They cross-checked the data entry against hard copies of case report forms and denominator data (scanned copies were sent by all sites to the central team via email). Any discrepancy/deficiency or incorrect entry was sent back to respective sites. The sites modified those entries and sent back the corrected CRF after approval of individual site Principal Investigators (PIs). Special training was provided to all sites on data entry in the portal and queries were addressed by the AIIMS team through specific email IDs and telephone numbers. The reporting mechanism is shown in Fig. 1.

Data analytics panel quality was checked by the central AIIMS team every month. Site support visits for data quality were also regularly conducted by the AIIMS team. Data validation is a necessary element to assure quality, accuracy, and reliability of reported surveillance events. Data validation was performed by:

1) Review of data collected in CRFs against primary data sources (e.g. medical chart) to ensure completeness of data collection
2) Review of events entered into surveillance database to determine if they met the VAP surveillance definitions
3) Review of microbiology results and comparison with reported cases to ensure sensitivity of the system, and
4) Monitoring trends of patient days and ventilator days to ensure accurate denominator collection and avoid internal errors (for example, the number of ventilator days does not exceed patient days in a particular month).

These were done periodically and reports on errors or misclassified cases were discussed with appropriate personnel of each site by the central AIIMS team. The overall purpose of data validation was to monitor the use of VAP definitions and accuracy of data submitted by hospitals to the central database, assess the surveillance system capacity of reporting hospitals, and identify opportunities to improve future data collection and reporting. Data collected in the database was cleaned, validated, and analyzed.

The primary data analyzed was:

1) Patient days: total number of days that all patients were in the ICU during the selected time period;
2) Ventilator days: total number of days of exposure to a ventilator for all the patients during the selected time period;
3) Device utilization ratio (DUR): ratio of ventilator days to patient days;
4) VAP cases: defined as presence of infection criterion together on or after the third day of ICU admission.
5) Microbiology culture data.

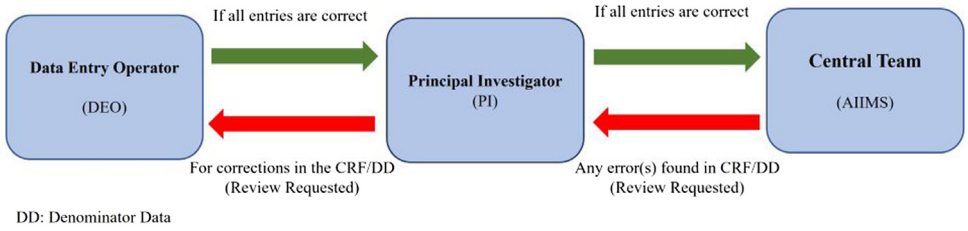

Fig. 1: Workflow in the surveillance database.

Data analyses

VAP rate

VAP rate per 1000 ventilator days was calculated by dividing the number of events of VAP by number of ventilator days and multiplying the result by 1000.

VAP rate per 1000 ventilator days = *No. of VAP events/No. of Ventilator* days X 1,000.

Device utilization ratio (DUR)

Ventilator Utilization Ratio was calculated by dividing the number of ventilator days by number of patient days.

DUR = No. of ventilator days/No. of patient days.

A questionnaire was sent to sites regarding the VAP protocol

A questionnaire was sent to all the sites at the time of analysis of the data. This asked the sites' lead investigator questions about performance of the VAP definitions. The following questions were asked:

1) Of the different sections of VAP definition, which was the most difficult to identify/apply?
2) What, according to you was the reason for this difficulty?
3) What changes do you suggest to VAP definitions?
4) Do you think this definition can be applied nationally?

Answers to these questions were analyzed to understand if the same protocol can be used for all hospitals in the HAIS network (www.haisindia.com).

Statistical analysis

Standard descriptive statistics (mean, median, and ranges) and absolute frequencies were used for analyzing continuous and categorical variables respectively.

Ethical considerations

The study was approved by AIIMS Institutional Ethics Committee (IEC 633/03.09.2021).

Role of funding source

Among the authors involved in the conceptualization and implementation of the study and manuscript development, PS, SS, and SM were employed under the CDC GHSA project (code N-2270) while KVS was employed under the ICMR project (code I-1203) and SG was employed under ICMR Pfizer project (code I-1188). Staff nurses who conducted surveillance were also employed under the CDC GHSA project (code N-2270). ICMR and non-ICMR authors were not precluded from accessing aggregated analyzed data in the study, agreed to proceed with manuscript development, and accepted the responsibility to submit it for publication.

Results

This report summarizes the results for 27 months, from February 2021 to April 2023. Surveillance for VAP was carried out in 34 different ICUs of 13 hospitals across India. Of the 34 ICUs, 12 (35.3%) were Medical ICUs; 5 (14.7%) were medical-surgical ICUs; 4 (11.7%) were neurosurgical ICUs; 3 each (8.8% each) were surgical, pediatric medical & Covid ICUs respectively; two (5.9%) were cardiac ICUs and one (2.9%) each were trauma and gastrointestinal ICUs respectively.

A total of 133,445 patient days and 40,533 ventilator days were recorded from these surveillance ICUs during the study period. The distribution of patient days and ventilator days in different ICUs is listed in Table 1. A total of 261 events of VAP were reported in the surveillance database, from 40,533 ventilator days. This gave the overall rate of VAP to be 6.4 per 1000 ventilator days. The average DUR was 0.30.

SL no	ICU	Patient days (n = 133,445)	Ventilator days (n = 40,533)
1	Medical ICU	58,131	19,136
2	Neurosurgical ICU	21,560	8447
3	Medical/Surgical ICU	14,465	4801
4	Gastrointestinal ICU	11,503	1508
5	surgical ICU	7928	1828
6	COVID ICU	7123	846
7	Cardiac ICU	6084	1597
8	Trauma ICU	4625	2190
9	Pediatric Medical ICU	2026	180

Table 1: **Distribution of patient days and ventilator days in ICUs reporting surveillance data.**

S. No.	Features	Adults	Pediatrics
1.	**Total VAP events**	244/261 (93.5%)	17/261 (6.5%)
2	**Gender**		
	• Male	187/244 (76.6%)	9/17 (52.9%)
	• Female	57/244 (23.4%)	8/17 (47%)
2.	**Age**		
	• Male	48.6 years (19–93)	15.1 (9–18 years)
	• Female	48.3 years (19–83)	15 (13–18 years)
3.	**Time to infection**		
	• 3–7 days	146/244 (59.8%)	14/17 (82.3%)
	• 8–14 days	53/244 (21.7%)	1/17 (5.8%)
	• 15–21 days	24/244 (9.8%)	2/17 (11.7%)
	• 21+ days	21/244 (8.6%)	0/17 (0%)
4	**Length of stay**		
	• 5–7 days	14/244 (5.7%)	0/17 (0%)
	• 8–14 days	52/244 (21.3%)	5/17 (29.4%)
	• 15–30 days	79/244 (32.4%)	7/17 (41.2%)
	• 31–45 days	26/244 (10.6%)	1/17 (5.9%)
	• 46–60 days	9/244 (3.7%)	0/17 (0%)
	• >60 days	13/244 (5.3%)	1/17 (5.9%)
	• Not reported	51/244 (20.9%)	3/17 (17.6%)
5	**Outcome**		
	14 days outcome		
	• Still in a surveillance unit	70/244 (28.7%)	7/17 (41.2%)
	• Died	101/244 (41.4%)	3/17 (17.6%)
	• Transferred to other ward/unit within the hospital	56/244 (22.9%)	5/17 (29.4%)
	• Unknown	5/244 (2.0%)	0/17 (0%)
	• Left against advice	5/244 (2.0%)	0/17 (0%)
	• Transferred to other hospital	1/244 (0.4%)	1/17 (5.9%)
	• Discharged	6/244 (2.4%)	1/17 (5.8%)
	Final outcome		
	• Died	123/244 (50.4%)	3/17 (17.6%)
	• Transferred to other hospital	7/244 (2.9%)	1/17 (5.9%)
	• Discharged	53/244 (21.7%)	8/17 (47%)
	• Unknown	10/244 (4.1%)	0
	• LAMA	8/244 (3.3%)	0
	• Not reported	43/244 (17.6%)	5/17 (29.4%)

Table 2: **Demographic data of events of VAP.**

Of the 261 events of VAP, 244 (93.5%) events were in adults and 17 (6.5%) in children. Of the total 244 events in adults, 187 (76.6%) occurred in males and 57 (23.4%) occurred in females.

The mean age of adult male patients who developed VAP was 48.6 years and in the female patients, it was 48.3 years. The age of pediatric patients who developed VAP ranged between 9 and 18 years with a mean age of 15 years. The maximum number of VAP events (160 [146 in adults and 14 in pediatrics]) occurred between 3 and 7 days of admission in the surveillance unit, with a median of 6 days.

Amongst the 261 VAP events reported, 126 (48.3%) events (123 in adults and 3 in pediatrics) had a fatal outcome. When we analyzed the 14-day outcome of VAP events, 104 of 261 events (39.8%) had a fatal outcome. These were associated mortality and could not be directly attributed to the VAP event.

The length of stay (LOS) for patients with VAP in the surveillance unit ranged from 5 days to 396 days with a median of 18 days. The median value of LOS for elderly patients (n = 36, Age ≥70 years) with VAP was 20 days. LOS did not vary based on gender of the patient. Table 2 summarizes the demographic details, outcomes, and length of stay of the 261 episodes of VAP.

The adult patients most frequently presented with lung infiltrates (150/158, 94.9%)/consolidation of lungs (117/167, 70%); fever (161/175, 92%); leukopenia (167/191, 87.4%); worsening gas exchange (121/141, 85.8%); increased respiratory secretions (93/135, 68.8%); rales in bronchial breath sounds (37/93, 39.7%); and tachypnea (14/66, 21.2%). The pediatric patients presented with infiltrates (8/8, 100%) and consolidation (10/14, 71.4%) of lungs; leukopenia (13/14, 92.8%); fever (12/14, 85.7%); and increased respiratory secretion (10/12, 83.3%). The complete list of signs and symptoms in 261 VAP events is given in Table 3.

A total of 344 bacterial pathogens were identified from these 261 VAP events. Out of these, 322 (93.6%) were from adults and 22 (6.4%) were from pediatric patients. Two or more pathogens were identified from 73 events of VAP (68 in the adult population and 5 events in the pediatric population). A total of 20 different bacterial species were identified. *Acinetobacter* spp was the most frequently isolated pathogen (102; 29.6%), followed by *Klebsiella* spp (92; 26.7%); *Pseudomonas* spp (66; 19.1%); and *Escherichia coli* (24; 6.9%). Table 4 gives the distribution of pathogens isolated from VAP.

Antibiotic susceptibility pattern was evaluated to identify the resistance pattern of pathogens causing VAP. Carbapenem resistance was seen in 98% (99/101) of *Acinetobacter* spp, 85.5% (100/117) of Enterobacterales and 64.6% (42/65) of *Pseudomonas* spp. A high level of resistance was also seen in *Acinetobacter* spp and Enterobacterales against fluoroquinolones, third-generation cephalosporins and beta-lactam-beta lactamase inhibitors as shown in Table 5. Isolates of *Acinetobacter* spp and Enterobacterales showed 3.2% (2/63) and 6% (2/33) resistance to colistin respectively. *Pseudomonas* spp showed a relatively lower resistance to these antimicrobial categories.

On asking lead investigators from each site about the suitability of VAP definition, most sites replied that interpretation of X-ray findings was the most difficult component. This was especially seen in new infiltrates, since comparison with baseline X-rays was subjective. Sites also felt that surveillance nurses found it difficult to retrieve X-rays, especially if the patients died. The sites suggested that to make these definition more sensitive, ventilator-associated lower respiratory tract (LRT) infection (with two subheadings of

A. New and persistent or Progressive and persistent	Number (%)
• Infiltrate	158 (60.5)
• Consolidation	127 (48.7)
• Cavitation	5 (1.9)
B1. Sign and symptoms	
• Fever (>38.0 °C or >100.4 °F)	173 (66.3)
• Leukopenia or Leukocytosis	180 (69.0)
• Adults (>70 years); altered mental status	3 (1.1)
B2. Sign and symptoms	
• New onset of purulent sputum	48 (18.4)
• Change in character of sputum	45 (17.2)
• Increased respiratory secretions	103 (39.5)
• Increased suctioning requirements	75 (28.7)
• New onset or worsening cough	28 (10.7)
• Dyspnea	4 (1.5)
• Tachypnea	15 (5.7)
• Rales or bronchial breath sound	43 (16.5)
• Worsening gas exchange	126 (48.3)
C. Lab findings	
• Organism identified from blood/pleural fluid	46 (17.6)
• Positive culture from BAL/endotracheal aspirate	223 (85.4)
• ≥5% BAL-obtained cells having intracellular bacteria upon direct microscopic Gram's staining	42 (16.1)
• Definitive diagnosis of fungal infections through histopathology/culture; definitive diagnosis	2 (0.8)
• Of Bordetella/Legionella/Mycoplasma/Chlamydia/ Viral pneumonia through Molecular/serological tests	
• For Immuno-compromised patients, isolation of a matching *Candida* spp from blood and sputum/ endotracheal aspirate/BAL	1 (0.4)

Table 3: **Presence of diagnostic parameters used for VAP surveillance (n = 261).**

Organism	Adults (n = 322)	Pediatric (n = 22)	Total (n = 344)
Acinetobacter spp	95 (29.5%)	7 (31.8%)	102 (29.6%)
Klebsiella spp	85 (26.4%)	7 (31.8%)	92 (26.7%)
Pseudomonas spp	63 (19.6%)	3 (13.6%)	66 (19.1%)
Escherichia coli	21 (6.5%)	3 (13.6%)	24 (6.9%)
Staphylococcus aureus	13 (4%)	2 (9.1%)	15 (4.3%)
Stenotrophomonas maltophilia	10 (3.1%)		
Proteus mirabilis	8 (2.5%)		
Candida spp[a]	5 (1.6%)		
Burkholderia spp	4 (1.2%)		
Elizabethkingia meningoseptica	4 (1.2%)		
Serratia marcescens	3 (0.9%)		
Others	11 (3.4%)		

[a]From BAL and matching culture from blood as per the definitions in Box 1.

Table 4: **Organisms isolated from events of VAP.**

VA-Tracheobronchitis [VAT] and VAP) could be tried. The inclusion of Biomarkers like Procalcitonin (PCT) was also one of the suggestions. Sites also felt that the VAE definition (which some sites had used previously in their ICUs) was specific but missed many events of VAP. There was mixed response on whether this definition could be applied nationally. Some sites also suggested that the component of "altered mental states (in B.1) in ≥70 years old" can be removed since this criterion was hardly ever used to link it to VAP by the intensivists. Another suggestion was to combine the criteria of "increased respiratory secretion" and "increased suctioning requirement" into one symptom.

Discussion

National surveillance of VAP has been a long-standing challenge, giving the issue of an objective, reliable, and implementable definition. NHSN has discontinued the VAP definitions for the adult and neonatal population; only the pediatric VAP definition is continued.

In low resource countries, getting trained manpower is a challenge. In our baseline assessment of infection control capacities using WHO's infection prevention and control assessment framework (IPCAF) tool, we found that in Indian hospitals, surveillance for HAIs and human resources was a common lacuna.[16]

Patients on mechanical ventilation are at a very high probability of acquiring VAP. This risk increases with days of ventilation and other co-morbidities, leading to high morbidity, mortality, and health care costs.[4,6] Conducting VAP surveillance, along with providing feedback on monthly rates and trends will help individual ICUs in developing and implementing preventive bundles for India and similarly resourced countries. Most hospitals in high-income countries have started conducting surveillance of VAE (VAC/IVAC/PVAP). However, VAP continues to cause fatal infections around the globe and there is a dire need to conduct surveillance of VAP and monitor its trend. There is also a need to assess the impact of preventive measures, if any, at facility and national levels. We felt that conducting VAE surveillance in India across a large number of hospitals was not feasible. As of January 2024, NHSN has also included a Pediatric VAE definition.

Therefore, we conducted this pilot study to test the modified definition of VAP surveillance in the HAI surveillance network of India, that consists of different types of specialist ICUs.

Microbiological diagnostics are an optional criterion in the NHSN. In India, in tertiary care setups, microbiology services are robust and clinicians depend on culture and sensitivity testing for treating patients suspected of VAP or other HAIs. Therefore, we included microbiological confirmation (primarily cultures) as an essential criterion in our definition, retaining the other findings like altered respiratory findings, radiological manifestations, and fever/leucocytosis from the previous NHSN definitions.

We found that the rate of VAP was 6.4 per 1000 ventilator days in our network hospitals. Higher rates

	Meropenem[b]	Colistin	Piperacillin-tazobactam[c]	Ceftriaxone[d]	Ciprofloxacin[e]
Enterobacterales[a] (n = 118)	100/117 (85.5%)	2/33 (6.0%)	97/112 (82.9%)	102/109 (93.5%)	105/114 (92.1%)
Acinetobacter spp (n = 102)	99/101 (98.0%)	2/63 (3.2%)	97/102 (95%)	93/99 (93.9%)	96/99 (96.9%)
Pseudomonas spp (n = 66)	42/65 (64.6%)	0/21 (0%)	29/59 (49.1%)	41/65 (63.0%)	43/65 (66.1%)

[a]*Klebsiella* spp, *Escherichia coli*, *Enterobacter cloacae*. [b]Resistant and intermediate to meropenem. [c]Resistant and intermediate to pipercillin-tazobactam. [d]resistant and intermediate to ceftriaxone. [e]Resistant and intermediate to ciprofloxacin.

Table 5: **Antimicrobial resistance profile of micro-organisms against commonly used antibiotics.**

of VAP as compared to this study, have been reported in single institutional studies conducted in India.[9,17,18] This could have been due to different definitions, lesser denominators, or non-uniform application of definitions over time. Since our study was conducted in a large number of ICUs across India and uses a VAP surveillance definition adjusted for resource-limited settings, the rate reported in this current study is a better representation of VAP incidence in the Indian context.

The incidence of VAP is directly associated with device utilization ratio. In our study, the DUR was found to be 0.30, which is relatively lower than that reported in other surveillance studies conducted in some other Indian hospitals.[18]

Almost 50% of reported events in this network had a fatal outcome, which emphasizes the contribution of VAP in outcomes of ventilated patients in ICUs. Prevention of VAP therefore needs to be prioritized. VAP also increased the length of stay in elderly population (59 days) as compared to adult population (28 days). Increased length of stay corresponds to increased cost of treatment and less availability of beds (which are already scarce in LMICs).

Almost three-fourths of the VAP events were caused by multidrug-resistant *Acinetobacter* spp (29.6%), *Klebsiella* spp (26.7%), *Pseudomonas* spp (19.1%), and *E. coli* (6.9%). Similar findings have been reported from other single-center studies on VAP surveillance.[9,19] A high level of AMR in our ICUs is leaving colistin as the only antimicrobial available to treat these sick patients. Even colistin was found to be resistant in 3.2% of Enterobacterales and 6% of *Acinetobacter* spp. This high level of resistance is concerning due to possibilities of treatment failure and emphasizes the need to plan and implement site-specific preventive strategies based on local surveillance data.

Data generated from hospitals can be used to monitor and evaluate the effectiveness of various preventive measures applied for VAP and for emergence of drug resistance. The present study was contextualized because unlike in high resource settings, where surveillance is moving towards VAE, in low resource settings, a system of surveillance for VAP is much needed. In one of the tertiary care & teaching hospitals of northern India, where two studies were conducted in two separate ICUs to compare VAP with VAE, it was found that 53.5% of VAE cases progressed to VAP while 46.4% did not.[20] Among the VAP cases that did not develop VAE, a majority were characterized by absence of an increase in positive end-expiratory pressure (PEEP) or fraction of inspired oxygen (FiO_2). An increase in FiO_2 was a key factor in identifying VAE among VAP cases. However, VAP and VAE are two separate definitions that cannot be used as replacements for each other. The sensitivity and positive predictive value of VAE for VAP were found to be lesser than specificity and negative predictive value.[20] In a trauma ICU of this same hospital, the authors aimed to find the predictive value of VAE and the sensitivity of VAE definitions to VAP. In 4046 patient days and 3031 mechanical ventilation days, the incidence rate of PVAP, IVAC, VAC, and VAP was 2.97, 6.60, 10.23, and 9.24 per 1000 ventilator days, respectively. Sensitivity, specificity, positive predictive value, and negative predictive value of diagnosing VAP were 0.61, 0.97, 0.68, and 0.97 for VAC; 0.80, 0.97, 0.57, and 0.99 for IVAC; and 0.78, 0.94, 0.25, and 0.9 for PVAP, respectively.[9]

Although NHSN has stopped surveillance for VAP, the last reported rates in ICUs of the United States of America were 1.1/1000 mechanical ventilator days.[3] In contrast, the International Nosocomial Infection Control Consortium (INICC) network of the developing countries reported a 10 times greater VAP rate of 11.47/1000 ventilator days.[21] The crude mortality in the INICC network in patients with VAP is around 42.3% (95 CI 40.6–44.09).[3,21,22] The differing rates between different countries may reflect differences in type of hospitals, variations in definitions, variations in application of defining criteria, or an actual difference in rates. Low resource countries are report to a higher rate of VAP and other HAIs compared with high resource settings[4,5]

In the current study, only two case report forms (0.8%) mentioned a positive diagnostic test for Bordetella/Legionella/Mycoplasma/Chlamydia/viral pneumonia/fungal infections (which are mentioned as a diagnostic criterion in Box 1). Considering the profile of infections caused by these organisms, they mainly cause community-acquired pneumonia and are rarely a cause of VAP, which has a very different pathogenesis. In one of the two case report form (CRF) that mentioned a "yes" for fungal infection/Bordetella/Chlamydia/Legionella/Mycoplasma/viral pneumonia, one also had a positive

bacterial culture for *E. coli* (10^5/ml) from tracheal aspirate. The other case report form mentioned a "yes" for fungal pathogens (*Aspergillus species*) and had also marked a "yes" for positive quantitative/semiquantitative culture from BAL with *Klebsiella pneumoniae* (10^5/ml). In both these cases, both criteria were marked as yes in the database. In a single case where the criteria of "*Candida species* isolated from blood and BAL from immunocompromised patient" was marked as a "yes", the CRF also mentioned presence of ">/ = 5% BAL-obtained cells having intracellular bacteria upon direct microscopic Gram's stain". This indicates that the above two criteria (detection of *Candida* spp in immunocompromised patients and detection of pathogens that cause community-acquired pneumonia) may not be stringent enough or diagnostic enough (as stand-alone criteria) to be included in the diagnostic algorithm of VAP.

Based on these findings, considering the low response obtained for diagnosis based on histopathology/detection of Mycoplasma/Bordetella/Chlamydia/Legionella/viral pneumonia, there is a need to change the definition.

Since this was a pilot study, we felt that feedback from the sites would be important as we plan to roll out this protocol to a larger section of hospitals. Interpretation of X-ray findings is a limitation of VAP surveillance globally, as was suggested by some participating sites. A way out can be the model used by the Trauma Center of AIIMS (the central site of this study), where the critical care consultants have fixed two days per week to review X-rays of culture-positive cases. Once they confirm the findings (as per our criteria), we enter that in our case report forms. The critical care consultants of ICUs follow up on serial X-rays and are always present and available for discussion. Regarding the suggestion of including ventilator-associated lower respiratory tract infection (with two subheadings of VA-Tracheobronchitis [VAT] and VAP), this would be difficult to implement on a larger scale. Any surveillance system used on a large scale should have simple, as well as sensitive, and specific definitions as far as possible. The generated data should ultimately be used for improvements and implementation of data-driven preventive measures.

The suggestion of removing "altered mental states (in B.1) in ≥70 years old" may be considered while advocating a wider application of this protocol. The suggestion of combining the criteria of "increased respiratory secretion" and "increased suctioning requirement" into one symptom was also considered as practical and simpler in implementation.

Other tests or criteria like PCT, need more scientific validation and it may not be feasible to apply them on a larger scale, considering the limitation of diagnostics manpower.

The strengths of this study include a large network-based approach; the use of a robust database that facilitated real-time on-site data entry and automated data analysis through the option of exporting to Excel. We also ensured data accuracy through various rigorous quality control measures. The staff were provided with support through online- and on-site training and there was constant communication between the central and site teams. Trained and dedicated staff performed surveillance, which was another strength of this study.

There are limitations in the present surveillance study. To meet VAP definitions, subjective criteria such as an increase in respiratory secretions, change in the character of sputum, and progressive/new and persistent X-ray changes were applied. Due to this, VAP cases may have been missing. The data generated was only from selected ICUs of the HAI network, so it may not be generalized to all ICUs. We may need further simplification of the definitions for ICUs of secondary care hospitals in India. We included microbiology diagnostics in our definition since the network hospitals had a strong laboratory support. This may be a challenge if we want to enroll in secondary care hospitals. We had trained manpower to conduct surveillance for VAP, which needs to be sustained, which will be another challenge for wider application in India. In the current study, all the case report forms were checked manually against the entry in the database. As the network grows, we will need to develop a more efficient way of data validation.

The sensitivity and specificity of the definitions also need to be evaluated from a sample of our network ICUs. We could not compare the VAP definitions against NHSN's VAE definitions.

We could successfully pilot-test the modified surveillance definitions of VAP in a section of Indian ICUs. Before these definitions can be applied on a larger scale in India, further validation would be required by enrolling all the ICUs from our existing HAIs network. Moreover, a few criteria like diagnostics for pathogens that mainly cause community-acquired pneumonia; molecular diagnostics or altered mental status in the elderly may be deleted, since very few hospitals can use thsese as diagnostic criteria.

Contributors

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Data sharing statement

De-identified datasets relevant to this study can be made available upon request following the submission of a proposal to the corresponding author and review and approval by network collaborators. Study protocols and affiliated reference materials are available on the HAI surveillance network's website at www.haisindia.com.

Declaration of interests

The authors declare no competing interests.

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