**Clinical and microbiological impact of implementing a decision support algorithm through microbiologic rapid diagnosis in critically ill patients. An epidemiological retrospective pre/post-intervention study**

**Supplementary material**

e-Table 1: Risk Factors for Multidrug-Resistant Pathogens according to IDSA guidelines (1)

* Prior intravenous antibiotic use within 90 days
* Septic shock at time of VAP
* ARDS preceding VAP
* Five or more days of hospitalization prior to the occurrence of VAP
* Acute renal replacement therapy prior to VAP onset

( 1 )Andre C. Kalil, Mark L. Metersky, Michael Klompas, John Muscedere, Daniel A. Sweeney, Lucy B. Palmer et al. Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society. Clinical Infectious Diseases 2016;63(5):e61–111

**Definitions**

*Frequency measures*

The definitions and calculation formula are those of the National Epidemiological Registry of Intra-ICU Acquired Infection (ENVIN-HELICS). <https://hws.vhebron.net/envin-helics/>

Incidence rates (IR) were calculated for each of the controlled infections expressed in relation to the number of patients at risk or the number of days at risk.

In all cases, the numerator includes the absolute number of cases of the infection analysed and the denominator uses 1000 days of exposure to risk or ICU stay.

* Incidence density(id) of invasive mechanical ventilation-associated pneumonia:

VAP id= Number of cases of pneumonia in MV X 1,000 / total days of mechanical ventilation.

* Incidence density(id) of Catheter-related bacteraemia (CRB) and bacteraemia of unknown origin (BUNK).

CRB/BUNK id= Number of CRB and BUNK episodes x 1,000 / total catheter days

* Incidence density (id) of Secondary bacteraemia (SB)

SB id= Number of SB episodes x 1,000/ total ICU days

* Incidence density Catheter Associated Urinary Tract Infection (CAUTI)

CAUTI id= Number of CAUTI episodes x 1,000 / total urinary catheter days

e-Figure 1: Flowchart of patients included in the study.



e-Table 2: Characteristic of 3635 critically ill patients included according to the study period.

|  |  |  |  |
| --- | --- | --- | --- |
| Study Period | Pre-intervention | Intervention | p-value |
| Variable |  2018 (n=987) | 2019-21(n=2648) |  |
| Demographics and severity |
| Age, mean (Q1-Q3) | 64 (52-73) | 63 (50-73) | **0.02**  |
| Male, n (%)  | 634 (64.2) | 1716 (64.8) | 0.78 |
| APACHE, mean (Q1-Q3) | 20 (15-25) | 19 (14-25) | **0.04** |
| SOFA, mean (Q1-Q3)  |  3.0 (2.0-5.1) | 2.9 (2.0-5.1) | **0.008** |
| Patients type  |
| Surgical, n (%) | 275 (27.9) |  680 (25.7) | 0.19 |
| Medical, n (%) | 712 (72.1) | 1968 (74.3) | 0.18 |
| COVID-19 within medical patients, n (%) | 0 (0.0) |  398 (20.2) | **NA** |
| Comorbidities |
| Obesity, n (%) | 123 (12.4) | 446 (26.8) | **<0.001** |
| Diabetes, n (%)  | 239 (24.2) | 586 (22.1) | 0.19 |
| Chronic heart disease, n (%) | 61 (6.2) | 100 (3.8) | **0.002** |
| COPD, n (%) | 126 (12.7) | 274 (10.3) | **0.04** |
| Chronic Rennal failure, n (%) | 93 (9.4) | 246 (9.3)  | 0.95 |
| Immunosupression, n (%) | 43 (4.3) | 116 (4.4) | 1.0 |
| Laboratory |
| Hemoglobin g/dL, median (Q1-Q3) | 10.3 (8.6-12.2) | 10.0 (8.5-11.9) | **0.003** |
| WBC count 103/uL, median (Q1-Q3) | 10.8 (8.1-13.9) | 10.4 (8.1-13.9) | 0.18 |
| Serum creatinine mg/dL, median (Q1-Q3)  | 0.7 (0.6-1.1) | 0.7 (0.6-1.1) | 0.05 |
| RCP mg/dL, median (Q1-Q3) | 9.9 (5.3-18) | 9.1 (4.7-16.6) | **0.006** |
| Microbiologically confirmed infections during ICU stay |
| Total number of infections, n (%) | 83 (8.4) | 380 (14.3) | **<0.001** |
| Ventilator-associated pneumonia (VAP)\*, n(%) | 21 (25.3) | 131 (34.5) | 0.06 |
| Bacteraemia secondary to other septic foci (BS), n(%) | 17 (20.0) |  40 (10.5) | **0.01** |
| Bacteraemia of unknown origin (BUNK), n (%)  |  9 (10.8) |  60 (15.8) | 0.25 |
| Catheter-associated urinary tract infection (CAUTI), n(%) |  8 (9.6) |  42 (11.0) | 0.70 |
| Ventilator-associated tracheobronchitis (VAT), n (%) |  5 (6.0) | 32 (8.4) | 0.46 |
| Catheter-related bacteraemia (CRB), n (%) | 4 (4.8) |  47 (12.3) | **0.04** |
| Intra-abdominal infections (IAI), n (%) | 4 (4.8) |  6 (1.6) | 0.08 |
| Skin and soft tissue infection (SSTI), n (%) | 4 (4.8) |  5 (1.3)  | 0.09 |
| Others, n (%)  | 11(13.2) |  6 (1.6)  | **<0.001** |
| Main micro-organisms isolated during ICU stay |
| Total number of microorganisms isolated, n (%) | 102 (10.3)  |  500 (18.9) | **<0.001** |
| *Staphylococcus aureus*  | 16 (15.7) |  70 (14.0) | 0.7 |
| *Escherichia coli* | 13 (12.7) |  49 (9.8) | 0.5 |
| *Klebsiella pneumoniae*  | 10 (9.8) |  58 (11.6) | 0.7 |
| *Pseudomonas aeruginosa* | 9 (8.8) |  78 (15.6) | **0.04** |
| *Enterobacter aerogenes*  | 7 (6.8) |  12 (2.4) | **0.02** |
| *Serratia marcescens* | 6 (5.8) |  20 (4.0) | 0.55 |
| *Haemophilus influenzae* | 5 (4.9) |  23 (4.6) | 1.0 |
| *Enterococcus faecium*  | 4 (3.9) |  9 (1.8)  | 0.33 |
| *Klebsiella oxytoca*  | 4 (3.9) |  11 (2.2) | 0.50 |
| *Proteus mirabilis*  | 3 (2.9) |  8 (1.6) | 0.60 |
| *Citrobacter* spp. | 3 (2.9) |  13 (2.6) | 1.0 |
| *Enterobacter cloacae* | 3 (2.9) |  29 (5.8) | 0.35 |
| *Enterococcus faecalis*  | 3 (2.9) |  30 (6.0) | 0.31 |
| Others | 16 (15.6) |  90 (18.0) | 0.67 |
| Incidence density of reported ICU-associated infections |
| VAP episodes/1000 mechanical ventilation days (95% CI) | 5.5 (3.5-8.3) | 7.3 (6.1-8.7) | 0.66 |
| CAUTI episodes /1000 urinary catheter days (95% CI) | 1.3 (0.6-2.6) | 1.6 (1.1-2.1) | 0.62 |
| BRC and BUNK episodes / 1000 catheter days (95% CI) | 1.7 (0.3-6.6) | 2.8 (2.2-3.7) | 0.89 |
| BS episodes / 1000 ICU days (95% CI) | 2.3 (1.4-3.7) | 1.3 (1.0-1.8) | 0.81 |
| Complications and Outcome |
| Invasive Mechanical ventilation , n(%) | 425 (43.1) | 1377 (52.0) | **<0.001** |
| LOS ICU, mean (Q1-Q3) | 4.0 (2.0-8.0) |  3.9 (2.1-7.9) | **0.009** |
| Crude ICU Mortality, n (%)  | 165 (16.7) | 460 (17.4) | 0.67 |

e-Table 3: Microorganisms isolated in patients with ventilator-associated pneumonia according to the study period.

|  |  |  |
| --- | --- | --- |
|  | **Pre-intervention**  | **Intervention**  |
| **Year**  | **2018**  | **2019** | **2020** | **2021** |
|  **Nº Patients/ Nº Microorganisms**  | 21 /27 | 12/20 | 38/56 | 92/132 |
| *Staphylococcus aureus* n (%) | 9 (33.3) | 4 (20.0) | 15 (26.8) | 28 (21.0) |
| *Klebsiella* sppn (%) | 4 (14.8) | ---- | 7 (12.5) | 16 (12.1) |
| *Escherichia coli* n (%) | 3 (11.1) | 3 (15.0) | 3 (5.3) | 12 (9.0) |
| *Pseudomonas aeruginosa* n (%) | 3 (11.1) | 4 (20.0) | 9 (16.0) | 24 (18.2) |
| *Haemophilus influenzae* n (%) | 2 (7.4) | 3 (15.0) | 3 (5.3) | 6 (4.5) |
| *Proteus mirabilis* n (%) | 1 (3.7) | ---- | 2 (3.5) | 2 (1.5)  |
| *Stenotrophomona maltophilia* n (%) | 1 (3.7) | ---- | 1 (1.8) | 2 (1.5) |
| *Streptococcus pneumoniae* n (%) | 1 (3.7) | 2 (10.0) | 1 (1.8) | 4 (3.0) |
| *Enterobacter* spp.n (%) | 1 (3.7) | ---- | 2 (3.6) | 12 (9.0) |
| *Acinetobacter* spp. n (%) | ---- | 1 (5.0) | 1 (1.8) | 3 (2.3) |
| *Staphylococcus aureus methicillin resistant* n (%) | ---- | 1 (5.0) | ---- | 2 (1.5) |
| *Serratia marcescens* | ---- | ---- | 3 (5.3) | 6 (4.5) |
| *Aspergillus* spp | ---- | ---- | ---- | 7 (5.3) |
| Others | 2 (7.4) | 2 (10.0) | 9 (16.0)  | 8 (6.0) |

e-Table 4: ATB consumption expressed in defined daily doses (DDD) according to the pre- and post-intervention period. Rate Ratio (RR) shows the variation of DDD between the periods compared.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **2018(1)** | **2019(2)** | **2020(3)** | **2021(4)** | **RR 2 vs 1 (95%CI)** | **RR 3 vs 1 (95%CI)** | **RR 4 vs 1 (95%CI)** |
| **Overall** | 128.7 | 124.2 | 113.8 | 66.0 | 0.96 (0.93-0.99)\* | 0.88 (0.80-0.91)\* | 0.51 (0.49-0.53)\* |
| **MRP** | 21.8 | 25.9 | 19.6 | 16.0 | 1.18 (1.11-1.27)\* | 0.89 (0.84-0.96)\* | 0.73 (0.68-0.78)\* |
| **PTZ** | 7.42 | 6.19 | 6.89 | 2.96 | 0.83 (0.73-0.94)\* | 0.92 (0.82-1.03) | 0.39 (0.34-0.45)\* |
| **CAZ** | 2.37 | 0.99 | 1.63 | 0.65 | 0.41 (0.31-0.54)\* | 0.68 (0.55-0.84)\* | 0.27 (0.20-0.35)\* |
| **CFP** | 1.06 | 0.60 | 0.31 | 0.09 | 0.56 (0.39-0.75)\* | 0.29 (0.22-0.49)\* | 0.08 (0.03-0.2)\* |
| **AZT** | 0.02 | 0.72 | 1.25 | 1.33 | 36.0 (7.1-180.0)\* | 62.5 (12.0-309.0)\* | 66.5 (13.2-329.3)\* |

MRP= Meropenem; PTZ= Piperacillin/Tazobactam ; CAZ= Ceftazidime CFP= Cefepime; AZT= Aztreonam. \* p-value <0.05

e-Figure 2: Resistance pattern of Pseudomonas aeruginosa strains in isolates from respiratory samples for the main antimicrobials comparing pre (2018) and post-intervention periods (2021).



PTZ= Piperacillin/Tazobactam ; CAZ= Ceftazidime; CFP= Cefepime ; IMI= Imipenem; MRP= Meropenem; AMK= Amikacine; CIPRO= Ciprofloxacin ; COL= Colistin; AZT=Aztreonam