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Admission screening and cohort care decrease carbapenem resistant enterobacteriaceae in Vietnamese pediatric ICU's

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Abstract

Objectives: To assess if admission screening for Carbapenem Resistant *Enterobacteriaceae* (CRE) and cohort care can reduce CRE acquisition (CRE colonization during hospital stay), Hospital Acquired Infections (HAI), hospital-stay, mortality, and costs in three Intensive Care Units (ICU's) at the Vietnamese National Children's Hospital.

Method: CRE screening using rectal swabs and *ChromIDCarbas* elective culture at admission and if CRE negative, once weekly. Patients were treated in cohorts based on CRE colonization status.

Results: CRE colonization at baseline point-prevalence screening was 76.9% (103/134). Of 941 CRE screened at admission, 337 (35.8%) were CREpos. 694 patients met inclusion criteria. The 244 patients CRE negative at admission and screened > 2 times were stratified in 8 similar size groups (periods), based on time of admission. CRE acquisition decreased significant (OR = 3.2, $p < 0.005$) from 90% in period 2 (highest) to 48% in period 8 (last period). Patients with CRE acquisition compared to no CRE acquisition had a significantly higher rate of culture confirmed HAI, $n = 20$ (14%) vs. $n = 2$ (2%), longer hospital stays, 3.26 vs. 2.37 weeks, and higher total treatment costs, 2852 vs. 2295 USD.

Conclusion: Admission CRE screening and cohort care in pediatric ICU's significantly decreased CRE acquisition, cases of HAI and duration of hospital-stay.

Keywords: Cohort care, Carbapenem resistant *Enterobacteriaceae*, Hospital acquired infections, Admission screening, Pediatric and neonatal care

Introduction

Antibiotic resistance is resulting in increased morbidity, mortality and healthcare costs [1]. In South East Asia, the situation is especially severe [2, 3]. Hospital acquired infections (HAI) with Carbapenem Resistant *Enterobacteriaceae* (CRE) are resistant to most antibiotics [4, 5] and very difficult to treat even with last resort antibiotics including tigecycline, gentamicin, amikacin and colistin [4, 6].

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CRE colonization and HAI are common in Vietnamese intensive care units (ICU's) [2,7,8]. CRE colonized patients with HAI has high mortality [7,9,10,6,9–12], 12–14,15,12,14,

Materials and methods

Design

This was a prospective intervention cohort study with a quasi-experimental design at the Vietnamese National Children's Hospital (VNCH) ICU's. It was performed to assess the effectiveness of CRE admission screening and cohort care on CRE acquisition and colonization, HAI, treatment outcome and costs. Implemented from 2018-03-20 to 2018-06-20 (Fig. 1). Conventional Infection Prevention and Control (IPC) measures were already in place in the ICU's, including instructions for

hand hygiene, availability of alcoholic hand rub, personal protective equipment, gloves and shoe protection, and an active antibiotic stewardship group. The project promoted and strengthened these IPC measures.

According to CRE colonization status in the baseline PPS in the ICU's, patients were moved to CRE positive (CREpos) or CRE negative (CREneg) cohorts. Following the PPS, all new admissions were CRE screened and cohorted in a separate area for newly admitted patients with unknown colonization status. The fecal screening samples were transported to the microbiology lab and cultured. According to screening result, patients were moved to either the CREpos or CREneg cohort. The cohort care intervention started at the same time as the admission screening as it was considered unethical to not cohort patient once their CRE-status was known. Patients

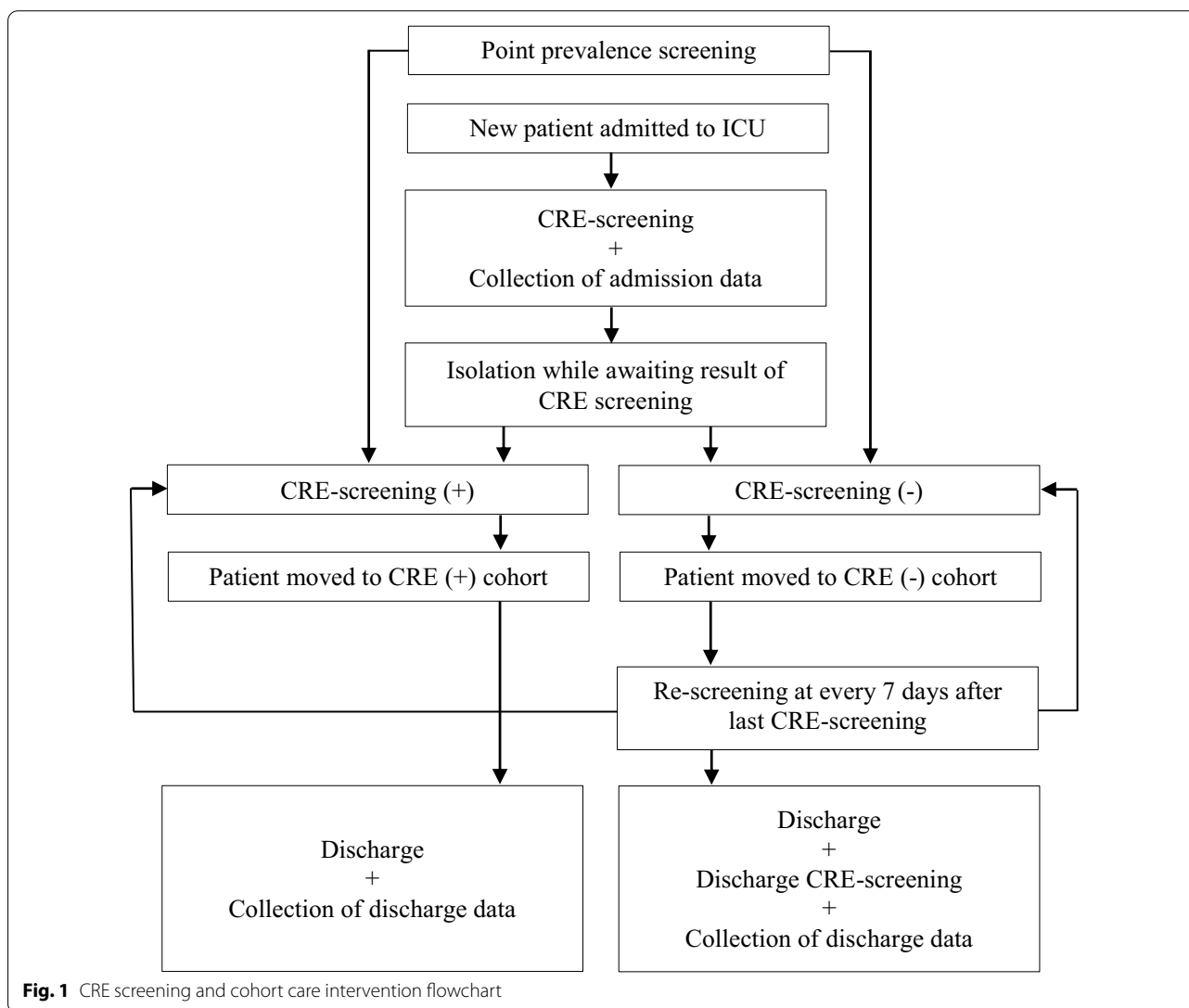


Fig. 1 CRE screening and cohort care intervention flowchart

screening CREneg were re-screened every 7 days of ICU care and discharge screened if > 48 h after admission. All patients diagnosed with a HAI were isolated in a separate area with designated staff according to pre-existing ICU protocols. ICU staff implemented the intervention and collected patient data on paper forms in Vietnamese.

Participants

Inclusion criteria

1. All patients admitted to the ICU's.
2. For newborns admitted to the Neonatal Intensive Care Unit (NICU), CRE admission screening was performed at the earliest 24 h after birth (as detectable bacterial intestinal colonization is not established < 24 h).
3. Patients already admitted before the start of the intervention were screened and treated in cohorts according to CRE status but were not included in the intervention.

Setting

The study was implemented at the VNCH's 3 main pediatric ICU's: the general Pediatric Intensive Care Unit (PICU); the Surgical Intensive Care Unit (SICU) and the NICU. In total, there were 176 beds (NICU n = 80, PICU n = 62, SICU n = 34), all typically occupied. There were up to 20 beds in the same room in the NICU, up to 10 in the PICU and 3–6 beds in the SICU. Each ward was divided into three sections: for newly arrived patients awaiting screening results; for patients screened CREneg and for patients screened CREpos.

Bacterial culture

Fecal samples were collected using rectal swabs (*ESwabs: Copan, Brescia, Italy, ChromID Carba: Biomérieux, Marcy-l'Étoile, France*). Incubation time 18 h as per manufacturer's instructions [16,

Economic outcomes

Data on the cost of hospital stay was obtained from the hospital economic division after patient discharge. The total cost was assessed in relation to CRE colonization and HAI. CRE screening cost was estimated at 3 USD per patient / two screenings.

Sample size

The sample size was based on admission CRE colonization rate of ~ 30% and at discharge ~ 80% [7,

Statistics

The *primary outcome, Secondary outcomes, Microsoft Corp*) was used for preliminary data input. The *IBM SPSS Statistics software (version 22 IBM, CA, Free Statistics and Forecasting Software [17] and Social Science Statistics [18]*. *p*-value of < 0.05 was considered significant.

Results

Baseline CRE point prevalence survey

Baseline CRE PPS was performed on the 20th of March 2018 in the NICU: 21st in the SICU and 22nd in the PICU. 103/134 patients (76.9%) were CRE colonized: NICU 79.4% (54/68), SICU 60.7% (17/28) and PICU 84.2% (32/38) (Table 1).

Admission CRE screening

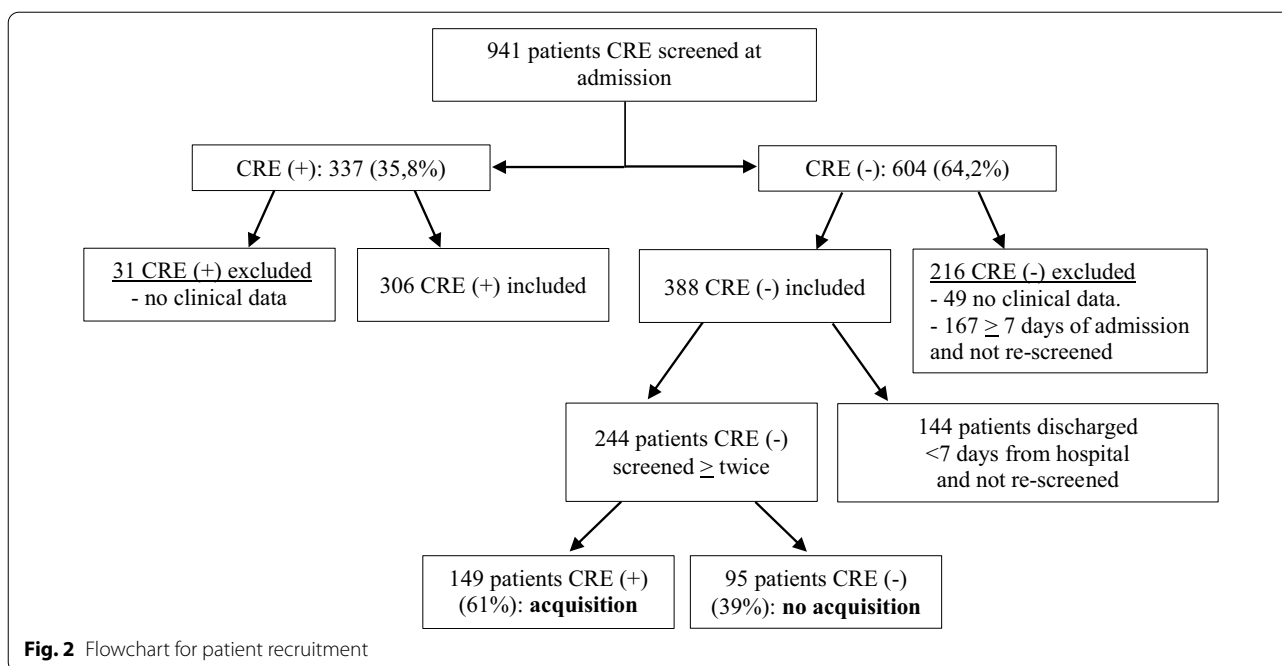
A total of 941 patients were CRE screened at admission to the ICU's. 337 (35.8%) were CRE colonized: NICU 39.6% (165/417), PICU 40.6% (91/224) and SICU 27.0% (81/300). Of the 694 patients (73.8%) that met the inclusion criteria, 306 (44.1%) were CREpos: NICU 46.7% (151/323), PICU 48.8% (84/172) and SICU 35.7% (71/199). Of the 247 patients excluded, 80 lacked clinical data: 31 (38.8%) CREpos; another 167 were CREneg and admitted > 7 days and not rescreened, hence acquisition status could not be determined. Of the 388 patients screened CREneg at admission and included, 244 (62.9%) were screened > 2 times and could be included

Table 1 Point prevalence data

| Variables | NICU N (%) | PICU N (%) | SICU N (%) | Total N (%) |
|--------------------------------|------------|------------|------------|-------------|
| CRE + | 54 (79) | 32 (84) | 17 (60) | 103 (77) |
| Crude mortality | 15 (22) | 13 (34) | 6 (21) | 34 (25) |
| Total | 68 (100) | 38 (100) | 28 (100) | 134 (100) |
| <i>Klebsiella pneumoniae</i> | 43 (80) | 16 (50) | 7 (41) | 66 (49) |
| <i>Escherichia coli</i> | 33 (61) | 20 (62) | 2 (12) | 55 (41) |
| KESC* | 6 (11) | 10 (31) | 5 (29) | 21 (16) |
| Other** | 6 (11) | 8 (25) | 7 (41) | 21 (16) |
| <i>Acinetobacter baumannii</i> | 3 (6) | 0 | 0 | 3 (2.2) |
| <i>Pseudomonas aeruginosa</i> | 1 (2) | 0 | 1 | 2 (1.5) |

* KESC *Klebsiella* species., *Enterobacter* species, *Serratia marcescens* and *Citrobacter* species

** Other = culture growth, bacteria not identifiable



in the acquisition assessment cohort. 144 (37.1%) of the CREneg patients were admitted <7 days and not rescreened (Fig. 2).

There was a significant correlation between CRE colonization and HAI ($p < 0.005$) as well as HAI related mortality ($p < 0.05$) when compared to CREneg patients. CREpos patients had a significantly higher number of hospital days and healthcare cost compared to CREneg patients, 23.4 days and 2568 USD vs. 8.1 days and 1351 USD, respectively (Table 2). For patients with a mortal outcome, the average duration of hospital stay was significantly longer for CREpos patients (27.6 days) vs. CREneg (8.8 days).

CRE acquisition

244 patients CREneg at admission were rescreened. An average 2.35 screenings were performed per patient, with 147 (60%) CREpos in rescreening (acquisition). Patients with CRE acquisition vs. no acquisition were screened on average 2.5 and 2.1 times, respectively. The cohort of 244 CREneg patients were stratified according to ICU: NICU (109), PICU (60) and SICU (75). In each ICU, all patients were split in 8 similar size groups, (periods), based on time of admission, roughly corresponding to weeks. A significant negative correlation between CRE acquisition and periods was seen ($p < 0.0005$), corresponding to a significant decrease in acquisition in univariate- and multivariate analysis (OR = 3.2, $p < 0.005$). A significant decrease of CRE acquisition was seen from the 2nd to the 8th period in the PICU ($p < 0.05$) and SICU ($p < 0.005$),

however not in the NICU ($p < 0.2$). When assessing CRE acquisition in NICU from the 2nd up to the 6th period ($n = 68$), a significant ($p < 0.05$) decrease of CRE acquisition was seen (Fig. 3).

CRE acquisition was significantly correlated with culture confirmed HAI ($p < 0.005$), weeks of hospital stay ($p < 0.0005$) and total treatment cost ($p < 0.05$), but not with mortality and bacterial infections based on CD10 codes (Table 3). In multivariate analysis, a significant correlation between CRE acquisition and weeks of hospital stay was seen ($p < 0.001$), however not with healthcare cost, the latter likely due to highly significant ($p < 0.00001$) co-variation between healthcare cost and weeks of hospital stay. A significant correlation ($p < 0.001$) was seen between periods and decreased healthcare cost (cost decreased with time), but no significant correlation with HAI or weeks of hospital stay.

Microbiological findings

The most common colonizing CRE were *E. coli* (41% of patients and 35% of isolates), *K. pneumoniae* (38% of patients and 32% of isolates), *KESC* (*Klebsiella* spp., *Enterobacter* spp., *Serratia marscescens*, and *Citrobacter* spp.) (26% of patients and 22% of isolates) and “finally” other G-bacteria such as *Acinetobacter baumannii* and *Pseudomonas aeruginosa* (14% of patients and 12% of isolates). In culture confirmed HAI, *K. pneumoniae* (59%) and *E. coli* (33%) were the most common (Table 4). Several patients had growth of more than one bacteria in

Table 2 General characteristics in groups as per CRE-status, department, crude mortality, culture confirmed HAI, HAI related mortality, duration of hospital stay, total cost and most common primary diagnosis during ICU care

| Variables | NICU | PICU | SICU | Crude mortality | HAI* | HAI mortality | Total | Hospital stay (days) | Cost |
|---|-----------------|-----------------|-----------------|------------------|------------------|------------------|--------------|----------------------|---------------|
| Female (%) | 117 (40) | 82 (28) | 91 (31) | 73 (25) | 18 (6) | 10 (3.5) | 290 | 16 | 1909 |
| Male (%) | 206 (51) | 88 (22) | 108 (27) | 94 (23) | 39 (10) | 16 (4) | 402 | 19 | 2311 |
| CRE + at admission (%) | 151 (49) | 84 (27) | 71 (23) | 65 (21) | 30 (10) | 15 (5) | 306 | 24.2 | 2419 |
| CRE—at admission (%) | 172 (44) | 88 (23) | 128 (33) | 102 (26) | 29 (7) | 11 (3) | 388 | 14.2 | 1917 |
| CRE Acquisition (%) | 82 (56) | 39 (27) | 26 (18) | 19 (13) | 20 (14) | 5 (3) | 147 | 24.3 | 2852 |
| No CRE acquisition (%) | 27 (28) | 21 (22) | 49 (51) | 21 (28) | 2 (2) | 1 (1) | 97 | 14.6 | 2295 |
| CRE—not re-screened** (%) | 63 (44) | 28 (19) | 53 (37) | 63 (44) | 7 (5) | 5 (3.5) | 144 | 3.8 | 712 |
| CRE + total (%) | 233 (51) | 123 (27) | 97 (21) | 84 (19) A | 50 (11) B | 20 (4) C | 453 T | 23.4 D | 2568 E |
| CRE—total (%) | 90 (37) | 49 (20) | 102 (42) | 83 (34) A | 9 (4) B | 6 (2.5) C | 241 T | 8.1 D | 1351 E |
| Total (%) | 323 (46) | 172 (25) | 199 (29) | 167 (24) | 59 (8.5) | 26 (3.7) | 694 | 18.0 | 2141 |
| Age at screening (months) | 0.32 | 22.2 | 32.6 | 13.1 | 3.88 | 1.16 | 12.9 | NA | NA |
| Pneumonia + bronchiolitis (J12–21) | 44 | 65 | 18 | 14 (11) | 11 (9) | 1 (1) | 127 | 20 | 2344 |
| Congenital malformations (Q01–99) | 25 | 11 | 59 | 24 (25) | 8 (8) | 3 (3) | 95 | 20 | 2303 |
| Extreme immaturity + Other preterm infants (P07–07.3) | 51 | 3 | 0 | 13 (24) | 8 (15) | 1 (2) | 54 | 19 | 2644 |
| Bacterial sepsis of newborn (P36) | 45 | 0 | 0 | 18 (40) | 9 (20) | 6 (13) | 45 | 20 | 2006 |
| Birth asphyxia + Respiratory distress (P21–P22.1) | 38 | 0 | 2 | 10 (25) | 5 (13) | 5 (13) | 40 | 14 | 1531 |
| Malignant neoplasms (C22–C92) | 1 | 6 | 28 | 8 (23) | 1 (3) | 0 | 35 | 18 | 1707 |
| Neonatal jaundice (P55.0–P59.0) | 23 | 1 | 1 | 0 | 0 | 0 | 25 | 16 | 701 |
| Sepsis + Septic shock (A41.0–41.9 + R57.2) | 1 | 16 | 4 | 12 (57) | 1 (5) | 1 (5) | 21 | 25 | 3303 |
| Intracerebral haemorrhage (I61) | 1 | 0 | 18 | 5 (26) | 0 | 0 | 19 | 13 | 1040 |
| Acute respiratory failure (J96.0) | 2 | 7 | 3 | 10 (83) | 0 | 0 | 12 | 12 | 4035 |

* Culture confirmed HAI caused by *Enterobacteriaceae*

** CREneg at admission and not re-screened and discharged < 1 week

CREpos total vs CREneg total:

A. Crude mortality vs Total mortality, significant $p < 0.001$ Chi²B. HAI (n), significant $p < 0.002$ Chi²C. HAI mortality vs Crude mortality, significant $p < 0.005$ Chi²D. Hospital stay days, significant $p < 0.001$ t-testE. Cost, significant $p < 0.001$ t-test

cultures. Repeated cultures with same strain from the same patient was excluded from the data set.

Hospital acquired infections

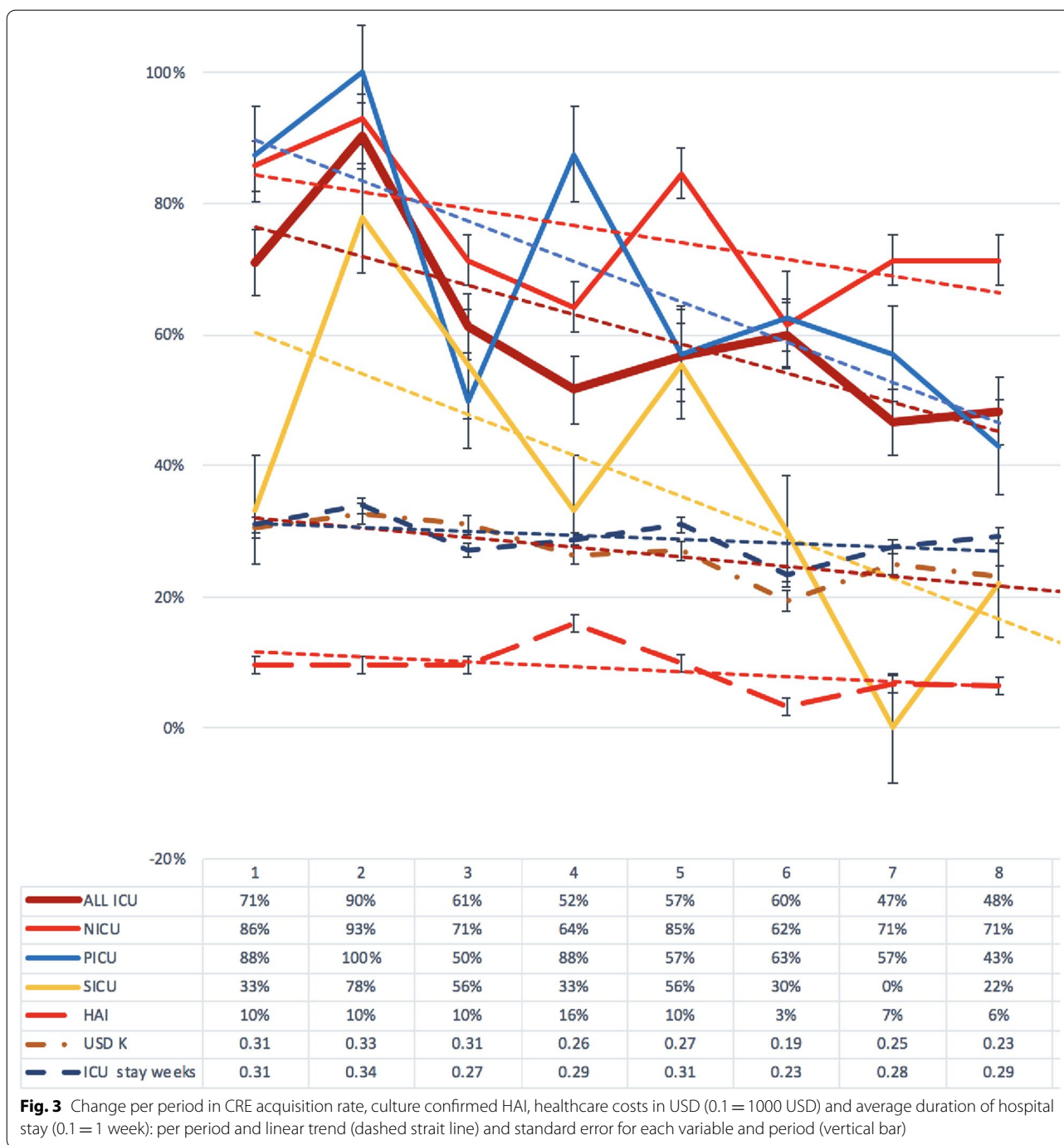
Of the 694 patients screened for CRE, 59 (8.5%) acquired culture confirmed HAI caused by *Enterobacteriaceae* (Table 2). *K. pneumoniae* HAI was the most common: (n=37), with 15 cultures from blood and 22 from tracheal aspirate. Antibiotic susceptibility data was available for 18 cultures, 15 (83%) carbapenem resistant and 13 (72%) gentamycin resistant. HAI with *E. coli*: 21 cultures, 7 blood and 14 tracheal aspirate, antibiotic susceptibility data available for 10 cultures, 6 (60%) resistant to both carbapenem and gentamycin (Table 4). Patients with culture confirmed HAI with *Enterobacteriaceae* when

compared to all other patients, had significantly higher mortality ($p < 0.001$), 32% vs. 13%; CRE colonization ($p = 0.016$), 62% vs. 50%; CRE acquisition ($p = 0.0078$), 85% vs. 57%; longer hospital stay ($p = 0.012$), 23.2 days vs. 17.7 days and costs ($p = 0.029$), 2876 USD vs. 2116 USD (Table 2).

Discussion

Main findings

In all ICU's combined, CRE acquisition decreased significantly from 90% in period 2 to 48% in period 8 during the intervention. The decrease was most pronounced in the PICU and SICU: from 100 and 78% period 2, to 43% and 22% period 8, respectively. In the NICU, a significant decrease of CRE acquisition was detected from period 2



(93%) to period 6 (62%), however an increase to period 8 (71%). The NICU has the most beds per room, highest rate of admission, several concurrent cohorting of respiratory syncytial virus (RSV) infections, HAI and preterm neonates, and suffered from overcrowding towards the end of the study, likely explaining the increase seen in latter periods. In the SICU, the CREpos cohort was treated

in an isolation room. Smaller cohorts and isolation rooms with designated personnel could further decrease the risk for CRE acquisition. [19].

Point prevalence survey result

[7,7] have shown a constant high- and increasing rate of CRE colonization in Vietnamese hospitals and ICU's.

Table 3 Uni- and multi-variate analysis (Pearson correlation and multiple linear regression) based on CRE acquisition vs. no acquisition in relation to time (periods)

| Variable | CRE Acquisition | No CRE Acquisition | Uni-variate | | | Multi-variate | | | |
|-----------|-----------------|--------------------|-------------------------|--------------|--------------|---------------|------------|------------------------|------------------------|
| | | | Pearson <i>p</i> -value | CI 95% lower | CI 95% upper | S.D | Odds ratio | 2-tail <i>p</i> -value | 1-tail <i>p</i> -value |
| PERIOD | 149 (61%) | 95 (39%) | < 0.0005 | -0.33 | -0.09 | 0.0123 | -3.19 | 0.0016 | 0.0008 |
| HAI | 20 (14%) | 2 (2%) | < 0.005 | 0.07 | 0.31 | 0.1031 | 2.73 | 0.0067 | 0.0034 |
| Mortality | 19 (13%) | 20 (21%) | 0.12 NS | -0.24 | 0.006 | | | | |
| Infection | 49 (33%) | 21 (22%) | 0.13 NS | -0.004 | 0.24 | | | | |
| USD | 2855 | 2287 | < 0.05 | -0.012 | 0.236 | 0.0197 | -1.22 | 0.22 NS | 0.11 NS |
| WEEKS* | 3.26 | 2.37 | < 0.0005 | 0.109 | 0.347 | 0.0226 | 3.54 | 0.00048 | 0.00024 |
| NICU | 82 (75%) | 27 (25%) | 3.66 NS | 0.14 | 0.37 | | | | |
| PICU | 39 (65%) | 21 (35%) | 0.47 NS | -0.08 | 0.17 | | | | |
| SICU | 28 (37%) | 47 (63%) | 2.23 NS | -0.43 | -0.21 | | | | |

HAI = culture confirmed HAI, Infection = bacterial infection ICD10 diagnosis, USD = treatment cost, WEEKS* = duration of hospital stay in weeks

Table 4 Bacterial growth from CRE screenings and culture confirmed HAI (N = 694 patients)

| | <i>E. coli</i> N (%) | <i>K. pneumoniae</i> N (%) | <i>KESC</i> # N (%) | Other## N (%) | Total N isolates N (%) | Mortality N (%) |
|-----------------------|------------------------|----------------------------|------------------------|----------------------|-------------------------------|----------------------|
| CREpos screening (%) | 185 (41)P 185 (35)I | 173 (38)P 173 (32)I | 116 (26)P 116 (22)I | 62 (14)P 62 (12)I | 453 (118) P* 536 (100) I * | 167/694(24) |
| HAI isolates (%) | 21/59 (36) | 37/59 (63) | 1/59(2) | 0 (0) | 59/59 (100) | 26/59 (44) |
| Blood (%) | 7/21 (33) | 15/37(41) | 7/17 (41) | 0 (0) | 22/59 (37) | 10/22 (45) |
| Tracheal aspirate (%) | 14/21 (66) | 22/37 (59) | 10/17 (59) | 3/3 (100) | 37/59 (63) | 16/37 (43) |
| Carbapenem R/S (%R) | 6/4(60) | 15/3(83) | 7/0 (100) | 2/2 (100) | 22/7 (76) | R12/22(55); S3/7(43) |
| Gentamycin R/S (%R) | 6/4 (60) | 13/5 (72) | 7/0 (100) | 2/2 (100) | 20/9 (69) | R11/20(55); S4/9(44) |
| Mortality CREpos (%) | 36/185 (19) | 34/173 (20) | 20/116 (17) | 10/62 (16) | 71/453 (16) | 71/694 (10) |
| Mortality HAI (%) | 8/21 (38) | 17/37(46) | 8/17 (47) | 3/3 (100) | 26/59 (44) | 26/694 (4) |

R = resistant, S = sensitive. EC = *Escherichia coli*, KP = *Klebsiella pneumoniae*, HAI = Culture Confirmed HAI

P = patients (n = 453), I = isolates (N = 534) *In average 1,18 isolates per screening culture (534/453)

KESC (*Klebsiella spp.*, *Enterobacter spp.*, *Serratia marscescens*, and *Citrobacter spp.*)

Other including *Pseudomonas Aeruginosa* and *Acinetobacter baumannii*

Italicized area CC HAI isolates among screening positive patients (CC both *Escherichia coli*, *Klebsiella pneumoniae* CC and *Enterobacter*)

CRE colonization secondary endpoints

,4]. Colonization was associated with increased risk for HAI and mortality [7,8,3,5,9,20,21–24] This strategy has been successful in high income country hospitals [25,7,2,3,7,26]. CRE surveillance in province hospitals is needed to contain the transmission.

HAI

Patients with CRE colonization and acquisition had significantly higher rates of culture confirmed HAI with *Enterobacteriaceae*,2). Correlation between colonization and HAI was shown in our previous study [7] and has been established in other studies also [27,25,28].

Microbiology findings

,*E. coli*; 38% *K. pneumoniae*; 26% *KESC* and 13% for other G-negative bacteria. In our previous PPS from 2017 [7,*K. pneumoniae*, and 58.5% for *E. coli* [7],*K. pneumoniae*,*Enterobacteriaceae*, such as *Acinetobacter baumannii* and *Pseudomonas aeruginosa*, which are also an important cause of severe HAI with high mortality in Vietnamese pediatric ICU's [8].

Treatment outcome

The mortality rate in CRE colonized patients with culture confirmed HAI was significantly higher (24%) compared to non-colonized patients with HAI (7%). Similar results was seen in our previous 2017 study [7,7]. Other studies have also shown high mortality rates in patients with infections caused by CRE [12,20,*Enterobacteriaceae*,,

Costs

,9,23,29–31,

The hospital cost in Vietnam is to a high extent covered by the health insurance, provided for free to children up to 6 years of age. At the time of the intervention, the costs for CRE screening were not reimbursed, despite potentially being able to save large resources for the health insurance. Patients with HAI occupy an ICU place for a longer time and blocks new admissions that require more investigations, hence pose an economic burden for the hospitals, in addition to increased patient mortality and morbidity.

The intervention was performed at a low cost, about 3 USD per agar plate, which can be used for two cultures. Costs for laboratory and ICU labor was however not accounted for. The aim of this intervention was to perform it at a cost level, which would allow a continuous CRE screening and cohort care.

Strengths and limitations

One major limitation in this study is that it was an interventional study with no control group. Further, the intervention, for ethical reasons, started immediately after a patient's CRE status was revealed. As this was no randomized controlled trial of CRE screening and cohort care, the results of this study can only be interpreted as indicative. The intervention was performed in pre-existing facilities and without extra staff, beside the research team. The cohorts could in most situations not be completely physically separated and it was not always possible to have designated staff. The high CRE colonization rate at admission made it challenging to isolate patients. Of 604 patients screened CREneg at admission, only 244 (40.4%) were re-screened. Reasons for this include that many patients were admitted for <48 h, patients were moved with short notice when discharged from ICU, lack of staff and reluctance to rectal swab patients after death. Despite these limitations, which in LMIC are a realistic actual setting, our study showed that admission CRE screening and cohort care intervention significantly *can* reduce the rates of CRE acquisition and HAI as well as shorten hospital stays and decrease costs.

Higher levels of HAI, higher treatment costs and a higher level of HAI-related mortality was seen in CREpos patients when compared to CREneg. One possible confounder is whether CREpos patients represents a group of patients with higher levels of co-morbidities (more ill patients) and therefore more prone to get colonized, have longer treatment periods in the hospital and be more likely to get nosocomial infections (HAI's) and suffer a mortal outcome from these. The intervention design without a control group does not allow for determining whether associations of CRE colonization

(initial) and acquisition with HAI, costs, and mortality (later), are causal. The group of patients treated in a separate cohort while awaiting their admission CRE screening results contained both CREneg and CREpos patients. Although it was the ambition to distance the patients in the group, possibly exposure could not be excluded, providing a risk of patients initially screening CREneg becoming colonized while awaiting their screening results. Some patients were likely colonized during this waiting period, which was deemed non-preventable in this intervention. In ideal conditions, complete isolation of patients from one another would be preferred but was not possible within the VNCH ICU's. The 7-day follow-up screening on all admitted patients was used, to limit the transmission of CRE in the CREneg cohort.

Conclusion

The admission CRE screening and cohort care intervention showed that CRE acquisition can be reduced with limited resources and be cost-effective by reducing CRE colonization, HAI and duration of hospital stay. As large proportions of patients were CRE colonized at admission, indicating a significant CRE spread in non-tertiary level hospitals, CRE screening should be implemented in all healthcare levels in the endemic Vietnamese system, however likely not applicable to other countries with lower levels of CRE. To enable permanent CRE admission screening and cohort care implementation, economic incentives for the health care sector to use CRE screening as a tool (such as reimbursement for screening costs from the health insurance system) should be warranted. The significant reduction in CRE acquisition found in this study is indicative, as there was no control group and further since the intervention, for ethical reasons, started as soon as patient's CRE status were known. To create evidence, a randomized controlled trial in a larger patient material assessing the effects of CRE screening and cohort care would be recommended.

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Authors' contributions

Conceptualization: K. Garpvall, Dung T.K. Khu, Ngai K. Le, Ngoc T.B. Hoang, L. Olson, M. Larsson; Data curation: K.G, D. Mucchiano, S. Modeen, L. Lagercrantz, L.O, M.L; Formal analysis: K.G, M.L; Funding acquisition: L.O, M.L and student authors for SIDA minor field study grant; Investigation: K.G, V. Duong,

T.N. Quốc, D.M. S.M, L.L, A.E, N.K.L, T. Huong, N.T.B.H, H.T.Le, D.T.K.K, D.M Tran, P.H Phuc, H. Hanberger, L.O. M.L; Methodology: N.K.L, D.M.T, L.O. M.L; Project administration: D.T.K.K, N.K.L, P.H.P, L.O. M.L; Resources: N.K.L, P.H.P, N.T.B.H, D.M.T, H.H, L.O. M.L; Supervision: K.G, N.K.L, N.T.B.H, H.T.L, D.M.T, L.O. M.L; Validation: L.O. M.L; Visualization: K.G, V.D, T.N.Q, D.M, S.M, L.L, A.E; Writing—original draft: K.G, M.L; Writing—review & editing: All authors. All authors read and approved the final manuscript.

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Availability of data and materials

All data is stored in a secure place with all patient information unidentifiable, for patient security reasons. All data can be accessed only after written permission to the hospital and Mattias.Larsson@ki.se.

Declarations

Ethics approval

This study followed the ethical standards of the Helsinki declaration of 2008. Ethical approval was obtained from the VNCH Ethics Committee (reference number 812/QD-BVNTU, 23rd March 2017). Informed consent was given on an opt-out basis and all caregivers were informed about the study.

Consent for publication

Not applicable.

Competing interests

There is no reported conflict of interest. All authors have agreed to participate in the paper.

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