Bacteriological Profile of Health Care Associated Infection and Antibiotic Resistance Pattern of Isolates at Picu in a Tertiary Care Hospital

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Abstract

Background: Healthcare Associated Infections (HAIs) are a major cause of morbidity and mortality in Pediatric intensive care units (PICUs). The aim was to determine bacteriological profile of HAI and to establish an antibiogram of isolates in our PICU.

Materials and Method: This was a retrospective study conducted at the Department of Pediatrics (Pediatric Intensive Care Unit) of AIIMS, Jodhpur. Data was collected over 2 years from January 2017 to December 2018. Among the114 culture positive isolates, 50% (57/114) were gram negative and 22.8% (26/114) were gram positive organisms. Culture positivity for fungal growth was 14 % (17/114) and rest 12.2% (14/114) were contaminants. The most common isolate in gram negative organism was Acinetobacter baumannii and in gram positive organism most common isolates were Enterococcus. Most commonly detected HAI types were ventilator associated pneumonia (VAP) - 34% (20/59). All gram negative organisms were resistant to carbepenems except Pseudomonas (100% sensitivity). Among gram positive organisms, methicillin resistant staphylococcus aureus (MRSA) was 100% sensitive to gentamicin, amikacin, vancomycin and linezolid.

Conclusion: The retrospective study showed that both gram positive and negative bacteria as well as fungal organisms are responsible for HAIs. Most of the strains were multi drug resistant.

Key words: *VAP- ventilator associated pneumonia, CRBSI- catheter related blood stream infection, CAUTI - catheter associated urinary tract infection, PICU - Pediatric intensive care units*

Introduction

Healthcare Associated Infections (HAIs) are a major cause of morbidity and mortality in Pediatric intensive care units (PICUs).Centers for Disease Control and Prevention –(CDC) defines a HAI as a localized or systemic condition resulting from an adverse reaction to the presence of an infectious agent(s) or toxin(s). There must be no evidence that the infection was present or incubating at the time of admission. [(1)]This is due to the increased use of medical instruments such as mechanical ventilators, blood and urine catheters, invasive monitoring devices and increased resistance of the microorganisms isolated from Intensive care unit (ICU) patients to most commonly used antibiotics, which in turn is a result of overt use of broad-spectrum antibacterial agents.[(2)]

HAIs are common among children in ICUs and have been reported to occur in 9% to 21% of critically ill children.[(3)] The most common HAIs in ICUs include bacteremia particularly CLABSI (central line associated blood stream infection), ventilator associated pneumonia (VAP), and Catheter associated Urinary Tract Infections (CAUTIs), the former being the leading cause of death in ICU patients. (2) Catheter-related blood stream infections (CR-BSIs) (defined as the growth of the same

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pathogen from catheter tip and peripheral blood culture), which represent up to 30% of cases, and primary blood stream infections (BSIs), accounting for around 35% of cases, are the most common types of BSI in ICUs.[(4)]Ventilator-Associated-Pneumonia (VAP) is 2nd most commonHAI. CDC defines Ventilator-associated pneumonia (Pneumonia in persons who had a device to assist or control respiration continuously through a tracheotomy or by endotracheal intubation within the 48-hour period before the onset of infection.[(1)]According to the literature, pediatric VAP rates vary, with incidence reported up to 32% and rates up to 27.1 per 1000 ventilator days.[(5)] UTI is the third most common HAI after CLABSI and VAP. As per NHSN (National Health Safety Network) the incidence of catheter- associated UTI is 5 per 1000 catheter days.[(6)]

In the developed countries, gram positive organism such as CONS (Coagulase negative staphylococcus) is the most frequent pathogen isolated in patients with blood stream infections whereas gram negative organisms such as Pseudomonas and Escherichia Coli are common causative organisms for VAP and UTI.[(7)] In our country, gram negative organisms such as Klebsiella, Acinetobacter, Pseudomonas and E. coli are the commonest organism isolates in children with various types of HAI.[(8)].

The infections caused by multidrug resistant (MDR) organisms are more likely to prolong the hospital stay, increase the risk of death and require treatment with more expensive antibiotics.[(9)]Therefore, this retrospective study was undertaken to determine bacterial flora of various HAIs and their antibiotic resistance pattern in our PICU.

Material and methods: This retrospective study was conducted at PICU at AIIMS, Jodhpur after the ethical clearance from institute`s ethical committee. Data was collected from medical record of the patient admitted between Jan 2017 to December 2018 retrospectively. Information regarding demography, presence of infection at admission, use of devices, type of devices, treatment details was collected. The study followed the Strobe guidelines. The inclusion criteria were children from one month to 18 years of age who were admitted in PICU. Blood sample, BAL and urine sample were taken after 48 hour of admission in PICU. Samples taken before 48 hour of admission were excluded. Three common HAIs (CLABSI/CRBSI, VAP, and CAUTI) were diagnosed according to the CDC definitions.[1]

1. A bloodstream infection was defined as CLABSI when it was associated with a central intravascular line. Diagnosis includes laboratory-confirmed bloodstream infection.

Laboratory-confirmed bloodstream infection was defined when either of the following criteria was observed:

a) A recognized pathogen was cultured from one or more blood cultures of a patient, and this pathogen was not related to an infection at another site.

b) A patient had signs or symptoms of infection not related to an infection at another site, and a common skin contaminant (such as coagulase-negative Staphylococcus) was cultured from two or more blood cultures drawn on separate occasions. [1]

2. CDC defines VAP (Pneumonia in persons who had a device to assist or control respiration continuously through a tracheostomy or by endotracheal tube within the 48-hour period before the onset of infection. Briefly pneumonia was defined when all of the below were satisfied.

a) There was new or progressive and persistent infiltrate, or consolidation, or cavitation (for all ages), or pneumatoceles (for infants ≤1 year of age) on a chest radiograph.

b) A patient had one of the following signs or symptoms: fever (temperature ≥38 °C), leucopenia (<4000 WBC/mm^3 and leukocytosis>12000WBC/mm^3

c) There were at least two of the following signs or symptoms: (i) new onset of purulent sputum or a change in property of the sputum, increased respiratory secretions and increased suctioning requirement (ii) new onset or worsening cough, dyspnea, or tachypnea, (iii) rales or bronchial breath sounds, or (iv) worsening gas exchange.(1)

3. CAUTI was briefly defined when a patient with a urinary catheter (UC) had one or more of the following signs or symptoms, with no other recognized infection: fever (temperature ≥38 °C), urinary urgency, frequency,

dysuria, or suprapubic tenderness, and this patient had a positive urine culture (≥10^5 colony-forming units per ml) with no more than two pathogens isolated. [(1)]

4. Bronchoalveolar lavage (BAL), non bronchoscopic BAL and aspiration of tracheal secretions was performed if required according to the patient's condition using an aseptic technique.

5. We used a closed drainage system for urinary catheterization. A urine sample was aseptically obtained from the sampling port of the UC or by bladder catheterization if required.

6. The incidence of HAI per 100 patients was calculated by dividing the number of patients with infections by the total number of patients and then multiplying the result by 100.

7. Antibiotic susceptibility of each pathogen was recorded for the purpose to create an antibiogram.

Statistical Analysis

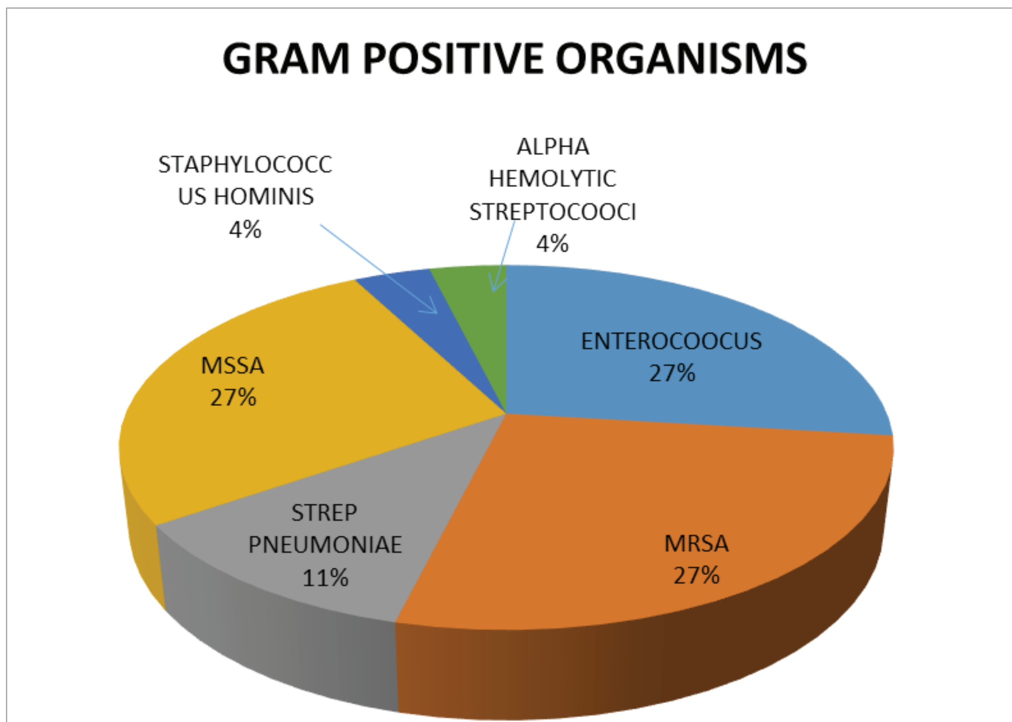
Data was analyses using SPSS software version 20.

Results and Discussion

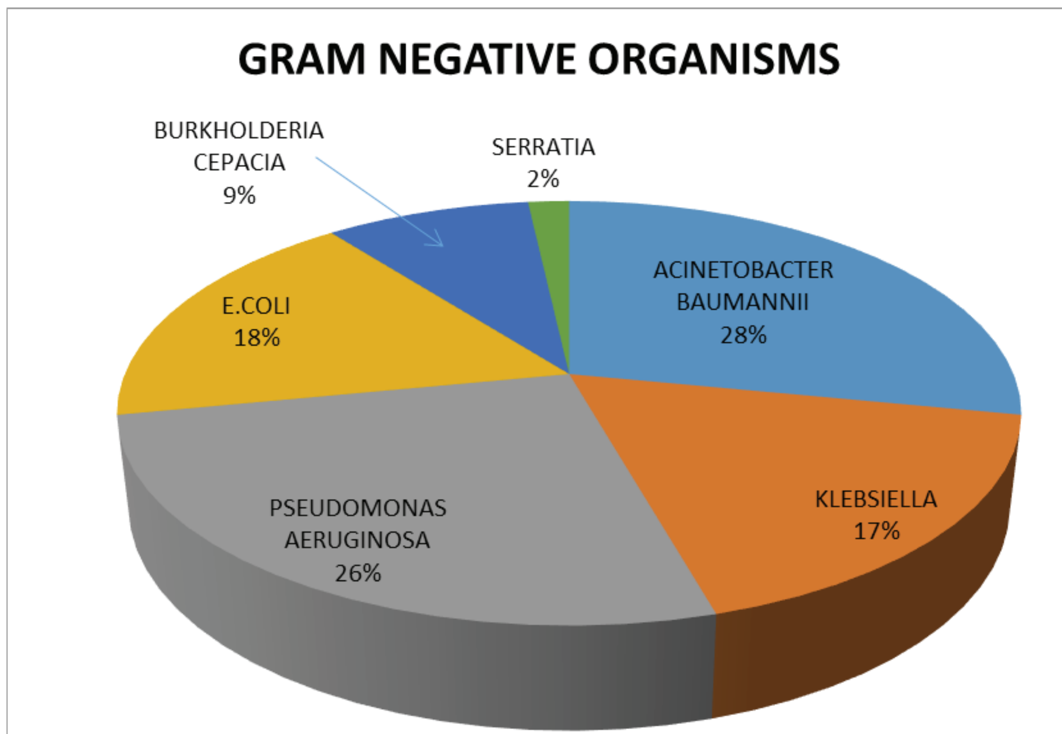
A total of 255 patients were admitted during the study period. Out of these, 155 (60%) were male children.610 samples were from different sites were analyzed during the study period.Samples were collected blood from peripheral line as well as central line, BAL, mid-stream urine sample, central line tip, peritoneal fluid, pleural fluid and wound swab whenever indicated. Total number of positive cultures obtained in the conducted study was 114 (18.6%). Among the culture positive isolates, 57 (50%) were gram negative and 26 (22.8%) were gram positive organisms.Culture positivity for fungal growth was 17 (14 %) and rests were contaminants. Fig 1 and 2 are showed species distribution according to culture. In the two years period of study, 59 HAI were detected from 255 patients. Based on the retrospective data, annual HAI rate for each year from 2017 to 2018 were 19.4% and 26% respectively. The overall HAI rate was 23.2%.

The most common isolate was Acinetobacterbaumannii (14.4%, n-16) followed by Pseudomonas (13.2%, n- 15), Klebsiella (8.7%, n-10) and E. coli (8.7%, n-10). Among Gram positive organisms Enterococcus(6.1%,n-7),*Methicillin-resistant*staphylococcus aureus (MRSA) (6.1%,n-7) and *Methicillin*-sensitive staphylococcus aureus (MSSA) (6.1%,n-7) were common. Culture positivity for fungal growth was 14 % (17). Candida Albicans was the most common fungus responsible for HAI.

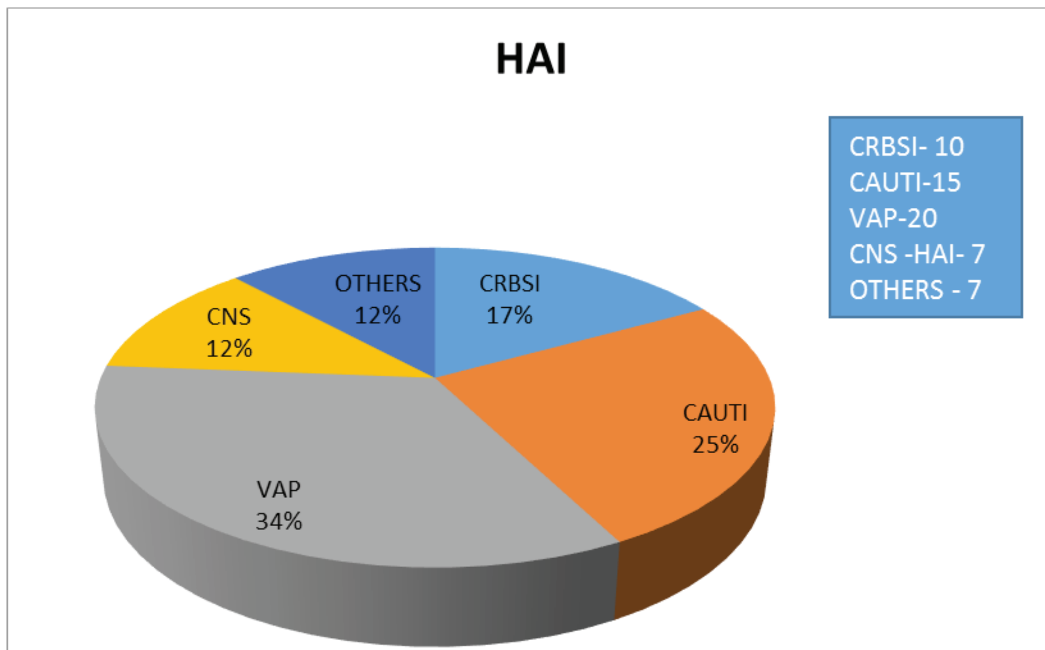
Regardless of years of observation the three most commonly detected HAI types were VAP (34%), CAUTI (25%), and CRBSI (17%). Most common organisms responsible for VAP were Pseudomonas Aeruginosa 11% (7/59) and Acinetobacterbaumannii 11% (7/59). CAUTI was most commonly caused by E. coli 5% (3/59) and Candida Albicans and tropicalis 10%(6/59). CRBSI/CLABSI was most commonly caused by Burkholderiacepacia(n=2), Klebsiella(n=2),Acinetobacterbaumannii (n=1) and E. coli(n=1). Species distribution in health care associated infections is shown in table no 1.



Graph 1: Gram positive organism distribution according to culture



Graph 2: Gram negative organisms distribution according to culture



Graph 3: Health care associated infection distribution

Table 1: Species distribution in health care associated infections

Organism	HAI –BC CRBSI (n)	CAUTI(n)	VAP(n)	HAI-CSF(n)	Others (n)	Total (n)
AcinetobacterBaumannii	1	0	7	2	1	11
Klebsiella	2	1	1	0	0	4
Pseudomonas Aeruginosa	0	0	7	1	1	9
E. Coli	1	3	0	0	2	6
BurkholderiaCepacia	2	0	1	0	0	3
Serratia	0	0	1	0	0	1
Enterocoocus	0	2	0	0	0	2
Methicillin resistant staphylococcus aureus	1	0	2	0	0	3
Strep. Pneumoniae	0	0	0	0	0	0
Methicillin sensitive staphylococcus aureus	0	0	0	1	1	2
Staphylococcus Hominis	0	0	0	0	0	0
Alpha HemolyticStreptocooci	0	0	0	0	0	0
Fungal	2	6	0	1	2	11
Mixed And Commensal	1	3	1	2	0	7
Total	10	15	20	7	7	59

Table 2: Antibiotic sensitivity pattern of gram negative organisms

Antibiotics	Acinetobacter Baumannii(%)	Klebsiella (%)	Pseudomonas Aeruginosa(%)	E.Coli(%)	Burkholderia Cepacia(%)	Serratia(%)
Ceftazidime	15	0	83.3	0	50	ND
Ceftriaxone	0	50	ND	0	ND	0
Amikacin	0	50	85.7	25	0	ND
Meropenam	12.5	50	100	50	50	ND
Piptaz	8.3	55.5	81.8	50	75	0
Imepenem	0	20	100	50	50	100
Colistin	100	100	100	100	ND	ND
Tigecycline	100	100	ND	100	ND	ND

Table 3: Antibiotic sensitivity pattern of gram positive organism

Antibiotics	Enterococcus (%)	MRSA (%)	MSSA (%)	Strep. Pneumoniae (%)	Staph. Hemolyticus (%)	Alpha Hemolytic Streptococci (%)
Linezolid	100	100	100	100	100	100
Vancomycin	100	100	100	ND	100	100
Teicoplanin	ND	100	100	ND	100	100
Clindamycin	ND	0	100	100	ND	ND
Gentamycin	50	100	100	ND	ND	100
Amikacin	ND	100	ND	ND	ND	ND
Cotrimoxazole	0	37.5	16	66	ND	ND
Erthyromycin	ND	0	50	100	ND	ND
Ciprofloxacin	ND	0	ND	ND	ND	0
Penicillin	ND	0	ND	100	ND	ND

Antibiotic sensitivity patterns

We attempted to correlate the organisms isolated with the antibiotic sensitivity pattern so as to formulate antibiotic protocols. Most of the gram negative organisms were resistant to multiple groups of antibiotic including Carbapenem. Acinetobacter baumannii and Klebsiella were sensitive to colistin and tigecycline only, however pseudomonas was sensitive to Carbapenems. Among gram positive organisms, MRSA was sensitive to gentamicin, amikacin, vancomycin and linezolid. Out of 17, antifungal sensitivity was done only for 4 isolates. In which Candida was sensitive to caspofungin and amphotericin B and resistance to fluconazole and Voriconazole. Antibiotic sensitivity pattern of gram positive and gram negative organisms are summarized in table 2and 3.

In the present study culture positivity rate was seen in (114/610) 18.6% samples and HAI was diagnosed in 59 (23.2%),whereas in other similar report prevalence of HAI varies from 6.6 – 37%. [8-12] In the current study, the incidence of infections due to gram negative organisms was 50% while 22.8% isolates were gram positive organisms. It is in accordance with other study. [(8, 10-12)] In present study, Acinetobacter baumannii was isolated in 14% of samples and Pseudomonas in 13.2%. It is in accordance with the study conducted by Kepenekli et al. However Deep et al.,Atici et al and Armouret et al. reported Klebsiella as the most common organism in 33.3%, 19.4% and 25% of the HAIs respectively. Acinetobacter species is emerging as an important nosocomial pathogen in PICU environment.This high prevalence observed in our study may be related to non-compliance with the recommendations for mastery the hospital environment, lack in hands hygiene and misuse of antibiotics.Difference in the incidence in different institutes is because of difference in set up and the type of antibiotic policy used in these hospitals.

In present study, fungal infection was reported 14.9%. It is in rising trend because of the increasing use of broad spectrum antibiotics, longer duration of hospital stay, use of central line catheter, urinary catheter and peritoneal catheter, mechanical ventilation, total parenteral nutrition, immune-compromised conditionsand multifocal colonization. We should have high index of suspicion and advocate early use of anti-fungal in high risk patients to prevent catastrophic events.

In present study, VAP is most common HAI because suction procedures and mechanical ventilationthe infectious particles lodged within thetracheal tubes can get dislodged into distalairways causing VAP. The risk of VAP increases if ET/TT is colonized. Prior respiratory disorders may put thepatients at a higher risk as there is a greaterchance of airway colonization by gramnegative bacilli in these patients andcompounding factors like impairment ofmucosal clearance and loss of mucosalintegrity also exists.The incidence of VAP increased with the durationof ventilation.Our study corroborated this fact as proven by Salata, *et al.*[13] and Schaberg, *et al.*[14]

In this study, mortality rate was higher in patients who did not develop HAI and it is contradictory finding compared with study done by Gupta A. et. al.[15]This could be explained by the fact that most of the patients who died in our PICU were referred from other hospitals and had already received antibiotics for more than 3 daysin other centers and hence their cultures were not positive andfew were post-operative patients with surgical complications.

In this study, another important finding was antimicrobial resistance which was very high and this may cause a serious therapeutic challenge to the management of common infections. Most of the GNB were multi drug resistant with a very high resistance to betalactam antibiotics (100% resistance to amoxyclav, 50 to 85% to ceftazidime). Carbepenem resistancewas detected in 88.5% isolates of Acinetobacter spp., 50% of Klebsiella spp. and 50% of E.coli spp. All gram negative organisms had developed resistance tocarbepenem except Pseudomonas (100% sensitivity). Klebsiella and Acinetobacter spp. were 100% sensitive to colistin and tigecycline. These findings correlated with findings of Kepenekli E. et. al.[10]

Among the gram positive organisms maximum resistance was seen with penicillin and erythromycin. MRSA displayed markedly high level of drug resistance to most commonly used antibiotics like penicillin, erythromycin, cotrimoxazole, ciprofloxacin and clindamycin.

Enterococcus, MRSA, MSSA, Streptococcus pneumoniae and Staphylococcus hominis were sensitive to vancomycin, linezolid and teicoplanin. These findings were in accordance to the study by Jamshidi M. et. al.[2] This higher degree of antibiotic resistanceis probably because of indiscriminate use of antibiotics in our city and patientsreaching our hospital after receiving broad spectrum antibiotics at various other hospitals on many occasions.

Conclusion

So it is concluded that HAI is an important cause of morbidity and mortality. The causative agents of HAI are acquired in hospitals. This retrospective study showed both gram positive and negative bacteria as well as fungal organisms are responsible for HAIs, but most commonly the gram negative organisms. Most of the strains are multi drug resistant. To bring down the incidence of HAI, judicious use of antibiotics according to the prevalent resistance pattern is essential. Moreover, there is a need for strict aseptic precautions on the part of health care workers.

Limitations

1. Since it is retrospective study, so the results may not be truly representative.

2. Antibiotic sensitivity pattern of all fungal pathogens were not doneat our institute and so resistance pattern of allfungal organisms to various anti-fungal could not be studied.

Conflict of Interest: Nil

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