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Nosocomial Bloodstream Infections in Children in Intensive Care Unit: Organisms, Sources, Their Sensitivity Pattern and Outcome of Treatment

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Summary:

Background: Nosocomial bloodstream infection in paediatric ICU is a leading, preventable infectious complication in critically ill patients and has a negative impact on patient's outcome. This study was done to determine the type of pathogens responsible for nosocomial infections and its sensitivity pattern, to evaluate the probable sources (fomites) of nosocomial infections and also to compare the outcome of treatment between children with and without nosocomial bloodstream infections in terms of length of ICU stay and mortality

Material and methods: This study was conducted in the intensive care unit of Dhaka Shishu(children) hospital. Children between 0-5 years of age were included in the study. Blood culture positive case at the time of admission and Children discharged or died within 48 hours of admission were excluded. When children clinically suspected to have nosocomial infections, their blood culture and swab culture of probable sources were done.

Results: Out 110 patients, 23(20.9%) patients developed nosocomial BSI. Neonates were found to be more susceptible to develop nosocomial BSI. Most of the organisms (86%) were Gram negative bacilli. Klebsiella was the most common pathogens (30.78%) followed by acinatobacter (21.73%), E-coli (13.04%), Pseudomonas (8.7%). Type of micro-organisms and their sensitivity pattern obtained from blood culture and sources culture of corresponding patient were almost similar which indicate the clue for probable source of nosocomial infection. Microorganisms were almost sensitive to Imipenem but there were high resistance to commonly used antibiotics including third generation cephalosporins. ICU acquired infections increase hospital mortality and duration of hospital stay.

Conclusion: Nosocomial bloodstream infections in children in ICU are associated with high mortality rate and prolong hospital stay. Neonates are more susceptible to develop nosocomial BSI than children aged above 28 days. Gram negative organisms are predominant isolates and are developing resistance to commonly used antibiotics including third generation cephalosporin. Imipenem is the most effective and reliable antibiotic option. Fomites especially health care device including IV canula, suction catheter, endotracheal tubes, oxygen mask are the important probable sources of nosocomial infections.

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Introduction:

Nosocomial infections (NI) constitute a major health problem associated with high morbidity, mortality and increase of health cost, especially in pediatric intensive care unit (PICU).[1] Nosocomial infections or hospital acquired infections defined as those not present or incubating at the time of hospital admission and developing 48 hours or more after admission.[2] The most NI occurred in pediatric intensive care unit.[3] A Majority of it occur in preterm and term infant that require intensive care.[4] Blood stream infections (BSI) is the most common nosocomial infections in PICU.[5] It is independently associated with a three-fold increased risk of death.[6]

Device associated nosocomial infections frequently occur in pediatric and neonatal intensive care unit. [7] The isolation of known pathogens from some of the equipment and other fomites shows that they can be sources of infection to patients.[8] Health care–associated infections are often due to multidrug resistant pathogens and are different from those encountered in community-acquired infections.[2] Empiric antibiotic treatment from

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the first hour reduces mortality in severe sepsis and septic shock.[9] But in empiric treatment, Knowledge about local pathogens and their sensitivity is essential. Pourakabari et al[5] have shown, Gm negative bacilli are the most frequent pathogen in nosocomial infections in pediatric patients. But in according to NNISS (USA) report[10], coagulase negative Staphylococcus were the most common isolates. The antibiotic resistance of nosocomial infections is rapidly iccreasing.[11] Nosocomial BSI with multidrug resistant pathogens are difficult to treat and are associated with increased mortality.[12] Progressive antimicrobial resistance threatens the previous knowledge of our primary treatment approach against bacterial pathogens.[13]

To minimize the infection in PICU with optimal cost effective care, every ICU should have its own strategy for prevention and treatment of BSI.[14] There is very little data from Bangladesh documenting the prevalence and trend of nosocomial blood stream infections in children in intensive care unit. This study was done to determine the type of pathogens responsible for nosocomial infections and its sensitivity pattern, to evaluate the probable sources (fomites) of nosocomial infections and also to compare the outcome of treatment between children with and without nosocomial bloodstream infections in terms of length of ICU stay and mortality which would serve as a reference based recommendation.

Material and method:

This study was conducted in the intensive care unit of Dhaka Shishu (children) hospital which was a combined ICU for all age group of children during the study period from January 2008 to November 2008. All the children between 0-59 months of age admitted to ICU during the study period were included in the study. Exclusion criteria were (1) blood culture positive case at the time of admission, (2) children discharged or died within 48 hours of admission,(3) attendants of those children not interested to continue participate in the study.

Blood samples of all study patients were sent for culture on admission. Patients who had positive blood culture on admission were excluded from the study. Remaining were followed up and examined everyday to observe the development of any sign-symptoms of nosocomial infections. When clinically suspected to have nosocomial infections, their blood sample were taken aseptically and culture and sensitivity was done. Those children who were culture positive, considered development of nosocomial infections. Swab were taken from the probable source such as Endotracheal tube, Suction catheter, I/V canula, oxygen musk from all culture positive cases and their culture and sensitivity test were done. Other investigations also were done as necessary.

PICU acquired nosocomial infections were defined according to the centre for Diseases Control and Prevention (CDC).[15] Infections that commenced at or after 48 hrs of admission to the PICU were included as PICU acquired infections. Bloodstream infections were defined as the biological documentation of infection, i.e., the result of a positive blood culture.

Permission of ethical board of Dhaka Shishu Hospital was taken. Informed written consents were taken from the parents/attendance after explanation.

Data were analyzed using SPSS version 12. Association between nosocomial BSI status and socio-demographic factors were sought through cross tabulation and chi square test. Quantitative variables were compared by comparison of mean through independent t test. The association was considered significant at p value < 0.05.

Result:

During the study total 110 patients were enrolled and analyzed for the study. Out of 110 patients, neonates were 67 (60.9%), 31 (28.2%) were aged between 29-365 days 12 (10.9%) aged above 365 days. About two third (67.3%) of the patients were male and rest (32.7%) of the patients were female giving a male-female ratio about 2:1. Out of 110 patients, 73 (66.4%) patients were from urban area and remaining 37 (33.6%) were from rural area. Majority of the patients (71.8%) were belonging to middle income group.Lower income group were 19(17.3%) and upper income group were the least (10.9%). (Table-I)

During study period 23 (20.9%) patients out 110 patients developed nosocomial BSI confirmed by blood culture and rest of 87 (79.1%) were found to be culture negative (Table-ll). Out of 23 patients found positive for blood culture, predominate isolates (20, 86.95%) of were Gram negative Bacteria. Klebsiella pneumoniae was the most common pathogens (8, 34.78%) in blood culture followed by acinatobacter spp (5, 21.73%), E-

Table-I

Demographic characteristics of the study patients

Age of the child	Frequency	Percent
0 - 28 days	67	60.9
29 - 365 days	31	28.2
>365 days	12	10.9
Total	110	100
Sex		
Male	74	67.3
Female	36	32.7
Total	110	100.0
Place of Residence		
Urban	73	66.4
Rural	37	33.6
Socio-economic status		
Lower income group	19	17.3
Middle income group	79	71.8
Higher income group	12	10.9
Total	110	100.0

Table-II

Distribution of the children by Blood culture status during the study period

Blood culture status	Frequency	Percent
Positive	23	20.9
Negative	87	79.1
Total	110	100.0

coli (3, 13.04%), Pseudomonas areuginosa (2, 8.7%), Serratia spp (2, 8.7%), Candida (2, 8.7%) and Staphylococcus spp (1, 4.35%) (Table-III). Swab culture from the probable sources (fomites) used by the culture positive children as endotracheal tube, Suction catheter, I/V canula, oxygen musk showed that Gram negative Bacteria were the predominate microorganisms. The most common pathogens in swab culture were Klebseilla pneumoniae (6, 30%) followed by Acinatobacter spp (4, 20%), E.coli(2, 10%), Pseudomonas (2, 10%), Serratia (2, 10%), Staphylococcus spp (15%) and Candida (5%) (Table-IV). Type of organisms obtained from blood culture and swab cultures of probable sources (fomites) of corresponding patient were almost similar. Frequency of microorganisms obtained from blood culture and their sources culture and their sensitivity pattern were also almost similar. Most of the organisms obtained from blood culture and sources culture were almost sensitive to Imipenem but there were high resistance to commonly used antibiotics including Ceftriaxon, Ceftazidim, Amikacin, Gentamycin, Chloramphenicol and Ciprofloxacin. E. Coli, serratia, pseudomonas and Staphylococcus were 100% sensitive to Imipenem but Klebsiella were 87% sensitive to Imipenem in blood culture and 83% sensitive to sources culture. In blood culture, Ceftriaxon, 25% sensitive to Klebsiella, 20% sensitive to Acinatobacter, 50% sensitive to E-coli, 50% sensitive to Serretia, 0% sensitive to Pseudomonas and 33% sensitive to Staphylococcus and in sources culture, Ceftriaxon, 33% sensitive to Klebsiella, 25% sensitive to Acinatobacter, 50% sensitive to E-coli, 50% sensitive to Serretia, 0% sensitive to Pseudomonas and 100% sensitive to Staphylococcus. These organisms were 100% resistant to Amoxicillin, Cotrimoxazol and Cephradin. Ceftazidim and amikacin were relatively better sensitive to Pseudomonas and E coli than Klebsielle and Acinatobacter. (Table –V).

In the study, 19 (28.35%) children aged 0-28days (neonates) developed nosocomial BSI and 4 (9.3%) children aged above 28 days developed nosocomia BSI indicating that neonates are more susceptible to develop nosocomial BSI than children aged above 28 days (P <0.02) (Table-Vl). During the study, out of 110 patients, 6 (5.45%) patients were discharged on risk bond (DORB). Among 104 patients, 90 (86.5%) patients improved and 14 (13.5%) patients died. Among the 23 patients who developed nosocomial bloodstream infections, 6 (26.1%) died and among 81 patients without nosocomial bloodstream infections, 8 (9.9%) died. The difference is statistically significant. The proportion of fatality is significantly higher in children with nosocomial BSI (P<.05) (Table-Vll). Length of hospital stay of children with nosocomial BSI in ICU in our study was about four days more than Children without nosocomial BSI (P<.01) (Table -VIIl).

Table-III

Pattern of micro-organisms in blood culture positive cases (n=23)

Micro-organisms in blood Culture		Number	Percent
Gm(-)ve	Klebsiella	8	34.78
	Acinotobacter	5	21.73
	E-coli	3	13.04
	Serratia	2	08.70
	Pseudomonus	2	08.70
Gm (+)ve	Staphylococcus	1	04.35
	Candida	2	08.70
Total		23	100

Table-IV

Micro-organisms isolated from probable sources (fomites) culture of the blood culture positive patients

Micro-organisms isolated from sources culture		Possible sources				Total (n)
		ET Tube	SuctionCath. Tip	I/V canula	Oxygen mask	
Gm (-) ve.	Klebsiella	2	2	1	1	06 (30%)
	Acinatobacter	2	1	1	0	04 (20%)
	E-coli	1	1	0	0	02 (10%)
	Serratia	0	0	1	1	02 (10%)
	Pseudomonus	1	1	0	0	02 10%)
Gm (+)ve.	Staphylococcus	1	0	2	0	03 (15%)
	Candida	0	1	0	0	01 (5%)
Total		7	6	5	2	20

Table-V

Sensitivity pattern of micro-organisms in blood culture and culture of the sources of corresponding patients

Organisms	Culture	Imipenem (%)	Ceftiaxon (%)	Chloramphenicol (%)	Amikacin (%)	Ceftazidim (%)	Ciprofloxacin (%)	Gentamycin (%)	Cefradine (%)	Amxicillin (%)	Cotrimoxazol (%)
KlebSeilla	Blood(8)	87	25	25	25	12.5	12.5	0	0	0	0
	Sources(6)	83	33	33	33	17	17	0	0	0	0
Acinatobacter	Blood(5)	80	20	0	0	20	0	0	0	0	0
	Sources(4)	75	25	0	0	25	0	0	0	0	0
E-coli	Blood (3)	100	67	33	33	33	0	33	0	0	0
	Sources (2)	100	50	0	50	50	0	50	0	0	0
Serratia	Blood (2)	100	50	0	0	50	0	0	0	0	0
	Sources (2)	100	50	0	0	00	0	0	0	0	0
Pseudomonas	Blood (2)	100	0	50	50	50	50	50	0	0	0
	Sources (2)	100	0	50	50	50	50	50	0	0	0
Staphylococcus	Blood (1)	100	100	0	100	0	100	100	0	0	0
	Sources (3)	100	33	0	33	0	33	0	0	0	0

(Candida is not shown in the table)

Table-VI

Distribution of the age of the child and nosocomial BSI status.

Age of the child	Nosocomial BSI		Total
	Positive	Negative	
0- 28days(Neonates)	19 (28.36%)	48 (71.64%)	67 (100%)
> 28 days(Non Neonates)	4 (9.3%)	39 (90.7%)	43 (100%)
Total	23	87	110

Chi-Square=5.75 df =1 P<0.02

Table-VII

Outcome of treatment between with and without nosocomial BSI.

Outcome of treatment	Status of nosocomial BSI		Total
	Positive	Negative	
Improved	17 (73.9%)	73(90.1%)	90(86.5%)
Deceased	06(26.1%)	08(9.9%)	14(13.5%)
Total	23(100.0%)	81(100.0%)	104(100.0%)

Chi-Square=4.014 df =1 P=.044

Table-VIII

Comparison of hospital stays in children with and without nosocomial BSI .

Nosocomial BSI	N	Days Mean	SD	T	P Value
Positive	23	12.2	4.24	2.94	0.004
Negative	87	8.8	5.02		

Discussion:

Nosocomial infections and antimicrobial resistance in the ICU is a major deterrent to patients outcome, increasing duration of patients stay in hospital as well as expense.[16] The risk of nosocomial infections depend on the host characteristics, the number of interventions, invasive procedure, asepsis of techniques, the duration of stay in PICU, and inappropriate use of antimicrobials.[17] First four weeks are the most susceptible period of getting nosocomial infection.[4,18,19] In our study showed neonates are more susceptible to develop nosocomial bloodstream infection than children age above 28 days.

Patients in ICU acquire nosocomial bloodstream infection faster than that of non ICU, probably it is due to the fact that patients in ICU are exposed to a greater number of reservoirs and sources of microorganisms.[20] In children those are likely to be more frequent and serious in developing countries. Some of possible factors for this may be malnourished state of patients, delayed presentation to referral centers and multi-organ involvement at admission.[21] The prevalence of nosocomial infections n ICU in our study is higher than the study of Dusgupta et al [22] (11.98%). Our study was comparable with the study with Porto et al[1] (22.1%) and Wahab et al[23] (21.4%).

According to the NNISS report[10], Gram positive pathogens responsible for majority of the nosocomial bloodstream infections. Common pathogens in pediatric intensive care units are- Coagulase-negative staphylococci followed by Enterococcus, Staphylococcus aureus, Enterobacter spp. Candida

albicans, Pseudomonas areuginosa, Klebsiella pneumoniae Escherichia coli, Acinetobacter spp. Streptococcus pneumoniae,Citrobacter, Fungi, Group B streptococcus. But most studies especially in developing countries showed, Gram negative organisms are the major pathogens in nosocomial BSI.[1.3,5,11,18] Pseudomonas areuginosa, Klebsiella pneumonia, Escherichia coli and Acinatobacter are the leading Gm negative isolates. [1,3,5,11,18,] Dal-Bo et al showed, [19] in neonatal ICU coagulase-negative staphylococci is common isolate in blood culture. Gram-negative bacteria, especially *Klebsiella* spp., were the predominant causes of neonatal NI, as has been described in other studies from developing countries.[23] In our study most of the isolated in culture were Gram negative organisms. Klebsiella were the common pathogen followed by Acinatobacter, Escherichia coli, Pseudomonas areuginosa, Serratia,, Candida and staphylococcus which has similarity with the result of Chowdhury et al.[18] and Wahab et al.[23]

According to WHO antimicrobial resistance global report 2014, antimicrobial resistance to common bacteria has reached alarming levels in many parts of the world.[24] Systematic reviews of the scientific evidence showed that antibacterial resistance had a negative impact on outcomes for patients and health-care expenditures.[24] Most bacteria isolated from ICU of Fatmawati hospital In Indonesia were shown resistant to the third generation cephalosporins and quinolone antibiotics.[25] Ahmed at al[12] showed of all available anti-microbial agents, carbapenems are the most active and reliable treatment options for infections which are similar with our study. According to WHO report, [24] Klebsiella was 100% sensitive to Carbepenem in Bangladesh. E-coli are 59% resistant (41% sensitive) and Klebsiella was 97.8% resistant (2.2% sensitive) to Ceftriaxon in Bangladesh. In our study 25-33% Klebsiella (blood and swab culture) and 50% E-coli, were sensitive to Ceftriaxon. Ceftazidim and amikacin were relatively better sensitive to Pseudomonas and E coli than Klebsielle and Acinatobacter.

The possible contributory role of fomites in the spread of nosocomial infections in ICU patients has been demonstrated in different literature.[7,8, 26,] International Infection Control Consortium (INICC) study[26] conducted in Turkey showed that device-associated healthcare-acquired infections (DA-HAI) pose a threat to patient safety, particularly in the intensive care unit (ICU). Common device-associated healthcare-acquired infections (DA-HAI) were central line-associated bloodstream infections (CLABSIs), ventilator-associated pneumonias (VAPs) and catheter-associated urinary tract infections (CAUTIs).[26] The pathogenesis of device-related infection is not completely defined, but these infections are related to the development of biofilms, organized communities of microorganisms protected from the immune system and antimicrobial therapy, host susceptibility, device composition, duration of implantation, and exposure to colonizing organisms.[27] In our study fomites especially health care device including IV canula, suction tubes, endotracheal tubes, oxygen mask are considered to be important sources of nosocomial bloodstream infection in intensive care unit. Similarity of the types of micro organisms, frequency of micro organisms, and similarity of sensitivity pattern of the micro organisms obtained from blood culture and swab culture of probable sources (fomites) of corresponding patient indicating that fomites like ET tube, suction catheter, I/V canula, oxygen musk etc may be the probable sources of nosocomial bloodstream infections.

Nosocomial infections in PICU are associated with increased mortality and length of stay in hospital.[3] Crude mortality rate of children (median age 2.8 years) in a pediatric ICU was shown 12.9%.[28] Ahmed et al[12] showed, crude mortality rate with bloodstream infections in ICU was 38%. .Our study found 26.1% fatal outcome of children from ICU acquired bloodstream infection. The outcome of treatment is significantly better in children without nosocomial infection (9.9%). Mortality rate strongly correlate with nosocomial BSI. Prowly et al[6] showed that BSI was associated with an 18.7% increase in crude hospital mortality which is similar with our study (16.2%) Nosocomial infections leads to extra hospital stay. [26]. In patients with nosocomial infection in a tertiary care teaching hospital in India, the mean PICU stay was 17.31 days which was higher than our study.[29] Length of hospital stay of children with nosocomial BSI in ICU in our study was about four days more than Children without nosocomial infection. It increases the treatment cost of patient.The prevention of these infections in ICU through specific intervention may reduce the ICU treatment cost.

Limitations of the study

- Study was done in only one centre for a short period of time.
- Small sample size.
- Randomization in recruitment of subjects could not be achieved.
- Possible confounding factors were not adjusted for the study.

Conclusion:

Nosocomial bloodstream infections in children in ICU are associated with high mortality and hospital stay. Neonates are more susceptible to develop nosocomial BSI than children aged above 28 days. Gram negative Organisms are most common isolates and are developing resistance predominantly to commonly used antibiotics including third generation cephalosporins. Imipenem is the most effective and reliable antibiotic option. Fomites especially health care device including IV canula, suction catheter, endotracheal tubes, oxygen mask are the important probable sources of nosocomial bloodstream infections.

Recommendations

- Standard operating procedure with adequate protective protocol should be maintained in the ICU to reduce nosocomial infection and its consequences.
- The choice of antimicrobial agents in initial empirical treatment should be depend on the knowledge of local pathogens and their susceptibility.
- Large multi centre study can be done for further evaluating of these findings.

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