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Characteristics of Healthcare Associated Bloodstream Infections in Neonates Operated and Managed in a Tertiary care Paediatric Surgical Neonatal Intensive Care Unit

Medical Science

KEYWORDS : Operated neonatal congenital malformations; Healthcare associated bloodstream infections (HCABSIs); Paediatric Surgery NICU; Tertiary care centre

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ABSTRACT

Context: Healthcare associated primary bloodstream infections in operated neonates.

Aims: To characterise the primary healthcare associated bloodstream infections (HCABSIs) in neonates operated and managed in a neonatal intensive care unit of northern India, a critical aspect inadequately addressed till now

Settings and Design: Prospective, observational study

Methods and Material: Neonates were assessed and those with foci of infection prior to/ at admission were excluded.

Statistical analysis used: Statistical testing was conducted with the statistical package for the social science system version SPSS 17.0

Results: The infection rate was found to be 16.84 episodes per hundred admissions. The infection density was found to be 16.67 episodes per thousand patient days. Majority of the infections set within the first seven days of life. The maximum numbers of eleven HCABSIs were reported in operated cases of tracheoesophageal fistula, in which Acintobacter spp was the predominant pathogen. Klebsiella pneumoniae was the predominant pathogen in operated cases of intestinal obstruction and omphalocele. Eighteen percent of K.pneumoniae isolates and thirty seven percent of Acinetobacter spp were resistant to imipenem. Birth weight, duration of stay and positive C-reactive protein (CRP) were significant risk factors associated with primary HCABSIs ($p<0.05$), however according to multivariate analysis, duration of stay was found to be the only statistically significant factor ($p=0.005$, OR-1.169, 95% CI: 1.047-1.304).

Conclusions: Primary HCABSI infection rate was 16.84 episodes per hundred admissions and birth weight, duration of stay and positive CRP were significant risk factors.

Introduction:

Surveillance of healthcare associated infections in a specialized set up is a key activity in infection control[1]. Health care associated primary bloodstream infections (HCABSIs) are a major cause of neonatal morbidity and mortality in cases operated for neonatal surgical conditions[2-11]. To the best of our knowledge, there is no published study from the south- eastern Asian region (including India) on this aspect.

The present study aims to characterize primary HCABSIs including the risk factors in neonates operated and managed in a tertiary-care pediatric surgery neonatal intensive care unit (PSNICU).

Subjects & Methods:

A prospective observational study was carried out from November 2011 to March 2013 on neonates (0 days- 28 days age) admitted in the Pediatric Surgery Neonatal Intensive Care Unit (PSNICU) of Kalawati Saran Children Hospital (KSCH), New Delhi, India. This tertiary-level 350-bedded children's hospital has 30 beds in the pediatric surgery unit. Neonates operated in the pediatric surgery operation theatre (OT) and subsequently managed in the PSNICU were included in the study. Neonates having infection at the time of admission as shown by clinical examination and/ or the results of investigations, or manifesting any infective illness within 48 hours of admission were excluded from the study. Neonates diagnosed with necrotising enterocolitis (NEC) or referred from the pediatric nursery or NICU were also excluded from the study. These were excluded as this study wanted to study the primary HCABSI rate of cases handled in the paediatric surgery OT and managed in the PSNICU without any influence of the other units of the hospital.

The patients in the study group underwent surgery in the pediatric surgery OT which deals with both elective and emergency surgeries. All the cases were administered prophylactic parenteral antibiotics, the exact choice of antibiotics depending upon the indication for the surgery. The administered antibiotics included cefotaxime in a dose ranging from 50-100 mg/kg/day, ceftriaxone 75-100 mg/kg/day, amikacin 15mg/kg/day in 1-3 divided doses, and metronidazole 15mg/kg over one hour followed by 7.5mg/kg eight hourly. The operative time for the cases varied between 30 minutes and 200 minutes. After surgery, the patients were shifted from the OT on the third floor to the PSNICU located on the second floor of the KSCH building. Postoperatively, in the PSNICU, the patients were managed by the pediatric surgery team with necessary assessment and advice from the microbiologists.

Surveillance of these cases was conducted during the daily rounds by the medical team. Necessary investigations such as blood culture, radiological and other laboratory investigations (CBC, CRP, KFT, LFT) of these cases were carried out whenever indicated.

Data was collected on a predesigned, pretested proforma from every patient regarding the various intrinsic and extrinsic risk factors and the demographic details. The questionnaire included information on intrinsic risk factors such as age, birth weight, type of delivery (normal vaginal delivery/ cesarean section), gestational age at birth, antenatal diagnosis of any congenital malformation, and maternal anemia. Amongst extrinsic factors, aspects dealing with management and care of the cases were preoperative preparation of the patient, type of procedure (emergency/ elective), type of anesthesia (regional/general), preoperative antibiotic administration, duration of operation, transfusion of blood products, duration of preoperative and postoperative stay and antibiotic therapy. All the cases were followed up from the time of admission time till their discharge. Blood culture was done at admission followed by a second when suspicion of infection arose. For the purpose of this study, the neonates were assessed by classifying them into three groups on the basis of birth weight, gestational age and

duration of onset of the healthcare associated bloodstream infections (HCABSIs).

HCABSIs in the cases in the study group was defined if the operated case managed in the PSNICU developed bloodstream infection a minimum of 48 hrs[12] after admission and the onset of management. Bloodstream infection in the study was defined as isolation of a pathogen from a blood[12] sample collected after aseptic precautions. An automated blood culture system[13] (BacT/Alert™, Biomèrieux) and automated identification systems (Vitek 2 Compact, Biomèrieux) were used in the study.

Statistical testing was conducted with the statistical package for the social science system version SPSS 17.0. Univariate analysis was performed to determine the statistically significant risk factors. Multivariate logistic regression analysis was performed to determine the independent predictor of HCABSIs. For all statistical tests, a p value less than 0.05 was taken to indicate a significant statistical difference.

Results:-

The study group included 190 neonates operated for a variety of indications including hypertrophic pyloric stenosis (HPS), neonatal intestinal obstruction (NIO), anorectal malformations (ARM), omphalocele (Omp), gastroschisis (Gas), and esophageal atresia with/ without tracheoesophageal fistula (EA +/- TEF). The male: female ratio in the study group was 5.3:1 while the mean birth- weight of the patients in the study group was 2.31±0.41 kg. Twenty nine (15.26%) of the 190 patients underwent emergency surgery. All the neonates were operated under general anaesthesia. In the majority of cases (62.1%), the duration of surgery was ≥150 minutes. The duration of surgery was in the range of 144±18 minutes in neonates having HCABSIs as compared with 135±18 minutes in cases who did not have. Most of the neonates (96.8%) had a 'clean contaminated surgical wound' as the surgical procedure often involved the gastrointestinal tract. Only one patient belonged to the category of 'clean wound' and none to the 'contaminated and dirty wound category'. Maternal anemia was corrected prior to delivery in 13.7% cases.

Table 1: Profile of healthcare associated bloodstream infections (HCABSIs) in the study group (n=32/190)

		Birth weight			Gestational age		Duration of onset				Isolates				
Diagnosis	HCABSI episodes	VLBW	LBW	NBW	T	PT	≤7d	8-14d	15-21d	22-28d	K. pneumoniae	*Acinetobacter spp*	CONS	E. coli	Others
Hypertrophic pyloric stenosis (HPS) [15]*	1	-	-	1/15	1/15	-	1	-	-	-	1	-	-	-	-
Neonatal intestinal obstruction (NIO) [37]*	6	-	5/23	1/13	2/19	4/18	5	1	-	-	4	-	-	1	1
Omphalocele (Omp) [24]*	5	1/1	3/17	1/6	2/12	3/12	4	-	-	1	3	-	-	2	-
Gastroschisis (Gas) [11]*	2	-	2/7	-	1/8	1/3	1	1	-	-	-	1	1	-	-
Anorectal malformation (ARM) [41]*	5	-	4/22	1/18	4/32	1/9	5	-	-	-	1	1	1	1	1
Esophageal atresia with/ without tracheoesophageal fistula (EA +/- TEF) [43]*	11	-	9/32	2/10	5/21	6/22	8	3	-	-	2	5	3	-	1
Others [19]*	2	-	2	-	1	1	1	1	-	-	-	1	1	-	-
Total [190]*	32	1/6	25/114	6/70	16/118	16/72	25	6	-	1	11	8	6	4	3

Others include *Citrobacter koseri* and *Staphylococcus aureus* CONS: Coagulase negative Staphylococcus VLBW: <1.5kg, LBW: ≥1.5 kg - <2.5 kg, NBW: ≥2.5 kg; T: Term (Gestational age ≥37 wks), PT: Preterm (Gestational age < 37 wks). *[ ] indicates total number of neonates diagnosed with included in the study.

During the study period thirty two neonates developed healthcare associated BSI (HCABSI) according to the CDC criteria[12] (Table 1). The majority of these infections (43.75%) occurred between the months of July to September in the study period. In patients developing HCABSI, the mean haemoglobin was within normal limits while in 40% of these patients, the platelet count was low (<1.5 lakhs/ cu mm). C- reactive protein levels were raised (>0.6 mg/dl) in 53.1% of these cases and these were designated as being CRP positive. Approximately seventeen percent of neonates who had undergone elective surgery and fourteen percent of neonates who underwent emergency surgery had acquired the infections. Twenty five percent of neonates delivered by ceaserean section and eleven percent of neonates delivered normally had HCABSIs. The infection rate of the HCABSI was found to be 16.84 episodes per hundred admissions. The infection density of HCABSI was 16.67 episodes per thousand patient days.

According to the surgical procedure, in cases operated for EA +/- TEF, 11 HCABSI episodes were reported, followed by cases operated for NIO in whom 6 HCABSI episodes occurred. There were five episodes of HCASBI each in patients operated for an ARM and those operated for an omphalocele. Majority of cases presenting with hypertrophic pyloric stenoses were beyond the neonatal period, hence only those presenting within the same and confirming to the criteria were included.

The majority of the infections (78.1%) set within the first week of stay and in the low birth weight neonates (78.1%). In cases operated for EA +/- TEF, the onset of the HCABSI in the majority of cases was ≤7 days. *Acinetobacter spp* was the predominant pathogen in this group. However *K.pneumoniae* was the predominant pathogen in the other groups.

The mean birth weight of neonates with HCABSIs was low, in the range of 2.14±0.38 kg whereas the mean birth weight of neonates who did not have HCABSIs was in the range of 2.39±0.4 kg. This was a significant risk factor ($p<0.001$) associated with occurrence of the HCABSI. According to univariate analysis, the other significant risk factors for occurrence of HCABSI were duration of hospital stay and

positive C-reactive protein (p<0.05). However according to multivariate analysis, only duration of stay was found to have a positive statistical significant association with HABSIs (p=0.005, OR- 1.169, 95% CI: 1.047- 1.304).

The *K. pneumoniae* isolates did not show any resistance to colistin and 18.18% of the isolates were resistant to imipenem. Decreased susceptibility to imipenem was seen in 37.5% of *Acinetobacte*r isolates. Methicillin resistance was seen in approximately 50% of the coagulase negative and *S.aureus* isolates.

Discussion:

The current study was a unicentric study carried out on 190 neonates operated and managed in PSNICU of KSCH, New Delhi. In the current study, the neonates were assessed on the basis of birth weight, gestational age and age at onset of the HACBSIs. No such categorization was performed in two other similar studies reported in the literature[10,11]. The majority of cases in our study presented with respiratory distress or intestinal obstruction[14]. The neonates underwent various operative procedures such as thoracotomy (for EA +/-TEF), repair of an anterior abdominal wall defect (for omphalocele or gastroschisis), bowel resection and anastomosis (for NIO), and anoplasty or colostomy for an ARM. This is in contrast to the US based multicentric study reported by Bhattacharya et al[10] which had a heterogenous study group with the population comprising of neonates, infants and older children who had undergone thoracotomy, repair of anterior abdominal wall defects, bowel resection, inguinal herniorrhaphy, appendectomy and other similar operative procedures. Another study defined neonatal infections as infections occurring upto 28 days of life in full-term neonates and during the first 2 months of life in preterm neonates admitted in the NICU[11]. In contrast, our study described neonatal infections as those occurring upto 28 days of life irrespective of the gestational age. The study reported by an Iranian study group was a heterogeneous study comprising neonates with both medical and surgical entities being grouped together[11]. A significant finding of our study was that the majority of HCABSIs occurred between the months of July to September. This increased number of HCABSI may be attributed to the hot and humid condition prevalent in New Delhi during this season which promotes the growth of microorganisms. However, the study reported by Bhattacharya et al[10], which was conducted in New Mexico, southern USA, found an even distribution of infections with no seasonal predilection. This difference may be attributed to the varying conditions in the two places. This aspect has also not been addressed in the study from Iran reported by Salamati et al[11].

The incidence rate of primary HCABSI in our study was found to be 16.84 cases per hundred admissions. This high rate of infection may be attributed to the inferior immune system of neonates who have undergone surgical intervention. In addition, surgical neonates require additional physiologic adjustments to overcome further heat loss through vomiting or nasogastric aspiration, increased rate of respiration, and during the massive increase in surface area when the baby's abdomen is opened[14]. This parameter has not been addressed in the studies reported by Bhattacharya et al[10] and Salamati et al[11]. The infection density of HCABSIs in our study was found to be 16.67 episodes per thousand patient days. However, a lower rate of 1.8 infections per thousand patient days was reported in the study conducted by Salamati et al[11]. This may be attributed to differences in practices of infection control practiced in these two centres.

The maximum number of primary HCABSI in the current study occurred in neonates operated for EA +/- TEF. This characteristic may be attributed to invasion of two major systems of the body; namely the respiratory and gastrointestinal tracts. In addition, during surgical repair of this condition, a nasogastric tube is inserted transanastomoticaly into the stomach, a manoeuvre that necessarily causes contamination. In our study, the duration of onset in the majority of HCABSIs that occurred in the cases operated for EA +/- TEF was in the ≤7 day category. The other two similar studies[10,11] have not included this surgical entity in their studies.

The present study dealt predominantly cases with clean contaminated wounds. The studies reported by Bhattacharya et al[10] and Salamati et al[11] did not mention about this parameter. *Klebsiella pnemoniae* was the most predominant pathogen in our study followed by *Acinetobacter spp. Klebsiella pnemoniae* was the exclusive pathogen in cases operated for NIO or omphalocele. This is understandable as in these cases, the source of infection is likely to be of endogenous origin. This aspect could not be compared with the study of Salamati et al[11] as these authors did not demarcate the finding of cases undergoing surgery from those who had only medical conditions. In their study, *Enterobacter spp* was the commonest isolate. Bhattacharya et al[10] also did not comment on this aspect in their reported study.

In our study, primary HCABSI were found to occur predominantly in the low birth-weight category of newborns. This parameter has not been addressed in other studies[10,11]. A higher percentage of HCABSI were also seen in preterm neonates. This aspect has not been adequately addressed in the studies reported by Bhattacharya et al[10] and Salamati et al[11]. The other risk factors found to be statistically significant with HCABSI by univariate analysis were duration of stay and positive C-reactive protein. By multivariate logistic regression analysis, duration of stay was found to be the only independent predictor of HCABSI (p=0.005, OR- 1.169, 95% CI: 1.047-1.304). Increased duration of stay in a healthcare setting prolongs the duration of exposure to risks thereby increasing the risks of acquiring infections. Although Salamati et al[11] did not address this risk factor in their study, Bhattacharya et al[10] reported prematurity and the presence of a second anomaly as risk factors for occurrence of HCABSI.

Conclusion:

The current study performed in the PSNICU of neonates operated in KSCH, New Delhi had a high incidence rate of primary HCABSIs, with an infection rate of 16.884 per hundred admissions and infection density of 16.67 per thousand patient days. The risk factors for the BSIs were found to be birth weight, duration of stay, duration of surgery, and a positive CRP by univariate analysis. However, according to multivariate logistic regression analysis, duration of stay was found to be significant risk factor to be associated with BSIs. To reduce the current primary HCABSI rate, admitted cases need proactive management with strengthened infection control practices[15-18].

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