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CENTRAL VENOUS CATHETER RELATED BLOODSTREAM INFECTIONS IN NEONATAL INTENSIVE CARE UNIT

Paediatrics

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ABSTRACT

BACKGROUND: To study the occurrence of central venous catheter related bloodstream infections in neonatal intensive care unit (NICU) of tertiary care center.

METHOD: A tertiary care hospital based prospective study was done over a 2-year period. In the study 167 central venous catheters were placed in neonates and incidence of catheter related bloodstream infection was evaluated during admission.

RESULTS: Out of total 167 cases, peripherally inserted central catheter (PICC) was used in 150 neonates and Umbilical venous catheter (UVC) in 17 neonates. Median catheter duration was 9 with a range of 3 to 23 days. The most common indication of insertion in neonates was prolonged IV access. Total of 41 complications were noted during 1707 catheter days. The overall incidence rate of CRBSI was 4.68 per 1000 catheter days and that of other complications was 19.33 per 1000 catheter days.

CONCLUSION: In spite of all aseptic precautions by everyone complications of central venous catheterization occur and should be watched out for.

KEYWORDS

Central venous catheter related bloodstream infections (CRBSI), neonatal intensive care unit (NICU), peripherally inserted central catheter (PICC), and Umbilical venous catheter (UVC).

INTRODUCTION

Reliable vascular access is a necessity for pediatric practice and enables the delivery of medications and fluids, nutritional support, hemodynamic monitoring, renal replacement therapy, and easy sampling of the blood for diagnostic testing. Vascular access is difficult mainly due to anatomical factors in the pediatric population as small veins and excess subcutaneous fat leading to poor visualization can make cannulation difficult making intravenous (IV) access very challenging.[1] Forssmann introduced one of the first techniques for central venous catheterization in the year 1929 for which he shared the 1956 Nobel Prize for Medicine with W. Richards and A. F. Cournand.[2] Central venous catheter (CVC) since then has become indispensable in pediatric practice especially in critical care setting. But despite best efforts, CVCs are prone to infectious, thrombotic and mechanical complications.[3][4]

Catheter related bloodstream infection (CRBSI) is defined as the presence of bacteremia originating from an intravenous catheter.[5] The US Center for Disease Control and Prevention (CDC) defines CRBSI as bacteremia or fungemia in a patient who has an intravascular device and >1 or equal to 1 positive result of culture samples obtained from the peripheral vein with clinical manifestations of infection and no apparent source of bloodstream infection.[6] CRBSI is one of the most frequent, lethal, and costly complications of central venous catheterization and also the most common cause of nosocomial bacteremia. Incidence of CRBSI reported varies from country to country and even hospital to hospitals.[7][8][9] According to S Singh *et al*., (2010) the overall CRBSI rate was 0.48 per 1000 device days.[10] In another study by Chopdekar et all the CRBSI rate was 9.26 per 1000 catheter days with highest rate of 27.02/1000 days in neonatal intensive care unit (NICU).[11]

Several questions regarding CRBSI remain unanswered with the available pediatric literature. Especially there are very few studies reporting rate of CRBSI in the Indian literature. Hence the purpose of this study is to evaluate catheter-related blood stream infections in pediatric and neonatal patients and identify common organisms for catheter related blood stream infections. This study will also evaluate other complications that may arise due to central venous catheters like certain mechanical complications and systemic complications like venous thrombosis.

OBJECTIVES

1. To study the occurrence of central venous catheter related bloodstream infections in neonates of tertiary care center.
2. To identify common organism seen with CRBSI in neonates with CVC of any kind.
3. To determine the length of time that the catheter is inserted in neonates of tertiary care centre.
4. To identify complications related to CVC in neonates of tertiary care centre.

MATERIALS AND METHODOLOGY

STUDY DESIGN:

Prospective study where outcome (complications, etc) were evaluated during admission and within 15 days of hospital discharge.

STUDY SETTING:

This prospective study was conducted in the Neonatal intensive care unit (NICU) of a tertiary care institute. An approval from the Ethics Committee of the institute was taken. Written informed consent was obtained from the parents or the surrogate for participation. The duration of study was 2 years. The demographic data including age, sex was collected and recorded in the case record proforma along with the physical examination findings.

STUDY POPULATION:

All neonates admitted to the NICU of the tertiary care centre with central venous catheter of any kind.

SAMPLE SIZE:

Determined considering proportion of complication as the main outcome. N = 167

TIME FRAME: October 2017 – September 2019

INCLUSION CRITERIA:

All neonates admitted to the NICU of the tertiary care centre with central venous catheter of any kind that has been inserted for greater than 48 hours for the purpose of management of patient's condition.

EXCLUSION CRITERIA:

All neonates admitted to the NICU of the tertiary care centre in whom the central line, PICC line or Umbilical line is removed within 48 hours of insertion.

STATISTICAL ANALYSIS:

The data on demographic characteristics of neonates like gestational age and gender were obtained and summarized in terms of numbers and percentages. The distribution of neonates as per presence of sepsis was obtained. Further, the success rate of insertion and number of attempts required for insertion were obtained. The indication of insertion of catheter, type of CVC and site of insertion of catheter were also determined. The distribution of neonates as per the primary outcome i.e. CRBSI was obtained. The incidence rate for CRBSI was determined. The incidence rates were also determined for other complications. The distribution of organisms in CRBSI cases was reported.

The analysis was performed using R-3.0.0 programming tool and

Microsoft Excel 17.0.

OUTCOME MONITORING:
Data was reported per 1000 catheter days.Rate of complication per 1000 catheter days

$$= \frac{\text{Total number of complications} \times 1000}{\text{Number of catheter days}}$$

DETAILED METHODOLOGY:
All the neonates requiring and consenting for the insertion of Central venous line of any form were selected. Sample was withdrawn and sent for culture before start of antibiotics. Skin preparation for percutaneously drawn blood samples was carefully done with either alcohol or tincture of iodine. Adequate skin contact and drying time will be allowed to mitigate blood culture contamination. If neonate was already on antibiotics, reports of culture for which antibiotic child was on, was obtained. Catheter, either peripherally inserted central catheter (PICC) or Umbilical venous catheter (UVC) was inserted as per requirement of the neonate and indication of insertion.

1. PROCEDURE FOR PERIPHERALLY INSERTED CEN TRAL CATHETER (PICC) INSERTION: [12][13]
The vein to be inserted was selected. The length to be inserted was assessed by measurements taken from the site of insertion to umbilicus for lower limb and upto the medial end of clavicle for upper limb. Single lumen polyurethane catheter was used with breakaway needle. Appropriate lumen catheter size was used. 28G sized PICC was used for preterm neonates and 24G for older neonates and infants.[14][15]After hand wash, sterile gown and gloves were donned. The insertion site and surrounding skin along the course of vein was cleaned thoroughly with alcohol and betadine. Sterile towel was draped underneath and above the insertion site. First the introducer was inserted into the vein and after blood return; the catheter was advanced slowly through the introducer using forceps. After inserting the measured length of catheter, the needle was taken out. The catheter was secured with appropriate dressing. Tip position was confirmed by check X-ray whether it is in superior vena cava/inferior vena cava.[16] The tip of the PICC line should be in superior vena cava for upper extremity and in thoracic inferior vena cava for lower extremity insertions.[17] After confirming the position IV fluids or medications were started.

2. PROCEDURE FOR UMBILICAL VENOUS CATHETER (UVC) INSERTION: [18][19]
The umbilical cord stump and the surrounding abdomen were sterilized with a bactericidal solution. Sterile drapes were placed. A purse-string suture or umbilical tape was tied around the base of the stump to provide hemostasis and to anchor the line after the procedure. The cord was cut horizontally with the scalpel, approximately 1.5-2 cm from the abdominal wall. Two thick-walled small arteries and one thin-walled larger vein were identified. When identifying vessels, vein is usually located in the 12-o'clock position. The umbilical vein may continue to ooze blood. Hemostasis was achieved by tightening the umbilical tape or suture. The arteries do not usually bleed secondary to vasospasm. Forceps were then used to clear any thrombi and dilate the vein. A 3.5-French catheter was used for preterm newborns, and a 5-French catheter was used for full-term newborns. The catheter was then be grasped 1 cm from its distal tip with the iris forceps and gently inserted, with the tip aimed toward the right shoulder. The catheter was advanced only 1-2 cm beyond the point at which good blood return was obtained; this was approximately 4-5 cm in a full-term neonate. If resistance was initially met, the umbilical tape or suture was loosened and the angle of approach manipulated. Advancement was not forced. The catheter was secured with a suture through the cord. The position of the catheter was confirmed radiographically.[20]

Once the Central line was placed all precautions were taken to keep the catheter site aseptic and clean.

The diagnosis of CRBSI was suspected clinically in a patient using a CVC who presented with fever or chills, unexplained hypotension, and no other localizing sign. Mild symptoms include malaise and nausea, and severe symptoms include high fever with rigors, hypotension, vomiting, and changes in mental status in the setting of a normal catheter exit site or tunnel, on physical examination.

The next step was to diagnose CRBSI: [6] [21] There are multiple definitions that have been proposed for CRBSI. [21][22] The simplest definition of Catheter related bloodstream infection (CRBSI) is the presence of bacteremia originating from an intravenous catheter.[4]

OPERATIONAL DEFINITION:
A diagnosis of CRBSI requires that the same organism (species and anti-biogram) grows from at least 1 percutaneous blood culture and from a culture of the catheter tip , or that 2 blood samples drawn (one from a catheter hub and the other from a peripheral vein) that, when cultured, shows the same organism, or bacteremia/ fungemia in a patient with an intravascular catheter with at least one positive blood culture obtained from a peripheral vein, clinical manifestations of infection (that is, fever, chills, and/or hypotension), and no apparent source for the bloodstream infection except the catheter**.**

ETHICAL APPROVAL:
This study was approved by the Institutional Ethics Committee.

STATISTICAL ANALYSIS:
Data was analyzed using the SPSS version 25.0. Data were analyzed quantitatively and presented in the form of frequency tables and proportions.

RESULTS
Out of total 167 neonates, maximum babies were delivered beyond 36 weeks of gestation i.e 102(61.07%) followed by those between 30 to 35 weeks of gestation 57 (34.13%) and only 8 (4.79%) babies were less than 30 weeks of gestation. 111 (64.46%) were male and 56 (33.53%) were female. A total of 94 (56.28%) neonates were septic and 56 (43.71%) neonates were non-septic.

TABLE 1: GESTATIONAL, SEX WISE, AND SEPTICEMIA AGE WISE DISTRIBUTION.

Areas		N=167
GESTATIONAL AGE		
	25-30 WEEKS	8 (4.79%)
	31-35 WEEKS	57 (34.13%)
	36-40 WEEKS	102 (61.07%)
Sex wise distribution.		
	MALE	111 (64.46)
	FEMALE	56 (33.53%)
Distribution as per age and septicemia		
	SEPTIC	94 (56.28%)
	NON-SEPTIC	73 (43.71%)

Overall PICC insertion was attempted in 157 neonates and was successful in 155 neonates but 5 were excluded from the study. UVC insertion was attempted in 17 neonates and successful in all. Most of the PICCs and UVCs were inserted in the single attempt in 113 (67.66%) neonates followed by two attempts in 42 (20.28%). 12(7.12%) neonates required three attempts for insertion of catheter.

TABLE 2: SUCCESS RATE OF INSERTION.

	Attempted	Successful	Excluded From Study	Final Cases Included In Study
PICC	157	155	5	150
UVC	17	17	-	17

TABLE 3: NUMBER OF ATTEMPTS REQUIRED FOR INSERTION.

ATTEMPT			
1	**2**	**3**	**TOTAL**
113 (67.66%)	42 (20.28%)	12 (7.18%)	167

The most common indication of insertion in neonates was prolonged IV access in 126 (75.44%) followed by difficult venous access in 36 (21.55%) and least common was exchange transfusion in 5 (2.99%). In the neonates, PICC was the type of catheter used in 150 (89.82%) whereas UVC was used in remaining 17 (10.17%).

TABLE 4: INDICATION OF INSERTION OF CATHETER.

PROLONGED IV ACCESS	DIFFICULT VENOUS ACCESS	EXCHANGE TRANSFUSION	TOTAL
126 (75.44%)	36 (21.55%)	5 (2.99%)	167

TABLE 5: TYPE OF CVC.

PICC	UVC	TOTAL
150 (89.82%)	17 (10.17%)	167

4 (44.44%)	-	9
1 (3.25%)	-	31

TABLE 6: SITE OF INSERTION OF CATHETER.

SITE			
SAPHENOUS	POPLITEAL	BASILIC	UMBILICAL VEIN
133 (79.64%)	12 (7.18%)	5 (2.99%)	17 (10.17%)

The most common site of catheter insertion was Saphenous vein in 133 (79.64%) followed by umbilical vein in 17 (10.17%), Popliteal vein in 12 (7.18%) and Basilic vein in 5 (2.99%).

TABLE 7: NUMBER OF DAY'S CATHETER WAS IN SITU.

>48 HOURS – 5 DAYS	6-10 DAYS	11-15 DAYS	16-20 DAYS	>20 DAYS
26	77	39	19	6

In our study 167 catheters were placed over 1707 days. Median catheter duration was 9 with a range of 3 to 23 days.

TABLE 8: CRBSI- PRIMARY OUTCOME.

CRBSI POSITIVE (No. of days of catheter in-situ)	CRBSI NEGATIVE (No. of days of catheter in-situ)
8 (114)	159 (1593)

In neonates, 8 (4.79%) cases were positive.

TABLE 9: INCIDENCE RATE FOR CRBSI.

AGE	CRBSI POSITIVE (No. of days of catheter in-situ)	CRBSI NEGATIVE (No. of days of catheter in-situ)	INCIDENCE RATE of CRBSI / 1000 catheter days
Neonates	8 (114)	159 (1593)	8/1707*1000 = 4.68

The incidence of CRBSI was 4.68 per 1000 catheter days.

TABLE 10: OTHER COMPLICATIONS.

OTHER COMPLICATIONS	TOTAL NO OF CASES (No. of days of catheter in-situ)
BLOCKAGE	14 (162)
ERYTHEMA	9 (76)
INDURATION	8 (63)
EXTRAVASATION	2 (28)

Blockage was found to be the most common other complication seen in 14 (8.38%) neonates, followed by erythema seen in 13 (5.38%) neonates, induration seen in 8 (4.79%) neonates and extravasation was seen in 2 (1.19%). The overall incidence of other complications is 19.33 per 1000 catheter days.

TABLE 11: ORGANISMS OBSERVED IN CRBSI.

ORGANISM	NEONATES
CANDIDA	2
KLEBSIELLA	3
METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS (MRSA)	1
COAGULASE NEGATIVE STAPHYLOCOCCUS (CONS)	1
NON FERMENTER	1

Most common organism associated with CRBSI was klebsiella (3) followed by candida (2), CONS (1), MRSA (1), non-fermenter (1).

TABLE 12: ANTIBIOGRAM OF ORGANISMS OBSERVED IN CRBSI.

Sr No	Organism	Sensitive	Resistant
1.	CANDIDA	Fluconazole, Amphotericin B, Itraconazole	-
2	KLEBSIELLA ESBL	Ciprofloxacin, Ceftriaxone-sulbactum, Imipenem	Cefotaxime, Ceftriaxone, Cefuroxime, Gentamicin, Piperacillin-Tazobactum
3	KLEBSIELLA	Piperacillin-Tazobactum, Meropenem	Cetriaxone, Levofloxacin
4	NON-FERMENTER	Cefotaxime, Ceftriaxone, Ciprofloxacin, Ceftriaxone-sulbactum, Piperacillin-Tazobactum, Imipenem	Cefuroxime, Gentamicin
5	MRSA	Vancomycin	Amikacin, Ampicillin-Sulbactum, Ciprofloxacin
6	CANDIDA	Amphotericin B, Itraconazole	Fluconazole, Ketoconazole, Voriconazole
7	KLEBSIELLA ESBL (extended spectrum beta lactamase)	Colistin, Polymixin	Amikacin, Cefotaxime, Ceftriaxone, Cefuroxime, Ceftriaxone-Sulbactam, Gentamicin, Imipenem, Meropenem, Levofloxacin, Netilmycin, Piperacillin-Tazobactum
8	CONS	Erythromycin, Ciprofloxacin, Clindamycin, Cotrimoxazole	Amikacin, Ampicillin-Sulbactum

DISCUSSION

In this study, a prospective surveillance was done for CRBSI in the NICU during the study period from October 2017 – September 2019. Out of total 167 neonates, 111 (64.46%) were male and 56 (33.53%) were female. The male to female ratio was 1.98.Gestational age wise, maximum babies were delivered beyond 36 weeks of gestation i.e 102(61.07%) followed by those between 30 to 35 weeks of gestation 57 (34.13%) and only 8 (4.79%) babies were less than 30 weeks of gestation.

The various types of catheters used were PICCs and UVCs. PICC was the most common type of catheter used in 150 (89.82%). UVC was used only in remaining 17 (10.17%) neonates. Overall the successful insertion rate of PICC and UVC was 98.8%. The success rate of insertion varied from 88- 95% in similar other studies done.[23,24,25,26]

PICC insertion was attempted in 157 neonates and was successful in 155 neonates but 5 were excluded from the study. In these 5 children, PICC was removed within 48 hours of insertion and were hence excluded. Umbilical line insertion was attempted in 17 children and successful in all. Only 1 neonate had two CVCs during the stay rest all had only one CVC during their entire stay.

Most of the CVCs including PICC and UVC were inserted in a single attempt in 113 (67.66%) neonates followed by two attempts in 42 (20.28%).

12 (7.12%) neonates required three attempts for insertion of catheter. In a similar study by Neubauer et al., the success rate of insertion at first attempt was 63.6%.[27] Whereas in a study by Njere I et al., the success rate at first attempt was 71%, at the second attempts was 21%, at the third attempts was 6% and at fourth attempt was 2%.[28] The success rate of PICC insertion at first attempt was as high as 86% in one study.[29]

The most common indication of insertion in neonates was prolonged IV access in 126 (75.44%) followed by difficult venous access in 36 (21.55%) and least common was exchange transfusion due to Rh incompatibility in 5 (2.99%). In this study, we could not compare lower extremity vs. upper extremity insertion since majority of CVC lines were inserted in lower extremity. The most common site of catheter insertion was Saphenous vein in 133 (79.64%) followed by umbilical vein in 17 (10.17%), Popliteal vein in 12 (7.18%) and Basilic vein in 5 (2.99%). In our study 167 catheters were placed over 1707 days. Median catheter duration was 9 days with a range of 3 to 23 days. Total of 41 complications were noted during 1707 catheter days. The most important complication noted was CRBSI in 8 catheters (4.79%).

In present study 8 (4.79%) were CRBSI positive which means that 8 of blood culture samples grew same organism from the catheter tip as well as from the peripheral blood culture sample. The infection rate or the overall incidence rate of CRBSI in neonates was 4.68 per 1000 catheter days.The 2014 report of the European Centre for Disease Prevention and Control (ECDC) estimated a mean device-adjusted rate in patients staying in an ICU for more than two days was 3.0 CLABSI episodes per 1000 central line-days.[30] In a cohort study performed in 173 neonatal intensive care unit (NICU) and 64 PICU reporting data to the Centers for Disease Control and Prevention's National Healthcare Safety Network in United States from 2007 to 2012 showed a reduction of infection rates from 4.9 to 1.5/1000 central line-days in NICU and from 4.7 to 1.0/1000 central line-days in PICU in 5 years time.[31]

Most common organism associated with CRBSI was Klebsiella seen in 4 cases 3 cases followed by Candida seen in 2 cases. Other organisms seen were Coagulase negative staphylococcus (CONS), Methicillin resistant staphylococcus aureus and a Non-fermenter in 1 case each. The other complication were Blockage seen in 14 (8.38%) neonates, followed by erythema seen in 13 (5.38%) neonates, induration seen in 8 (4.79%) neonates and extravasation was seen in 2 (1.19%). The overall incidence of other complications is 19.33 per 1000 catheter days. Many studies reported complication rate of 1.1-19.3 per 1000 catheter days with infection rate of 0.2-6.4 per 1000 catheter days.[32,33]

Our study reports complication rates similar to those of prior studies that have reported rates ranging from 17% to 50%. [34] [35] [36] [37] [38] This large variation in complication rates may be in part explained by differences in types of complications reported (infectious, noninfectious, or both combined) and different populations studied.

CONCLUSION

In spite of all aseptic precautions by everyone complications of central venous catheterization occur and should be watched out for. CRBSI is one of the most common complications of central venous catheterization. Numerous guidelines exist on the prevention of CRBSI. Standard operating procedures and training for maintenance of CVC, PICC and UVC is of paramount importance. Local protocols to minimize CRBSI should be established and followed.

LIMITATION -

The results of this study "Central Venous Catheter Related Bloodstream Infections in Neonatal Intensive Care Unit" further require an area based research and future research to delineate and characterize frequency, and risk factors for central venous catheter related bloodstream infections in neonatal intensive care unit (NICU).

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CONFLICT OF INTEREST-

The authors declare that they have no conflict of interest.

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