

# Study of risk factors and therapeutic outcomes in Central Venous Catheter related Blood Stream infection in neonatal intensive care unit

Jayant Sargar<sup>1</sup>, Dilip Turbadkar<sup>2\*</sup>, Sujata Baveja<sup>3</sup>

<sup>1</sup>Assistant Professor, <sup>2</sup>Additional Professor, <sup>3</sup>Professor & HOD, Department of Microbiology, Lokmanya Tilak Municipal Medical College & General Hospital, Sion Mumbai, INDIA.

Email: [turbadkar@hotmail.com](mailto:turbadkar@hotmail.com) [sembaveja@gmail.com](mailto:sembaveja@gmail.com)

## Abstract

**Background:** Central Venous Catheter (CVC) use has been associated with an increased risk for developing hospital-acquired blood stream infections, also termed central line-associated blood stream infections (CLABSI). CLABSI in neonates are associated with longer stay in the hospital, unfavorable outcome, and mortality. Present study was aimed to study risk factors and therapeutic outcomes in central venous catheter related blood stream infection in neonatal intensive care unit at a tertiary hospital. **Material and Methods:** Present study was single-center, prospective, observational study, conducted in neonates on central venous catheters admitted in NICU and who developed systemic signs and symptoms of infections after 48 hours of admission. Specimens collected were catheter tip, blood for blood culture, urine and endotracheal secretions (for patients on ventilator) by standard method and processed. After incubation, individual bacterial colonies grown were further identified as per standard protocol (Gram staining, culture). **Results:** 35 neonates on CVC in NICU and who developed signs and symptoms of infections after 48 hrs of admission were analysed. Of these 35 patients, 23 developed Catheter related local infection (CRLI) and 12 patients developed Central line associated blood stream infections (CLABSI). Maximum patients having local catheter infection were distributed among age group of 6-10 days (34.8%), followed by 1-5 days (30.4%) and 11-15 days (21.7%). While those with systemic catheter infections age group of 6-10 days (50%) was common followed by 1-5 and 11-15 days (16.7% each). Male preponderance was seen in both local (60.8%) and systemic (62.8%) catheter infection. In present study, 85.7% were early preterm birth ( $\leq 32$  weeks of gestational age) 77.1% neonates were less than 1500 gram birth weight, 45.7% neonates were admitted for more than 30 days in NICU and 80% had catheters for more than 8 days. 30 (85.7%) of total patients had insertion at peripheral site. Triple lumen catheter was most commonly used (65.7%) followed by single lumen catheter in 34.3% of patients. Out of the 23 patients with local infection, three died. There was no significant association of local catheter infection with outcome of patients. Out of the 12 patients who developed systemic infections, 8 patients died showing highly significant correlation with the outcome with p value  $< 0.0001$ . **Conclusion:** CRBSI are responsible for a large number of nosocomial bacteremia cases and constitute one of the main infections affecting premature and low weight neonates.

**Keywords:** CRBSI, premature, low weight neonates, bloodstream infections, antimicrobials

## \*Address for Correspondence:

Dr Dilip Turbadkar, Additional Professor, <sup>3</sup>Professor & HOD, Department of Microbiology, Lokmanya Tilak Municipal Medical College & General Hospital, Sion Mumbai, INDIA.

Email: [turbadkar@hotmail.com](mailto:turbadkar@hotmail.com)

Received Date: 14/06/2021 Revised Date: 09/07/2021 Accepted Date: 28/08/2021

This work is licensed under a [Creative Commons Attribution-NonCommercial 4.0 International License](https://creativecommons.org/licenses/by-nc/4.0/).



## Access this article online

Quick Response Code:



Website:

[www.medpulse.in](http://www.medpulse.in)

DOI:

<https://doi.org/10.26611/10082014>

## INTRODUCTION

The integral component of provision of care to neonates in the Neonatal Intensive Care Unit (NICU) is to obtain a secure and reliable vascular access. As consequence of their increasing use, blood stream infection (BSI) resulting from CVC have become costly complication of health care. Central Venous Catheter (CVC) use has been associated with an increased risk for developing hospital-acquired blood stream infections, also termed central line-associated blood stream infections (CLABSI).<sup>1,2</sup> The gold standard is

**How to cite this article:** Jayant Sargar, Dilip Turbadkar, Sujata Baveja. Study of risk factors and therapeutic outcomes in Central Venous Catheter related Blood Stream infection in neonatal intensive care unit. *MedPulse International Journal of Microbiology*. September 2021;20(1): 16-22. <https://www.medpulse.in/Microbiology/>

the combination of a positive blood culture with the same organism isolated from the catheter. It nearly occurs infection generally within 48 hours of CVC insertion.<sup>3</sup> CVC related Blood stream Infection is a severe complication with a high morbidity and mortality; with infection ranging from 21.4% to 23.5%, often with a poor outcome.<sup>4</sup> There is a wide range of disparity in the infection rates in different studies which may depend on unit-associated factors such as size and settings, patient-associated factors such as type of illness and its severity and catheter-associated factors such as type of catheter, site of insertion and conditions under which the catheter was located.<sup>5,6</sup> Although, CVCs are essential for the treatment of sick neonates in neonatal intensive care unit and have many benefits, they have also important disadvantages. CLABSI in neonates are associated with longer stay in the hospital, unfavorable outcome, and mortality. Identification of these complications, as well as their risk factors is necessary in order to avoid them and improve the outcome of high risk infants in the NICU. Present study was aimed to study risk factors and therapeutic outcomes in central venous catheter related blood stream infection in neonatal intensive care unit at a tertiary hospital.

## MATERIAL AND METHODS

Present study was single-center, prospective, observational study, conducted in department of microbiology in collaboration with Neonatal Intensive Care Unit (NICU) at Lokmanya Tilak Municipal Medical College & General Hospital, Sion Mumbai, India. Study duration was of 1 year (January 2017 to December 2017). Study was approved by institutional ethical committee.

**Inclusion criteria:** Neonates on central venous catheters admitted in NICU and who developed systemic signs and symptoms of infections after 48 hours of admission.

**Exclusion criteria:** Patients with septicemia due to obvious causes other than central line. Patients developing systemic signs and symptoms < 48 hrs. of admission. Written informed consent was taken from parents/guardian of neonates who met inclusion criteria.

Central line related local infections (CRLI) was diagnosed as: 1. Any sign of local infection (induration, erythema, heat, pain, purulent drainage) and 2. Catheter tip colonization was defined as "Significant growth of a microorganism by >15 colony-forming units from the catheter tip by semiquantitative method or >10<sup>3</sup> by quantitative culture."

Central line associated blood stream infections (CLABSI) was diagnosed as: Recognized pathogen isolated from blood culture and pathogen not related to infection from

another site (other than site of an intravascular device i.e., it should not have been isolated from urinary tract / respiratory tract / wound, etc) OR One of the following – fever (>38.0 C), chills, hypotension AND any of the following: a. Common skin contaminant isolated from two blood cultures drawn on separate occasions, and organism is not related to infection at another site. B. Common skin contaminant isolated from blood culture from patient with intravascular access device and physician institutes appropriate antimicrobial therapy. C. Positive antigen test on blood or organism is not related to infection at another site.

Detailed clinical history of each patient was noted as per the clinical proforma, patient's clinical details including all risk factors, examination findings, laboratory investigations (complete hemogram, serum electrolyte, LFTs, RFTs) were recorded. Specimens collected were catheter tip, blood for blood culture, urine and endotracheal secretions (for patients on ventilator) by standard method and processed. After incubation, individual bacterial colonies grown were further identified as per standard protocol (Gram staining, culture).<sup>7,8</sup>

Antibiotic susceptibility of the bacterial isolate was done on Muller Hinton Agar (MHA) according to CLSI guidelines 2017 by using Kirby Bauer's Disc Diffusion Method (KBDDM) according to CLSI guidelines for all, except for catalase negative Gram positive cocci. For the later antibiotic susceptibility was put up on Blood agar.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Chi square analysis and Mid p test (wherever chi square cannot be applied i.e., failure to meet Cochrane's criteria) was applied for comparing cases (with infection) and control (without infection). P value less than 0.5 was considered as statistically significant.

## RESULTS

35 neonates on CVC in NICU and who developed signs and symptoms of infections after 48 hrs of admission were analysed. Of these 35 patients, 23 developed Catheter related local infection (CRLI) and 12 patients developed Central line associated blood stream infections (CLABSI). Maximum patients having local catheter infection were distributed among age group of 6-10 days (34.8%), followed by 1-5 days (30.4%) and 11-15 days (21.7%). While those with systemic catheter infections age group of 6-10 days (50%) was common followed by 1-5 and 11-15 days (16.7% each). Male preponderance was seen in both local (60.8%) and systemic (62.8%) catheter infection.

**Table 1: Age and gender wise distribution**

Age distribution (days)	CRLI (n=23) (%)	CVCBSI (N=12) (%)	Total
1 – 5	7 (30.4%)	2 (16.7%)	9
6 – 10	8 (34.8%)	6 (50%)	14
11 – 15	5 (21.7%)	2 (16.7%)	7
16 – 20	1 (4.3%)	1 (8.3%)	2
21 – 25	1 (4.3%)	1 (8.3%)	2
26 - 30	1 (4.3%)	0	1
Gender			
Male	14 (60.8%)	08 (66.7%)	22
Female	09 (39.1%)	04 (33.3%)	13

In present study, 85.7% were early preterm birth ( $\leq 32$  weeks of gestational age) 77.1% neonates were less than 1500 gram birth weight, 45.7% neonates were admitted for more than 30 days in NICU and 80% had catheters for more than 8 days.

**Table 2: Risk factors**

Risk factors	No. of cases (n=35)	Percentage (%)
Gestational age		
Early preterm birth ( $\leq 32$ weeks)	30	85.7%
Moderate and mild preterm ( $> 32$ and $< 37$ weeks)	04	11.4%
Term infants ( $\geq 37$ weeks)	01	2.8%
Birth weight (Gram)		
$\leq 1500$ g	27	77.1%
$> 1500$ g	08	22.8%
Length of stay (days)		
1 - 10 days	04	11.4%
11 - 20 days	06	17.1%
21- 30 days	09	25.7%
$> 30$ days	16	45.7%
Catheter dwell time (days)		
$< 4$ days	02	5.7%
4- 8 days	05	14.3%
$> 8$ days	28	80%

30 (85.7%) of total patients had insertion at peripheral site. Triple lumen catheter was most commonly used (65.7%) followed by single lumen catheter in 34.3% of patients

**Table 3: Association of CRLI with site of insertion**

Site	CRLI (%) (n=23)	CVCBSI (N=12) (%)	Total
Femoral venous catheter	1 (50%)	1 (50%)	2
Umbilical venous catheter	2 (66.7%)	1 (33.3%)	3
Peripherally inserted Central catheter	20 (66.7%)	10 (33.3%)	30
Type			
Single lumen	10	2	12
Triple lumen	13	10	23

Of total 35 catheter tips cultured, 23 (65.7%) were positive by Semiquantitative Maki's roll over technique, while 19 (54.3%) were positive by Quantitative endoluminal flush technique. Amongst signs and symptoms of local infection, Erythema (69.6%) was the most common finding, followed by oozing (39.1%), pain (26.1%) and induration (17.4%) respectively.

**Table 4: Distribution of all patients who developed central line related local infections**

Criteria	Positive	% Positivity	
CVC Tip Culture techniques (n=35)	Semiquantitative Maki's roll over	23	65.7%
	Quantitative endoluminal Flush	19	54.3%
Signs/Symptoms of local infection (n=23)	Erythema	16	69.6%
	Oozing	09	39.1%
	Pain	06	26.1%
	Induration	04	17.4%

Of 35 patients observed for infections attributable to catheter, 12 patients met criteria to be diagnosed as central line associated blood stream infections. None of them had growth in urine, ET secretions, induced sputum and pus. Fever was the common sign/symptom of systemic infection (66.7%) followed by chills (41.7%) and hypotension (16.7%).

**Table 5:** distribution of all patients with CRLBI

Criteria		Positive	% Positivity
Culture technique (n=35)	Blood culture	12	34.3%
	Fever	8	66.7%
Signs/Symptoms of systemic infection (n=12)	Chills	5	41.7%
	Hypotension	2	16.7%

Catheter related local infections were caused by Gram positive organisms in 12 (52.2%) cases while Gram negative organisms were isolated in 11 (47.8%) cases. Amongst Gram positive organisms, Coagulase negative Staphylococci were the most common isolate (30.4%) causing local infection, whereas, amongst Gram negative organisms *Klebsiella pneumoniae* was the most common isolate (21.7%).

**Table 6:** Distribution of organisms causing CRLI (n=23)

Gram positive Organisms	
CONS	7 (30.4%)
MSSA	2 (8.7%)
MRSA	2 (8.7%)
<i>Enterococcus</i> spp	1 (4.3%)
Gram negative Organisms	
<i>Klebsiella pneumoniae</i>	5 (21.7%)
<i>Acinetobacter</i> spp	2 (8.7%)
<i>Pseudomonas aeruginosa</i>	2 (8.7%)
<i>Escherichia coli</i>	1 (4.3%)
<i>Citrobacter</i> sp	1 (4.3%)

Central line associated blood stream infections were caused by Gram positive organisms in 7 (58.3%) cases while Gram negative organisms were isolated in 4 (33.3%) cases. One (8.3%) yeast (*Candida albicans*) was also isolated. Amongst Gram positive organisms, Coagulase negative Staphylococci were the most common isolates in 5 (41.6%) causing systemic infections, whereas, amongst Gram negative organisms *Klebsiella pneumoniae* and *Acinetobacter* spp. were the most common isolates in 2 (16.6%).

**Table 7:** Distribution of organisms causing CVCBSI

Organisms	No. of isolates (%)
Gram positive	7 (58.3%)
CONS	5 (41.6%)
MSSA	2 (16.6%)
Gram negative	4 (33.3%)
<i>Acinetobacter</i> spp	2 (16.6%)
<i>Klebsiella pneumoniae</i>	2 (16.6%)
Yeast	
<i>Candida albicans</i>	1 (8.33%)

Out of the 23 patients with local infection, three died. There was no significant association of local catheter infection with outcome of patients. Out of the 12 patients who developed systemic infections, 8 patients died showing highly significant correlation with the outcome with p value < 0.0001.

**Table 8:** Correlation of CRLI and CVCBSI with outcome

Type	Discharged	Died	P value	Significance
CRLI (n=23)	20	3	0.5361	Not significant
CVCBSI (n=12)	4	8	< 0.0001	Highly significant

## DISCUSSION

Neonates admitted to the Neonatal Intensive Care Unit (NICU) are often prematurely born and suffer from several life-threatening conditions. Supportive care measures such as the use of inotropic medication or total parenteral

nutrition are important and central venous catheter (CVC) insertion is often a necessary part of these. A CVC is also used when fluids or medication are to be administered intravenously for an extended period. In high-income-country NICUs, CLABSI rates declined dramatically

following wide spread implementation of central-line bundles.<sup>9</sup> A CLABSI bundle is a strategy for insertion and maintenance of central lines, which includes several evidence-based best practices implemented simultaneously.<sup>10,11</sup> Central-line care bundle elements include: hand hygiene, optimal catheter-site selection, maximal barrier precautions at insertion, chlorhexidine skin antisepsis, daily review of line necessity, sterile line access, use of closed needleless intravascular catheter systems and ensuring the line dressing stays clean and intact.<sup>10,11</sup> Reductions in NICU CLABSI rates have been achieved in developing countries.<sup>12</sup> Major risk factor for development these infections is the indwelling time of CVCs. Zingg *et al.*<sup>13</sup> presented that the median time to an infection for PICCs and umbilical catheters was 7 (5- 10 days) and 7 (5- 8 days) days, respectively. Hoang *et al.*,<sup>14</sup> reported a median time of 9 days for PICCs of the upper extremities, although the median time was longer (15 days) for PICCs of the lower extremities. The National Institute of Child Health and Human Development Neonatal Research Network showed that the risk of late-onset sepsis increased as the duration of CVC and parenteral nutrition increased, and infants who developed sepsis had higher mean indwelling times than infants without sepsis. The risk of late-onset sepsis increased significantly for catheters in place for 22 or more days.<sup>15</sup> Anticoagulants are used widely to prevent catheter thrombosis. Because thrombi and fibrin deposits on catheters might serve as a nidus for microbial colonization of CVC, the use of anticoagulants might have a role in the prevention of CRBSI. It is known that surface heparinization appears to have a great impact on bacterial colonization and can be a significant approach to the prevention of catheter-associated bacteremia or fungemia.<sup>16</sup> Newborns, especially preterm, are at increased risk of infection and are considered immunocompromised due to their immune system immaturity. Their immune response is characterized by a decrease in neutrophil-endothelial adhesion, low levels of complement factors, and immaturity regarding the different subpopulations of lymphocytes and mononuclear phagocytic system cells.<sup>17</sup> The incidence of neonatal infection is 3- to 10- fold higher in preterm infants than in full term normal birth weight infants. This may be explained by a higher frequency of intra-amniotic infection among mothers of infants with a short gestational age compared with full term infants. Moreover, maternal genital tract infection is considered to be an important cause of preterm labour and increased risk of infection of the fetus. In addition, preterm infants have a compromised immune system and they often require invasive procedures that provide a portal of entry.<sup>18</sup> Furthermore, preterm infants have a compromised skin barrier; their stratum corneum is 3 cell layers thick at 26 weeks of age compared to 16 layers in full term infants.

The thin keratin layer is easily damaged by handling, adhesives frequently applied to the skin and alcohol applications.<sup>19</sup> Gestational age was one of the factors associated with CVC-BSI in a US case-control study by Hruszkewycz V *et al.*<sup>20</sup> In present study, 27 (77.1%) neonates were less than 1500 gram birth weight whereas remaining 8 (22.8%) had birth weight more than 1500 gram. LBW infants are vulnerable to infections because of their immature immune systems, frequent contact with hospital personnel, and invasive procedures. Some authors reported that LBW is the most important factor for the occurrence of CLABSI/CRBSI. de Brito *et al.*<sup>21</sup> showed that neonates weighing less than 750 g revealed the highest CRBSI incidence rate (3.3/1,000 days CVC). In the National Healthcare Safety Network survey,<sup>22</sup> the rate of CRBSIs was 4.4 to 6.4 per 1,000 catheter days among neonates weighing less than 1,000 gram. LBW were factors associated with CVC-BSI in a US case-control study by Hruszkewycz V *et al.*<sup>20</sup>, Geldenhuys C *et al.* studied central-line-associated bloodstream infections in a resource-limited South African neonatal intensive care unit and observed that CLABSI cases occurred more commonly in babies with LBW less than 1500 gram.<sup>22</sup> In developed and developing countries, most nosocomial infections (NIs) in NICUs are related to a longer duration of hospitalization and medical treatments.<sup>23</sup> The hospitalization of infants in NICUs has been reported in the literature as being longer, and the susceptibility to infection has been greater than in other pediatric intensive care units.<sup>24,25</sup>

Longer duration of hospitalization is one of the factors leading to bloodstream infections in newborns.<sup>23</sup> Ertugrul S *et al.* studied risk factors for health care-associated bloodstream infections in a neonatal intensive care unit in Iran and observed that length of hospitalization was higher in the infected neonates.<sup>26</sup> Central vascular access through umbilical vessels in many cases still remains the first option. They can be very useful, especially in emergency situations (resuscitation) and for newborns of very low birth weight in the first days of life. However, the use of this catheter is frequently limited by the severe complications that can result, including thrombosis, vascular perforation, liver necrosis, cardiac perforation, necrotizing enterocolitis.<sup>27, 28</sup> In our study, triple lumen catheter was most commonly used (65.7%) followed by single lumen catheter in 34.3% of patients. In Khanna *et al.* study, the incidence of catheter-related infection was highest with triple lumen catheters when compared with double and single lumen catheters.<sup>29</sup> Daniela *et al.* observed that the likelihood of acquiring a bloodstream infection was approximately two and half-fold greater when a patient had used a multiple-lumen CVC compared to a single-lumen catheter.<sup>30</sup> The

knowledge of bacteriological profile and its antibiotic sensitivity patterns is of immense help in saving lives of neonates with septicemia.<sup>25</sup> In study by Thakur *et al.*, Gram-positive isolates were 60% and 40% were Gram-negative.<sup>31</sup> Similar findings were noted in present study. The bacteriological profile has changed worldwide from predominant Gram-negative to a predominant Gram-positive bacteria isolation.<sup>32,33</sup> Many recent studies have reported the emergence of some new emerging organisms such as CONS, Non-fermenters and *Candida* spp. as a cause of neonatal septicemia.<sup>34,35</sup> The high frequency of CONS in CRBSI is due to its ability to adhere to the exterior surface of the catheter and formation of biofilm and slime layer which protects them from phagocytosis and antibiotics. Furthermore, the presence of lipid emulsion in the infusate has been linked to CoNS bacteremia.<sup>32</sup> Central venous catheters are associated with increased morbidity and mortality in patients admitted to NICU. In the present study, the overall mortality observed was 31.4%. In a study by Thakur *et al.*, overall mortality was observed in 11.7%,<sup>31</sup> An early diagnosis of neonatal septicemia is important to initiate appropriate and prompt treatment. The correct and timely identification of infectious agents and their antibiotic sensitivity patterns are essential to guide the clinicians regarding both the empirical and definitive treatment.

## CONCLUSION

CRBSI are responsible for a large number of nosocomial bacteremia cases and constitute one of the main infections affecting premature and low weight neonates. At present Gram-positive microorganisms, in particular Coagulase negative Staphylococci, are major causative microorganisms in central venous catheter related bloodstream infections, although Gram-negative microorganisms and *Candida* species are also important. The training and education of the health team, approaching techniques in care, the maintenance and insertion of vascular catheters, as well as the rational use of antimicrobials and attention to protocols of catheters use, is of great importance to prevent CRBSI.

## REFERENCES

- Chien LY, Macnab Y, Aziz K, Andrews W, McMillan DD, Lee SK, et al. Variations in central venous catheter-related infection risks among Canadian neonatal intensive care units. *Pediatr Infect Dis J* (2002) 21(6):505-11.
- Auriti C, Maccallini A, Di LG, Di Ciommo V, Ronchetti MP, Orzalesi M. Risk factors for nosocomial infections in a neonatal intensive-care unit. *J Hosp Infect* (2003) 53(1):25-30.
- Fletcher SJ, Bodenhsn AR. Catheter-related sepsis: an overview-part 2. *Br J Intensive Care* 1999; 74-80.
- Urrea M, Pons M, Serra M, Latorre C, Palomeque A. Prospective incidence study of nosocomial infections in a pediatric intensive care unit. *Pediatr Infect Dis J* 2003; 22: 490-493.
- Horan T, Andrus M, Dudeck M. CDC/NHSN surveillance definition of Health care-associated infection and criteria for specific types of infection in the acute care setting. *Am J Infect Control* 2008;36(5):309-32.
- Decker MD, Edwards KM. Central venous catheter infections. *Pediatr Clin North Am* 1988; 35: 579-612.
- Collee JG, Fraser AG, Marmin BP, Simmons A. Mackie and McCartney practical medical microbiology. 14th edition. Churchill Livingstone Inc. 1996. ch7;pg 131-149
- Washington W Jr., Stephen A, Janda W, Koneman E, Procop G, Schreckenberger P, Woods G, Koneman's color atlas and textbook of diagnostic microbiology, ed 6, Washington, 2006, Lippincott, ch 2; 100-103
- Shepherd EG, Kelly TJ, Vinsel JA, et al. Significant reduction of central-line associated bloodstream infections in a network of diverse neonatal nurseries. *J Pediatr* 2015;167(1):41-46.e3. [17 SEP]
- Powers RJ, Wirtschafter DW. Decreasing central line associated bloodstream infection in neonatal intensive care. *Clin Perinatol* 2010;37(1):247-272.
- O'Grady NP, Alexander M, Burns LA, et al. Guidelines for the prevention of intravascular catheter-related infections. *Am J Infect Control* 2011;39 (4 Suppl 1): S1-S34. [17 SEP]
- Rosenthal VD, Dueñas L, Sobreyra-Oropeza M, et al. Findings of the International Nosocomial Infection Control Consortium (INICC), part III: Effectiveness of a multidimensional infection control approach to reduce central line-associated bloodstream infections in the neonatal intensive care units of 4 developing countries. *Infect Control Hosp Epidemiol* 2013;34(3):229-237.
- Zingg W, Posfay-Barbe KM, Pfister RE, Touveneau S, Pittet D. Individualized catheter surveillance among neonates: a prospective, 8-year, single-center experience. *Infect Control Hosp Epidemiol*. 2011;32:42-49.
- Hoang V, Sills J, Chandler M, Busalani E, Clifton-Koeppel R, Modanlou HD. Percutaneously inserted central catheter for total parenteral nutrition in neonates: complications rates related to upper versus lower extremity insertion. *Pediatrics*. 2008;121:e1152-e1159.
- Revelas A. Healthcare - associated infections: A public health problem. *Niger Med J* 2012;53(2):59-64.
- Cho HJ, Choi YH, Shin SS, Oh YJ, Hwang SC. Central venous catheter colonization and bloodstream infection: influence of catheter insertion site and duration. *Infect Chemother*. 2005;37:65-70.
- Marchant EA, Boyce GK, Sadarangani M, Lavoie PM. Neonatal sepsis due to coagulase-negative staphylococci. *Clin Dev Immunol*. 2013;2013:586076.
- Stoll BJ. Infections of the neonatal infant. In: Kliegman, Behrman, Jenson, Stanton, ed. 18th ed. Philadelphia: Saunders Elsevier; 2007:794-811.
- Kaufman D, Fairchild KD. Clinical microbiology of bacterial and fungal sepsis in very-low-birth-weight infants. *Clin Microbiol Rev*. 2004;17:638-80, table of contents.
- Hruszkewycz V, Holtrop PC, Batton DG, Morden RS, Gibson P, Band JD. Complications associated with central

- venous catheters inserted in critically III neonates. *Infect Control Hosp Epidemiol.* 1991;12:544-8. \
21. de Brito CS, de Brito DV, Abdallah VO, Gontijo Filho PP. Occurrence of bloodstream infection with different types of central vascular catheter in critically neonates. *J Infect.* 2010;60:128–132.
  22. Didier C, Streicher MP, Chognot D, et al. Late-onset neonatal infections: incidences and pathogens in the era of antenatal antibiotics. *Eur J Pediatr.* 2012;171:681–7.
  23. Yumani DF, van den Dungen FA, van Weissenbruch MM. Incidence and risk factors for catheter-associated bloodstream infections in neonatal intensive care. *Acta Paediatr* (2013) 102(7):e293–8.
  24. Blanchard AC, Fortin E, Rocher I, Moore DL, Frenette C, Tremblay C, et al. Central line-associated bloodstream infection in neonatal intensive care units. *Infect Control Hosp Epidemiol* (2013) 34(11):1167–73.
  25. Ting JY, Goh VS, Osioviich H. Reduction of central line-associated blood- stream infection rates in a neonatal intensive care unit after implementation of a multidisciplinary evidence-based quality improvement collaborative: a four-year surveillance. *Can J Infect Dis Med Microbiol* (2013) 24(4): 185–90.
  26. Mutlu M, Aslan Y, Kul S, Yilmaz G. Umbilical venous catheter complications in newborns: a 6-year single-center experience. *J Matern Fetal Neonatal Med* (2016) 29(17):2817–22.
  27. Sastre JBL, Cotallo GDC. Estudio prospectivo sobre el empleo de cateteres umbilicales en el recién nacido. Grupo de Hospitales Castrillo. *An Esp Pediatr.* 2000;53:470-478.<sup>11</sup><sub>SEP</sub>
  28. Macias AE, Munoz JM, Galvan A, Gonzalez JA, Medina H, Alpuche C, Cortes G, Ponce-de-Leon S. Nosocomial bacteremia in neonates related to poor standards of care. *The Pediatr Infect Dis J.* 2005;24:713-716.
  29. Khanna V, Mukhopadhyay C, KE Vandana, Verma M, Dabke P. Evaluation of central venous catheter associated blood stream infections: a microbiological observational study. *J Pathog.* 2013;2013:936864.
  30. Daniela BR, Guilherme H, Furtado. Risk factors for catheter-related blood stream infection: a prospective multicenter study in Brazilian intensive care units. *Braz J Infect Dis* 2011;15(4):328-331.
  31. Thakur S, Thakur K, Sood A, Chaudhary S. Bacteriological profile and antibiotic sensitivity pattern of neonatal septicaemia in a rural tertiary care hospital in North India. *Indian J Med Microbiol* 2016;34:67-71
  32. Kohli-Kochhar R, Omuse G, Revathi G. A ten-year review of neonatal bloodstream infections in a tertiary private hospital in Kenya. *J Infect Dev Ctries* 2011;5:799-803.
  33. Monjur F, Rizwan F, Asaduzzaman M, Nasrin N, Ghosh NK, Apu AS, et al. Antibiotic sensitivity pattern of causative organisms of neonatal septicemia in an urban hospital of Bangladesh. *Indian J Med Sci* 2010;64:265-71.
  34. Bhat YR, Lewis LE, Ke V. Bacterial isolates of early-onset neonatal sepsis and their antibiotic susceptibility pattern between 1998 and 2004: An audit from a center in India. *Ital J Pediatr* 2011;37:32.
  35. Sharma P, Kaur P, Aggarwal A. *Staphylococcus aureus* – The predominant pathogen in the neonatal ICU of a tertiary care hospital in Amritsar, India. *J Clin Diagn Res* 2013;7:66-9.

Source of Support: None Declared  
Conflict of Interest: None Declared