BRIEF REPORT

INCIDENCE AND RISK FACTORS OF CENTRAL LINE CATHETER-RELATED BLOODSTREAM INFECTIONS

Diego M. Cabrera[1,a], Fiorella K. Cuba[1,a], Roger Hernández[1,2,a], Yolanda Prevost-Ruiz[1,3,a]

[1] Facultad de Medicina Humana «Alberto Hurtado», Universidad Peruana Cayetano Heredia, Lima, Perú.
[2] Servicio de Infectología Pediátrica, Hospital Cayetano Heredia, Lima, Perú.
[3] Servicio de UCI Neonatal, Hospital Cayetano Heredia, Lima, Perú.
[a] Physician

RESUMEN

Central line catheter-related bloodstream infections (CLABSI) burdens great morbidity, mortality and unnecessary hospital expenses. Studies related to its incidence and epidemiological and clinical profile among neonates in Peru are scarce, not being clear it's actual impact. A prospective cohort study was conducted in a neonatal intensive care unit (ICU) of a public hospital in Lima, Peru between 2017-2018. 167 patients were included (52,7% male) with gestational age between 24-41 weeks, obtaining 1999 catheter-days and 16 cases of CLABSI. The incidence rate was 8/1000 catheter-days. Use of umbilical catheter (p=0,005) and multiple catheters (p<0,001) both showed a statistically significant correlation regarding the development of CLABSI. It's necessary to extend the study to other ICUs and stablish solid, efficient and long-lasting system of CLABSI surveillance that allows the evaluation of possible interventions to reduce the incidence of CLABSI.

Keywords: Catheter-Related Infections; Newborn; Risk Factors; Peru (source: MeSH NLM).

INTRODUCTION

Healthcare-associated infections (HAIs), or previously called hospital-acquired infections (HAIs), represent a range of pathologies that cause high morbidity and mortality rates. These events are most common in critical areas with vulnerable populations, such as a neonatal intensive care unit (NICU), where patients are prone to prolonged hospital stays and invasive procedures, such as catheter insertion (central and peripheral). The use of central catheters in the neonate corresponds to a common practice in medical management [1]. However, being an invasive device, catheters create an entry point for various microorganisms; furthermore, both its placement and maintenance have been associated with cases of superinfection [2].

In Peru, epidemiological reports describe important frequency measures of HAIs during the last decades. In 2013, it is described that 12.7% of the 9,812 HAIs occurred in neonatology services [3]. Similarly, in 2018, an incidence rate of central line-associated bloodstream infection (CLABSI) of 4.92 was reported, which is higher than other types of HAIs reported in that year [3].

The impact of CLABSI is important for both, patient prognosis and public health [4,5]. Warren *et al.* reported that the total hospital costs in neonates who have suffered from this pathology are almost three times those of unaffected neonates [4]. Nevertheless, it is recognized that preventive interventions can reduce the number of complications [6]. For this purpose, longitudinal studies are needed to explore the epidemiology of this disease. The aim of this study is to determine the incidence of CLABSI in the NICU of a public hospital in Lima, Peru, and to explore the risk factors associated with this pathology.

Cite as: Cabrera DM, Cuba FK, Hernández R, Prevost-Ruiz Y. Incidencia y factores de riesgo de infecciones del torrente sanguíneo asociadas a catéter central. Rev Peru Med Exp Salud Publica. 2021;38(1):95-100. doi: https://doi.org/10.17843/rpmesp.2021.381.5108.

Correspondence: Diego Cabrera Chávez; Av. Honorio Delgado 430, San Martín de Porres; diego.cabrera.c@upch.pe

Received: 16/01/2020
Approved: 10/11/2020
Online: 01/02/2021

THE STUDY

Study design and participants

We carried out a prospective cohort of patients admitted to the NICU of the Hospital Cayetano Heredia (HCH) between June 2017 and June 2018. HCH is a public hospital with a 10-bed NICU and responds to a significant demand of neonates annually. As this study was an open cohort, all neonates who met the eligibility criteria during the mentioned period were included, there was no formal sample size calculation, we worked with the population universe. All neonates admitted to the HCH NICU who carried a central catheter for at least 48 hours were included. A central catheter was considered to be one that ends up located in the heart or in a major vessel adjacent to the heart, regardless of the insertion site, whether it was an umbilical arterial catheter (UAC), an umbilical venous catheter (UVC) or a peripherally inserted central catheter (PICC). Patients transferred from other health institutions with these types of catheters at the time of admission were excluded.

Variables

The dependent variable was CLABSI, defined according to the criteria of the Centers for Disease Control and Prevention (CDC) as an infection in a patient carrying a central catheter for more than 2 calendar days before the event, where the day of insertion of the device is "day 1" and the catheter is implanted on the day of the event or the day before [7]. Follow-up started from central catheter placement (day 1) to the occurrence of the event (appearance of the first clinical signs of infection). The clinical picture compatible with infection was evaluated, in each shift, by the NICU medical team that follows an established protocol for suspected infection, which includes the evaluation of clinical signs and the corresponding laboratory tests (hemogram, PCR, cultures), as described by Haque [8]. Suspected infection was subsequently confirmed with a positive blood culture and catheter culture by the microbiology area of the HCH following standardized procedures [9]. Those who remained asymptomatic or had clinical signs suggestive of infection that were not confirmed by cultures were followed-up until catheter removal, death or discharge from the unit.

As independent variables, anthropometric data were collected, such as weight (in grams), gestational age (GA) (in weeks) and sex, following the definitions established by the World Health Organization (WHO) [10]. Central catheter-related data were collected, such as insertion site (UAC, UVC, PICC), use of total parenteral nutrition (TPN), days of use (catheter-days) and use of two or more catheters simultaneously. Overcrowding was recorded as a control variable, defined as the number of patients exceeding the allowed capacity in the NICU (>10 beds), where there is no minimum separation of two linear meters between two beds [11].

KEY MESSAGES

Motivation for the study: Catheter-associated infections generate a great burden for health systems and the patients who suffer them. In Peru, studies on their incidence and behavior in neonates are scarce and their current impact is not entirely clear.

Main findings: We found an incidence of infection of 8/1000 catheter-days, higher than previous national and international reports. Associated factors were umbilical catheter use as a protective factor and use of multiple catheters as a risk factor.

Implications: There is a need to establish efficient and long-lasting hospital-acquired infection monitoring programs that allow the approach and evaluation of preventive interventions.

Instruments and data collection

Two digitalized forms with a Microsoft Access© interface were used. Both forms were previously validated by the NICU service, taking into account risk factors previously reported in the literature [12,13]. The measurements were obtained by means of standardized procedures, using the same instrument for all participants; the data referring to the catheter were obtained from the patient's clinical history. The first form was used to collect information regarding anthropometric data, nutrition, and devices used in the patient, including data related to catheter placement and maintenance. The second form was used to collect information on patients with suspected infection and included clinical data, laboratory tests and cultures. If a patient with suspected infection did not have a catheter-associated infection, he/she returned to the cohort providing days of exposure.

Statistical analysis

Frequency measures, means, standard deviation, medians, and interquartile ranges were used to describe the independent variables. The association between risk factors

https://doi.org/10.17843/rpmesp.2021.381.5108

and CLABSI was analyzed using Student's t-test and Mann Whitney U-test for quantitative variables; chi-square and test of proportions were used for qualitative variables. Univariate regression with Poisson analysis was performed to explore the relative risk (RR) between risk factors previously reported in the literature (umbilical catheter use, catheter-days, weight, crowding, TPN, multiple catheter use) and CLABSI after normality analysis of quantitative variables. The incidence rate of CLABSI was calculated by dividing the number of device-associated infections by the sum of total catheter-days. We used the statistical package STATA 15.0 (StataCorp, Texas, USA). A value of $p<0.05$ was considered statistically significant.

Ethical considerations

The research was approved by the ethics committees of the Universidad Peruana Cayetano Heredia (155-08-19) and HCH. The identity of the participants was protected by assigning numerical codes in the database. Since we did not interact directly with the participants, the use of informed consent was not required.

FINDINGS

A total of 167 neonates were included, in which 322 central catheters were placed in 1,999 catheter-days; 47.3% neonates were female. The median GA was 32.3 (SD: 4) vs. 34.6 (SD: 3.5) weeks between the CLABSI and non- CLABSI group ($p<0.05$). Eighty-two percent were preterm (≤37 weeks) and the median weight at the time of catheter insertion was 1,990 grams (Table 1).

Sixteen cases of CLABSI were diagnosed (9.6% of the total cohort). Thus, the incidence rate was 8/1000 catheter-days. All cases of CLABSI were found in preterm infants and 56.3% of them had a birth weight of less than 1,500 grams. Fifty percent (8/16) were women. Gram-positive bacteria were isolated in 62.5% and gram-negative in 37.5% of the cases. *Staphylococcus aureus* was the most frequent bacterium (31.3%) (Table 2). Regarding catheter-related variables, 93.8% of participants with CLABSI carried multiple catheters at some time during their stay (50%, 3 catheters; 43.8%, 2 catheters) and the most frequent indication was TPN (81.3%). Regarding the catheter insertion site, 66.7% of the catheters associated with CLABSI were placed via the umbilical route and 33.3% via the peripheral route. The overcrowding control variable was present at some time during the hospital stay in 62.5% of the cases.

In the bivariate analysis, umbilical catheter use (RR: 0.25; 95% CI: 0.09-0.65; $p=0.005$) and multiple catheter use (RR: 4.98; 95% CI: 2.05-12.12; $p<0.001$) were shown to be statistically significant factors in the development of CLABSI. Female sex, increased catheter-days, presence of overcrowding and the use of TPN showed an increased risk, but not statistically significant (Table 3).

DISCUSSION

CLABSI is an adverse healthcare event whose magnitude nationwide is partially known, based on the epidemiological surveillance of the Ministerio de Salud (MINSA). However, at the hospital level, its exact incidence is unknown. This study proposes to fill a gap in knowledge by estimating the magnitude of CLABSI in a prospectively enrolled cohort over one year. The incidence rate of CLABSI in neonates admitted to the NICU of a Peruvian public hospital was 8/1000 catheter-days, an incidence higher than that described nationally and internationally [3,14].

Coinciding with several studies, the microorganisms found were *Staphylococcus aureus*, followed by coagulase-negative *Staphylococcus* [15]. Both are frequently found colonizing the skin, the main entry point for this condition [16]. Likewise, only 37.5% of the cases were caused by gram-negative bacteria. This is consistent with studies conducted by the National Healthcare Safety Network in the United States between 2016-2017 where low rates of infection by these bacteria were reported [7]. The low percentage of cases associated with gram-negative bacteria coincides with the more frequent choice of the head and upper limbs as the site of device insertion rather than the femoral insertion. This location is the most at risk due to its proximity to urinary and fecal flora [17].

Among the factors associated with CLABSI, gestational age less than 28 weeks and a weight less than 1,500 grams at the time of catheter insertion are identified as important risk factors [18]. In concordance with the reported cases of CLABSI, 100% had a gestational age of less than 37 weeks, although no statistically significant relationship was found regarding weight and the occurrence of CLABSI; despite the fact that both factors are frequently interrelated and represent severe conditions that require greater manipulation of the catheter, a fact that has been associated with bacteremia [13].

Table 1. Clinical characteristics of central line-associated bloodstream infections in the neonatal intensive care unit of a level III-1 public hospital.

Clinical characteristics	Total cohort (N=167)	CLABSI group (n=16)	No-CLABSI group (n=151)	p Value [d]
Clinical characteristics	**N (%)**	**n (%)**	**n (%)**	
Sex				
Male	88 (52.7)	8 (50.0)	80 (52.9)	0.872 [e]
Female	79 (47.3)	8 (50.0)	71 (47.1)	
Gestational age [a]	34,40 (3.6)	32.3 (4.0)	34.61 (3.5)	0.017 [f]
≤37 weeks	137 (82.1)	16 (100.0)	121 (80.1)	0.049
>37 weeks	30 (17.9)	0 (0.0%)	30 (19.9)	-
Weight (grams) [b]	1,990 (1,380 – 2,905)	1,415,5 (1,183.5 – 2,455)	2,078 (1,458 –2,990)	0.028 [g]
<1,000	10 (5.9)	2 (12.5)	8 (5.3)	0.716
1,000-1,499.9	40 (23.9)	7 (43.8)	33 (21.9)	0.228
1,500-2,499.9	55 (32.9)	3 (18.7)	52 (34.4)	0.576
>2,500	62 (37.3)	4 (25.0)	58 (38.4)	0.592
Catheter-days [a]	11.97 (7.6)	12,25 (5.6)	11.94 (7.8)	0.878 [f]
Catheter location [c]				
UAC	133 (79.6)	15 (93.8)	118 (78.1)	0.153
UVC	110 (65.9)	11 (37.5)	99 (65.6)	0.067
UL PICC	62 (37.1)	6 (37.5)	56 (37.1)	0.980
LL PICC	10 (5.9)	6 (37.5)	4 (2.6)	0.202
Head PICC	7 (4.2)	1 (6.3)	6 (3.9)	-

[a] Mean (standard deviation)
[b] Median (interquartile range).
[c] Participants used more than one type of catheter at the same time during recruitment; therefore, the total number of catheters used by each category is reported.
[d] Test of proportions
[e] Chi-square test
[f] Student's t test
[g] Mann Whitney U-test
CLABSI: central line-associated bloodstream infection; UAC: umbilical arterial catheter; UVC: umbilical venous catheter; PICC: peripherally inserted central catheter; UL: upper limbs; LL: lower limbs.

Regarding catheter-related variables, multiple use and umbilical insertion location were reported as predisposing factors for infection [15,18,19]. In the bivariate analysis, we found that the use of multiple catheters had a statistically significant relationship with the presence of CLABSI. However, contrary to the literature, umbilical insertion was a protective factor, possibly due to the short time of use compared to PICC.

Overcrowding is a measure that reflects the capacity of a hospital to adequately care for its patients [20]. We found that 62.5% of the group with CLABSI were in an overcrowded

Table 2. Microorganisms isolated in cases of central line-associated bloodstream infection in the neonatal intensive care unit of a level III-1 public hospital.

Microorganisms	n (%)
Gram-positive	10 (62.5)
Staphylococcus aureus	5 (31.3)
Staphylococcus epidermidis	4 (25)
Staphylococcus haemolyticus	1 (6.3)
Gram-negative	6 (37.5)
Pseudomona aeruginosa	2 (12.5)
Klebsiella spp.	2 (12.5)
Klebsiella pneumoniae	1 (6.3)
Stenotrophomonas spp.	1 (6.3)

Table 3. Bivariate analysis between independent variables and central line-associated bloodstream infection in the neonatal intensive care unit of a level III-1 public hospital.

Independent variables	Bivariate Analysis		p Value
	RR	95% CI	
Clinical characteristics			
Female gender	1.11	0.42-2.96	0.829
Use of umbilical catheter	0.25	0.09-0.65	0.005
Catheter-days	1.00	0.94-1.07	0.883
Weight (grams)	0.99	0.99-0.99	0.043
Overcrowding	2.61	0.95-7.19	0.063
TPN	2.25	0.64-7.87	0.207
Use of multiple catheters	4.98	2.05-12.12	<0.001

TPN: total parenteral nutrition; RR: relative risk; 95% CI: 95% confidence intervals.

https://doi.org/10.17843/rpmesp.2021.381.5108

condition at some time during their hospitalization. However, this was not statistically significant in the bivariate model. Previously reported causes are the lower availability of staff per patient and thus a potentially reduced implementation of infection prevention measures [20].

Limitations of our study include the absence of a sample size calculation and the use of an unadjusted bivariate analysis, which could have affected the analysis of the variables; and the single-center nature that affects extrapolation to other contexts. Although, there was difficulty in strictly complying with the microbiological criteria for the diagnosis of CLABSI due to the lack of equipment and personnel, we used the criteria established by the CDC and MINSA, mainly for epidemiological surveillance purposes.

In conclusion, the incidence of CLABSI was 8/1000 catheter-days, a figure higher than what is found in previous reports. This adverse event carries a high burden of morbidity and mortality for those who suffer it. Therefore, prospective multicenter studies with a larger population are proposed to allow the inference of other risk factors and the application of infection control strategies with subsequent measurement of the impact of these interventions on incidence. Finally, although the number of cases was limited, our findings suggest the establishment of an infection control program to reduce risk factors and decrease morbidity.

Author contributions: DMC and FKC contributed in the conception and design of the study, drafting of the protocol, collection, analysis and interpretation of data, review and approval of the final version of the manuscript. YPR contributed in the conception and design of the study, creation and design of the protocol, analysis and interpretation of data, drafting and critical revision of the manuscript, approval of the final version, technical and statistical advice. RH contributed to the analysis and interpretation of data, critical revision of the manuscript, approval of the final version, technical and statistical advice.

Funding: Self-funded by the authors.

Conflict of interest: None.

REFERENCES

1. Oliveira Gomes AV, Luca Nascimento MA. Central venous catheterization in Pediatric and Neonatal Intensive Care Units. Rev Esc Enferm USP. 2013;47(4):794-800. doi: 10.1590/S0080-623420130000400004.
2. Castro López F. Beneficios del catéter epicutáneo en el recién nacido. Rev Cubana Enfermer. 2004;20(2):1-1.
3. Quispe Z. Situación de las infecciones asociadas a la atención en salud, perú -2016. Dirección General de Epidemiología. Published 2016 (Accessed on December 14, 2019). Available at: http://www.dge.gob.pe/portal/docs/tools/teleconferencia/SE102017/02.pdf.
4. Warren DK, Quadir WW, Hollenbeak CS, Elward AM, Cox MJ, Fraser VJ. Attributable cost of catheter-associated bloodstream infections among intensive care patients in a nonteaching hospital. Crit Care Med. 2006;34(8):2084-2089. doi:10.1097/01.CCM.0000227648.15804.2D.
5. Estimating the Additional Hospital Inpatient Cost and Mortality Associated With Selected Hospital-Acquired Conditions | Agency for Health Research and Quality (Accessed on December 18, 2019). Available at: https://www.ahrq.gov/hai/pfp/haccost2017-results.html.
6. Bell T, O'Grady NP. Prevention of Central Line-Associated Bloodstream Infections. Infect Dis Clin North Am. 2017;31(3):551-559. doi:10.1016/j.idc.2017.05.007.
7. Haddadin Y, Regunath H. Central Line Associated Blood Stream Infections (CLABSI). In: StatPearls. StatPearls Publishing; 2019 (Accessed on December 14, 2019). Available at: http://www.ncbi.nlm.nih.gov/books/NBK430891/.
8. Haque KN. Neonatal Sepsis in the Very Low Birth Weight Preterm Infants: Part 2: Review of Definition, Diagnosis and Management. J Med Sci. 2010;3(1):11-27.
9. Hernandez L, Amaro C. Procedimiento Operacional Estándar Del Sistema de Gestión de Calidad Para Toma de Muestra Para Hemocultivo. Lima: Hospital Cayetano Heredia; 2016. Available at: http://www.hospitalcayetano.gob.pe/transparencia/images/stories/resoluciones/RD/rd2016/rd_767_2016.pdf.
10. Cutland CL, Lackritz EM, Mallett-Moore T, Bardají A, Chandrasekaran R, Lahariya C, *et al*. Low birth weight: Case definition & guidelines for data collection, analysis, and presentation of maternal immunization safety data. Vaccine. 2017;35(48Part A):6492-6500. doi: 10.1016/j.vaccine.2017.01.049.
11. Ministerio de Salud. Norma técnica de los servicios de cuidados intensivos de los hospitales del sector salud. Lima: MINSA; 2004. Available at: ftp://ftp2.minsa.gob.pe/destacados/archivos/46/Norma%20T%E9cnica%20Unidad%20Cuidados%20Intensivos.pdf.
12. García H, Romano-Carro B, Miranda-Novales G, González-Cabello HJ, Núñez-Enríquez JC. Risk Factors for Central Line-Associated Bloodstream Infection in Critically Ill Neonates. Indian J Pediatr. 2019;86(4):340-46. doi:10.1007/s12098-019-02896-6.
13. Mahieu LM, De Muynck AO, Ieven MM, De Dooy JJ, Goossens HJ, Van Reempts PJ. Risk factors for central vascular catheter-associated bloodstream infections among patients in a neonatal intensive care unit. J Hosp Infect. 2001;48(2):108-116. doi:10.1053/jhin.2001.0984.
14. Dudeck MA, Edwards JR, Allen-Bridson K, Gross C, Malpiedi PJ, Peterson KD, *et al*. National Healthcare Safety Network report, data summary for 2013, Device-associated Module. Am J Infect Control. 2015;43(3):206-221. doi: 10.1016/j.ajic.2014.11.014.
15. Dubbink-Verheij GH, Bekker V, Pelsma ICM, van Zwet EW, Smits-Wintjens VEHJ, Steggerda SJ, *et al*. Bloodstream Infection Incidence of Different Central Venous Catheters in Neonates: A Descriptive Cohort Study. Front Pediatr. 2017;5:142. doi:10.3389/fped.2017.00142.
16. Guía de Practica Clínica Prevención, diagnóstico y tratamiento de las infecciones relacionadas a lineas vasculares. México, D. F: Instituto Secretaría de Salud; 2012. (Accessed on December 14, 2019). Available at: http://www.cenetec.salud.gob.mx/descargas/gpc/CatalogoMaestro/IMSS_273_13_INFECCIONLINEASVASCULARES/273GER.pdf.
17. Hussain R, Cevallos ME, Darouiche RO, Trautner BW. Gram-negative intravascular catheter-related bacteremia in patients with spinal cord

injury. Arch Phys Med Rehabil. 2008;89(2):339-342. doi:10.1016/j.apmr.2007.08.151.

18. Yumani DFJ, van den Dungen FAM, van Weissenbruch MM. Incidence and risk factors for catheter-associated bloodstream infections in neonatal intensive care. Acta Paediatr. 2013;102(7):e293-298. doi:10.1111/apa.12256.
19. Concannon C, van Wijngaarden E, Stevens V, Dumyati G. The effect of multiple concurrent central venous catheters on central line-associated bloodstream infections. Infect Control Hosp Epidemiol. 2014;35(9):1140-1146. doi:10.1086/677634.
20. Kaier K, Mutters NT, Frank U. Bed occupancy rates and hospital-acquired infections--should beds be kept empty?. Clin Microbiol Infect. 2012;18(10):941-945. doi:10.1111/j.1469-0691.2012.03956.x.

https://doi.org/10.17843/rpmesp.2021.381.5108