

## Original Paper

# The Incidence Rate of Central Line-associated Blood Stream Infections Related to Peripherally Inserted Central Catheters and Its Related Factors in the Neonatal Intensive Care Units



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## ABSTRACT

**Introduction:** Preventing the incidence of central line-associated blood stream infections (CLABSI) related to peripherally inserted central catheters (PICCs) is a top priority in the neonatal intensive care units (NICUs), as it can reduce mortality, morbidity, and the length of hospitalization.

**Objective:** The current study aims to identify factors related to CLABSI associated with PICC in Iranian infants hospitalized in the NICUs.

**Materials and Methods:** This is a retrospective analytical study with a cross-sectional design. The medical records of 321 infants with PICC admitted to two NICUs of one maternal and neonatal hospital in Tehran, Iran, over 5 years (2018-2023) were reviewed, and their data were extracted using a researcher-made neonatal demographic/clinical checklist. Mann-Whitney U test and logistic regression analysis were used for data analysis.

**Results:** Among 321 infants with PICC, 168(52.3%) were male and 153(47.6%) were female. Their mean birth weight was 1219.23±447.68 g, and their mean weight on the day of PICC insertion was 1215.72±454.81 g. The mean catheter dwell time was 15.97±10.45 days. The total days of hospitalization was 40.9±24.7. The incidence rate of CLABSI was 7.60 in 1000 catheters/days. The total days of hospitalization ( $P=0.007$ ), duration of antibiotics therapy at the catheter dwell time ( $P=0.005$ ), infant age on the day of reaching full enteral feeding ( $P=0.002$ ), duration of mechanical ventilation at the catheter dwell time ( $P=0.007$ ), cause of catheter removal ( $P=0.001$ ), history of PICC insertion ( $P=0.003$ ), catheter dwell time ( $P=0.03$ ) and duration of antibiotic therapy ( $P=0.005$ ) were significantly different between infants with positive and negative blood culture tests for CLABSI. For every one day increase in the infant age on the day of reaching full enteral feeding, the risk of having a positive blood culture test for CLABSI increases by 0.06 units.

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⋮ **Conclusion:** Several factors can influence the PICC-related CLABSI rate in infants. The infant age on the day of reaching full enteral feeding can predict the increased risk of having a positive blood culture test for CLABSI.

## Highlights

- The incidence rate of peripherally inserted central catheters (PICCs) -related central line-associated blood stream infections (CLABSI) in Iranian infants is 7.60 in 1000 catheters/days.
- Several factors can influence the PICCs -related CLABSI rate in infants.
- The infant's age on the day of reaching full enteral feeding can predict the increased risk of central catheters -related CLABSI

## Plain Language Summary

The use of PICCs can reduce the excessive painful stimuli caused by repeated venepunctures in infants, ensuring timely intravenous nutrition and medication administration. However, the use of these catheters is associated with the risk of central line-associated bloodstream infections. The findings of the present study showed that, for every one day increase in the infant age on the day of reaching full enteral feeding, the risk of having a positive blood culture test for central line-associated stream infections increases by 0.06 units.

## Introduction

**T**he neonatal period, the first 28 days of life, is the most vulnerable time for an individual's survival [1]. Although the mortality rate in the neonatal period is nearly 30 times higher than in later stages of life [2], advancements in neonatology science have led to unprecedented improvements in neonatal survival [3]. With the increase in the survival of new-borns, the importance of vascular access in new-borns has also increased [4]. The use of peripheral vascular catheters is a common and invasive procedure in new-borns and is one of the most frequently performed painful procedures in neonatal care [5]. Routine vein access methods can have complications [6]. Repeated attempts to access peripheral veins can compromise the delicate skin of new-borns (which serves as the first line of defence against systemic infections) and puts the infant at risk of further injury [7].

The placement of a peripherally inserted central catheter (PICC) is a safe, convenient, and effective vascular access method due to its simplicity, high success rate, low complications, and the ability to administer hyperosmolar substances. It can reduce the excessive painful stimuli caused by repeated venepunctures in babies,

ensuring timely intravenous nutrition and medication administration. However, the use of PICCs is associated with the risk of central line-associated bloodstream infection (CLABSI). These complications may even more occur in new-borns with severe illnesses [8]. The rate of CLABSI in new-borns is in a range of 0.3-8.21 per 1000 catheter/days. The CLABSI is among the most significant causes of late-onset sepsis [9]. Therefore, preventing CLABSIs resulted from central venous catheterization is a top priority in neonatal care units, as it can reduce mortality, morbidity, and the length of hospital stays.

Several studies have attempted to identify the causes and factors associated with CLABSI in new-borns with PICCs, but these factors have not been definitively established yet [4, 10, 11]. Various variables such as weight, gender, gestational age [11], catheter dwell time, site of insertion, and the number of tries for catheter insertion have been introduced as potential factors associated with catheter-related infections [4]. The type of catheter, catheter tip position, gestational age, and birth weight are other risk factors, although there is no clear consensus on which factor truly affects the occurrence of this infection [12]. Trained nurses are responsible for PICC placement in clinical settings [13]. In the nursing interventions classification (NIC) system, PICC placement and care are considered a standardized nurs-

ing intervention [14]. This research aims to investigate the rate of CLABSI related to PICC in the neonatal intensive care units (NICUs) of hospitals in Tehran, Iran, and identify the associated factors.

## Materials and Methods

This is a retrospective analytical study with a cross-sectional design. The medical records of all infants with PICC admitted to two NICUs of one maternal and neonatal hospital in Tehran, Iran, over 5 years (2018-2023) were assessed, and the data of 321 cases that met the inclusion criteria were extracted. The inclusion criteria were having a PICC during hospitalization for more than 24 hours. The infants with catheters transferred to other hospitals for continued treatment (catheter removal in another hospital) were excluded.

For data collection, a demographic/clinical checklist was designed after identifying all possible factors associated with PICC-related infection from previous studies. The researcher-made checklist included three sections: a) Demographic/clinical information related to the infant (sex, birth weight, gestational age, cause of hospitalization, weight on the day of PICC insertion, post-natal age on the day of catheter insertion, weight on the day of PICC removal, age on the day of full enteral feeding, total days of hospitalization, days of mechanical ventilation at the catheter dwell time, days of antibiotic therapy days at the catheter dwell time); b) Information related to the catheter (catheter size, neonatal age at the catheterization time, number of catheterization attempts, site of insertion, location of catheter tip after insertion, dwell time, cause of catheter removal, and type of catheter-related complications), and c) Information related to CLABSI, including laboratory test results. The validity of the checklist was confirmed based on a content validity ratio of 0.87 and a content validity index of 0.88, according to the opinions of 10 nursing faculty members. The Mann-Whitney U test and the logistic regression analysis were used for data analysis in SPSS software, version 20.

## Results

Of 321 infants with PICC, 168(52.3%) were male and 153(47.6%) were female. Their mean birth weight was  $1219.23 \pm 447.68$  g, while their mean weight on the day of PICC insertion was  $1215.72 \pm 454.81$  g, and the mean weight on the day of PICC removal was  $1348.95 \pm 481.46$  g, which was not significantly different from the weight on the day of PICC insertion. These results indicate that the insertion of PICC was mostly done for infants with

weight  $<1500$  g, and the infants had weight  $<1500$  g until the time of PICC removal. The mean gestational age of the infants was  $29.2 \pm 2.7$  weeks, indicating that most of the infants were preterm. The mean post-natal age of the infants on the day of catheter insertion was  $6.79 \pm 11.38$ . It also showed that most infants had catheter insertion in the first week of life.

The mean catheter dwell time was  $15.97 \pm 10.45$  days, and the total days of hospitalization was  $40.9 \pm 24.7$ . The most common clinical diagnosis for infants was sepsis (49.53%). None of the infants had the clinical diagnosis of CLABSI. For 84.1% of the infants, a size 1 catheter had been inserted. Moreover, 62.3% of the infants had their PICC inserted at the first attempt. In 77.8% of cases, the catheter was placed in the upper extremities. Additionally, 85% of infants were under mechanical ventilation. The most common cause of catheter removal was “complications” (about 40%). In most cases, the catheter insertion was performed by a PICC team member (88.7%). Almost all infants (98.7%) were under antibiotic therapy at the time of catheter insertion. The majority of infants (25.86%) had an Apgar score of 9 at 1 minute, and 37% of infants had an Apgar score of 10 at 5 minutes. Other information is presented in Tables 1 and 2.

The rate of CLABSI caused by PICC was 7.60 per 1000 catheters/days. The Mann-Whitney U test results showed statistically significant differences between infants with positive blood culture test for CLABS and those with negative blood cultures in terms of total days of hospitalization ( $P=0.007$ ), antibiotics therapy at the catheter dwell time ( $P=0.005$ ), infant age on the day of reaching full enteral feeding ( $P=0.002$ ), mechanical ventilation at the catheter dwell time ( $P=0.007$ ), cause of catheter removal ( $P=0.001$ ), previous history of PICC insertion ( $P=0.003$ ), catheter dwell time ( $P=0.03$ ) and duration of antibiotic therapy ( $P=0.005$ ). In the rest of the variables, no significant differences were found between infants with positive and negative blood cultures (Table 3).

The variables that were significantly different between infants with positive and negative blood cultures were entered into the logistic regression model. Logistic regression with the likelihood ratio test was performed on all the covariates that had a significant effect. Only the variable of “infant age on the day of reaching full enteral feeding” remained in the model and was found to be significant. For every one day increase in the infant age on the day of reaching full enteral feeding, the risk of having a positive blood culture test for CLABSI increases by 0.06 units (Table 4).

**Table 1.** Qualitative demographic/clinical characteristics of infants hospitalized in the neonatal intensive care units (n=321)

Variables		No (%)
Sex	Male	168(52.34)
	Female	153(47.66)
Clinical diagnosis	Bronchopulmonary dysplasia	7(2.18)
	Intraventricular hemorrhage	8(2.5)
	Necrotising enterocolitis	3(4.05)
	Sepsis	159(49.53)
	Pneumothorax	16(4.98)
	Pneumonia	14(4.36)
	Seizure	6(1.87)
	Prematurity	98(30.53)
Size of catheter	1	270(84.11)
	2	51(15.89)
History of PICC insertion	Yes	22(6.85)
	No	299(93.15)
Number of PICC insertion attempts	1	200(62.31)
	2	80(24.92)
	3	3(4.05)
	>3	28(8.72)
Catheter insertion site	Lower limb vein	57(17.76)
	Upper limb vein	250(77.88)
	External jugular vein	6(1.87)
	Scalp veins	8(2.49)
Catheter tip placement	Central	301(93.77)
	Non-central	20(6.23)
The work shift when catheterization was done	Morning	118(36.76)
	Evening	78(24.3)
	Night	10(3.11)
	Unknown	115(35.83)
Frequency of catheter dressing change	1	105(32.71)
	2	72(22.43)
	3	23(7.17)
	>4	14(4.36)
	Not recorded	107(33.33)

Variables		No (%)
Type of infant nutrition	Breast milk	109(33.96)
	Formula milk	15(4.67)
	Breast milk + formula milk	193(60.12)
	Donated breast milk	4(1.25)
Clinical symptoms at the catheter dwell time	Apnoea	22(6.85)
	Bradycardia	5(1.56)
	Hyperthermia	4(1.25)
	Hypothermia	8(2.49)
	No symptom	282(87.85)
Another positive culture (other than blood)	Urine culture	8(61.54)
	Eye secretion culture	3(23.08)
	Ear secretion culture	1(7.69)
	Tracheal secretion culture	1(7.69)
	-	308(95.95)
Mechanical ventilation on the day of catheterization	Yes	273(85.05)
	No	48(14.95)
Cause of catheter removal	Accidental exit	4(1.25)
	No clinical need	160(49.84)
	Complications	127(39.56)
	Infants death	30(9.35)
Complications of catheterization	Obstruction	58(45.3)
	Phlebitis and oedema	16(12.5)
	Doubt of infection	52(40.6)
	Pericardial effusion	2(1.6)
Catheter inserter	Non-PICC team member	36(11.21)
	PICC team member	285(88.79)
Antibiotic therapy	Yes	317(98.75)
	No	4(1.25)
Intralipid administration	Yes	265(82.55)
	No	56(17.45)

PICCs: Peripherally inserted central catheters.

**Table 2.** Quantitative demographic/clinical characteristics of infants hospitalized in the neonatal intensive care units (n=321)

Variables	Mean±SD
Birth weight	1219.23±447.68
Weight on the day of PICC insertion	1215.72±454.81
Gestational age	29.2±2.7
Post-natal age on the day of catheter insertion	6.7±11.3
Weight on the day of PICC removal	1348.95±481.46
Infant age on the day of reaching full enteral feeding	25.2±14.6
Catheter dwell time	15.97±10.45
Total days of hospitalization	40.9±24.7
Days of mechanical ventilation at the catheter dwell time	10.9±10
Days of antibiotic therapy at the catheter dwell time	13.7±10.2

PICCs: Peripherally inserted central catheters.

## Discussion

Our research results showed that the incidence rate of CRBSIs was 7.6 in 1000 catheters/days. This finding is consistent with those of Dubbink-Verheij et al., who reported a CRBSI incidence rate of 5.3 in 1000 catheters/days in infants with central venous catheters [15]. In another study, the incidence rate of CRBSIs ranged from 4.4 to 6.4 in 1000 catheters/days in infants weighing less than 1000 g [16]. Hu et al. reported a CRBSI rate of 10.6 in 1000 catheters/days in 381 infants with PICCs [7]. Jansen et al., in a study conducted from 2012 to 2020, reported a CRBSI rate of 8.8-25.23 in 1000 catheters/days in preterm infants [17]. Njere et al. showed a CRBSI rate of 17 in 1,000 catheter/days [18], which is higher than the rate reported in our study. Khieosanuk et al. reported a CRBSI rate of 3.32 in 1000 catheters/days [19], which is lower than the CRBSI rate in our study. The different results reported in other studies clearly show the impact of care on the incidence of CRBSIs and, thus, the need to plan for better care to reduce infections. The statistics should be collected periodically because the proper planning for reducing CRBSIs relies on accurate data.

Different CLABSI-associated factors were investigated in the study. One was the total length of hospital stay, which was significantly associated with PICC-related CLABSI in the present study. Tavanaee Sani et al. demonstrated that CLBSI increased the length of hospital stay from 4.2 to 5.7 days and raised the mortality rate [20]. In Stoll et al.'s study, the infants with late-onset sepsis

had a longer length of hospital stay compared to infants without sepsis [21]. Nielsen's study also indicated that a longer NICU stay is associated with a higher incidence of CRBSIs. Their results suggest that the occurrence of CRBSIs contributes to the prolonged hospitalization of infants with PICCs [22]. Further studies focusing on this aspect may provide more insight into the exact relationship between these variables.

Another factor associated with PICC-related CLABSI in the present study was the catheter dwell time. Milstone et al.'s study demonstrated that a dwell time of more than 7 days was associated with an increased risk of CRBSIs [23]. This finding was also reported in other studies [7, 18, 21, 23]. Various studies have reported that in NICUs, PICC dwell time is an independent risk factor for CLABSI [24-26]. However, there are contradictory findings in a study that reported that catheter dwell time did not increase the incidence of CLABSI [27], possibly due to adequate nutritional support, reduced invasive procedures, and increased skin maturity in children. Some studies have indicated that regular catheter replacement does not reduce the risk of CLABSI [28, 29]. Different CLABSI rates during different periods following PICC insertion highlight the complexity of this relationship [30]. Therefore, the studies suggest that catheter dwell time is likely an important variable affecting the CRBSI rate, but other factors can influence it and may increase or decrease accordingly. Further research is needed to explore the complexities of this relationship.

**Table 3.** Mean levels of demographic/clinical variables in infants with positive and negative blood culture tests for CLABSI

Variables		Mean±SD	P*
Birth weight	Positive	1132.18±349.36	0.137
	Negative	1231.27±458.83	
Weight on the day of PICC insertion	Positive	1143.46±360.08	0.244
	Negative	1195.53±498.56	
Weight on the day of PICC removal	Positive	1362.31±481.28	0.93
	Negative	1313.62±520.51	
Gestational age	Positive	28.6±1.9	0.2
	Negative	29.3±2.8	
Postnatal age on the day of PICC insertion	Positive	9.03±14.01	0.478
	Negative	6.48±10.96	
Total days of hospitalization	Positive	54.38±36.71	0.007
	Negative	39.06±22.01	
Duration of antibiotic therapy at the catheter dwell time	Positive	16.9±9.3	0.005
	Negative	13.32±10.26	
Catheter dwell time	Positive	18.69±10.42	0.03
	Negative	15.59±10.42	
Infant age on the day of reaching full enteral feeding	Positive	34.35±22.53	0.002
	Negative	20.18±14.64	
Duration of mechanical ventilation at the catheter dwell time	Positive	16.17±11.77	0.007
	Negative	10.35±9.59	

PICCs: Peripherally inserted central catheters.

\*Mann-Whitney U test.

The variable of antibiotic therapy duration was also associated with PICC-related CLABSI in the present study. Jansen et al. found that, although there was no change in the reported rate of CLABSI related to PICCs over time, the use of antibiotics decreased [17]. The findings of Reynolds et al. [31] are against the results of the present study. Similarly, a study reported a 9.3% reduc-

tion in sepsis rates based on clinical symptoms in infants who received prophylactic antibiotics [32]. Bayoumi et al. found that impregnating the catheter with the antimicrobials before insertion had no significant effect on the reduction of CLABSI rate [33]. These results suggest that, not only the PICC-related CLABSI rate is likely associated with antibiotic therapy, but also prophylactic

**Table 4.** Regression coefficients for the factor of “infant age on the day of reaching full enteral feeding

Variable	β Standardized Coefficient	SE	Wald Test	df	P	OR	95% CI, Lower, Upper
Infant age on the day of reaching full enteral feeding	0.063	0.017	13.661	1	0.0001	1.065	1.03, 1.1

OR=Odds ratio.



antibiotic therapy may yield better results. In the present study, antibiotic therapy was recorded and assessed over time. Interventional studies may be needed to obtain more accurate results in this regard.

The duration of mechanical ventilation at the catheter dwell time was another factor significantly associated with PICC-related CLABSI in the present study. A study found that effective infection control interventions reduced PICC-related CLABSI and ventilator-associated pneumonia [34]. However, it is important to note that infants dependent on mechanical ventilation are likely to be in poor conditions and may stay in the hospital for several days, which can contribute to a longer PICC dwell time. Since both the length of hospitalization and the catheter dwell time were identified as significant factors related to CLABSI, they may have a synergistic effect on each other.

Our result showed that only the infant age on the day of reaching full enteral feeding was the significant predictor of PICC-related CLABSI in infants. In a study that examined the predictors of PICC-related CLABSI, the nurse-to-patient ratio in specialized care units was identified as the only predictive factor [35]. In Badheka et al.'s study, two factors of longer external catheter length outside the body and the catheter placement in the operating room were reported as predictive factors for the increased incidence of PICC-related CLABSI in children [36]. It seems necessary to conduct further studies on the predictors of PICC-related CLABSI in infants.

The retrospective design and the distortion and incompleteness of some items in the infants' files, such as the number of catheter dressings, were identified as limitations of the research. Overall, it can be concluded that the PICC-related CLABSI rate in infants can be influenced by multiple factors such as the duration of mechanical ventilation at the catheter dwell time, duration of antibiotic therapy, catheter dwell time, and total length of hospital stay. The infant age on the day of reaching full enteral feeding is the predictor of PICC-related CLABSI in infants. The findings can help in understanding the causes and factors related to PICC-related CLABSI in infants. More studies in Iran are recommended on the role of other variables, and longitudinal and systematic review studies should be conducted in this field.

## Ethical Considerations

### Compliance with ethical guidelines

The study was approved by the Ethics Committee of **Shahid Beheshti University of Medical Sciences**, Tehran, Iran (Code: IR.SBMU.PHARMACY.REC.1402.148).

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### Authors' contributions

Conceptualization and supervision: Hamide Jalali, Maryam Varzeshnejad, and Elahe Rastkar Mehrabani; Methodology: Azam Shirinabadi Farahani; Data collection: Hamide Jalali, and Zahra Roosta; Data analysis: Maliheh Nasiri; Literature review: Hamide Jalali, Elahe Rastkar Mehrabani; Writing the original draft: Maryam Varzeshnejad and Hamide Jalali; Final approval: All authors.

### Conflict of interest

The authors declared no conflict of interest.

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