Original Article

RISK FACTORS OF CENTRAL-LINE ASSOCIATED BLOODSTREAM INFECTIONS AMONG ADULT PATIENTS ON PARENTERAL NUTRITION

Pui Wun Fiona **Fong**[1], Sze Ling **Tan**[2]

1. Pharmacy Department, Hospital Queen Elizabeth, Kota Kinabalu, Sabah, Malaysia
2. Pharmacy Department, Hospital Queen Elizabeth II, Kota Kinabalu, Sabah, Malaysia

Submission Date:
12th February 2025

Acceptance Date:
21st May 2025

Publication Date:
30th May 2025

***Corresponding author:**
Pui Wun Fiona Fong
fionafong@moh.gov.my
Tel: +6088-517555

DOI:
https://doi.org/10.63719/imrj.2025.11.01.010

ABSTRACT

Central venous catheter is preferred for the administration of parenteral nutrition (PN) as it allows longer period of use and higher osmolarity cut-off. However, one of the common complications is central-line associated bloodstream infection, which increases mortality and healthcare burden. This study aimed to determine the prevalence and risk factors of central-line associated bloodstream infection among adult patients on parenteral nutrition. This was a retrospective study involving all adult patients at Hospital Queen Elizabeth, Sabah who received parenteral nutrition via central venous catheter from 1 April 2022 to 31 March 2023. Potential risk factors of central-line associated bloodstream infection were identified from medical records. The infection prevalence was calculated and associated risk factors were determined using multiple logistic regression. Of 112 patients, more than half were male (n=70, 62.5%) with mean age of 53.4±15.1. Majority of the patients were from surgical ward (n=61, 61.6%), followed by intensive care unit (n=25, 22.3%). Central-line associated bloodstream infection was present in 25 patients (22.3%). The median PN duration was nine days (interquartile range=5-19). Duration of parenteral nutrition was the only factor demonstrating statistically significant association with central-line associated bloodstream infection (adjusted odds ratio=1.08; 95% confidence interval=1.03-1.13; p=0.001). Approximately a quarter of patients in our study developed central-line associated bloodstream infection. Longer duration of parenteral nutrition indicates longer catheterisation which exposes patients to higher risk of infection, potentially via catheter manipulation or infusate contamination. Prospective studies should be considered in future to explore strategies in reducing the infection occurrence.

KEYWORDS: risk factor, central-line associated bloodstream infection, adult, parenteral nutrition

INTRODUCTION

Parenteral nutrition (PN) is the intravenous administration of macronutrients including protein, carbohydrates, and fats, as well as micronutrients such as minerals, electrolytes, vitamins, and other trace elements, bypassing gastrointestinal tract (GIT) (1). It is indicated for patients with impaired GIT function who cannot maintain optimal nutrition status via oral intake or tube feeding (1). Achieving adequate nutritional intake in a timely manner can help combat various metabolic and physiological complications, including downregulation of immunity, delayed wound healing, muscle wasting, prolonged hospitalisation and increased risk of mortality (2). Therefore, it is prudent to identify patients at risk of malnutrition using proper screening and assessment tool, with timely nutritional intervention either via enteral or parenteral nutrition according to patient's GIT function and tolerance.

When planning for PN, the choice of venous access is one of the most important considerations. Peripheral catheters have limited duration of use and reduced osmolarity cut-off, which may limit the composition in the PN admixture and lead to unnecessary underfeeding (3). To overcome these limitations, central venous catheter (CVC) is preferred for PN administration. CVC is a device inserted into a large central vein, namely internal jugular, subclavian or femoral vein, and advanced until it resides within the superior vena cava, at the atrio-caval junction, or in the upper part of the right atrium. These sites come with larger lumen diametre and greater flow rate, hence allowing the safe infusion of high osmolarity PN over a longer duration (4).

Nevertheless, PN administration via CVC is not without complication. One of the most common complications is central-line associated bloodstream infections (CLABSIs), which is defined as a primary bloodstream infection (BSI) in patient with a central line for more than 48 hours before the development of the BSI and is not bloodstream-related to an infection at another site.(5) In fact, CLABSI is one of the chief contributors of primary healthcare-associated BSI, which in turn increases hospital length of stay, mortality rates and subsequently healthcare burden(6,7).

Although PN has been identified as an independent risk factor of CLABSI (6), there has been limited literature looking into the possible factors pertaining to PN which may directly contribute to BSI. In Malaysia, while similar studies are scarce with results more than a decade ago, most of the relevant studies evaluating CLABSI among critically ill patients only(8,9). Therefore, this study aims to give an up-to-date overview on the CLABSI occurrence on patients receiving PN, and to explore the associated risk factors at local setting.

MATERIALS AND METHODS

Study Design and Data Collection

This is a retrospective study involving all adult patients aged 18 and above who received PN via CVC from 1 April 2022 to 31 March 2023 at Hospital Queen Elizabeth (HQE) in the state of Sabah, Malaysia. No sample size calculation was required since all patients fulfilling the inclusion criteria within the stipulated timeframe were included in the study. CLABSI was defined as a laboratory-confirmed positive blood culture in patients with central line inserted for at least 48 hours prior to symptom onset, as per the definition by the Centres for Disease Control and Prevention (6). The medical records of the patients who received PN via central-line during the aforementioned period were reviewed to collect information on multiple putative risk factors associated with CLABSI as shown by relevant literature. The information included age, gender, underlying medical conditions, body mass index (BMI), ward, duration of PN, CVC site (internal jugular, subclavian or femoral veins), baseline serum albumin level during PN initiation, and whether CLABSI developed after PN initiation. The occurrence

of CLABSI was cross-checked against blood investigation results on iLab, a commercial laboratory information system. Patients who received PN via peripheral line or those who were already developing CLABSI prior to PN initiation were excluded from the study. This study has been registered on the Malaysian National Medical Research Register (NMRR) with identification number NMRR ID-23-01470-E4N and has been granted ethical approval by the Medical Research and Ethics Committee (MREC).

Statistical Analysis

Descriptive analysis was employed to present the overall characteristics of subjects. Numerical data was presented in mean and standard deviation (SD) or median and interquartile range (IQR) depending on data normality. Categorical data was presented as frequency and percentage. Prevalence of CLABSI was calculated by confirmed cases of CLABSI divided by total number of subjects. As for the associated risk factors for CLABSI, simple logistic regression was first performed to select potential variables. Subsequently, variables which were biological plausible or with p-value < 0.25 were analysed with multiple logistic regression to adjust for the effects of one another. Assumptions were checked if there is significant variable found. Data analysis was performed using Statistical Package for Social Sciences (SPSS) software version 26.

RESULTS

A total of 112 patients were included in this study. More than half of the patients were male (n = 70, 62.5%) with a mean age and SD of 53.4 and 15.1. Mean BMI of patients is 23.08 kg/m2 with SD of 5.14. The median PN duration was nine days (IQR = 5-19). Majority of the patients were from surgical ward (n = 61, 61.6%), followed by intensive care unit (n = 25, 22.3%). Hypertension was the most common underlying condition, which appeared in 41 patients (36.6%). Internal jugular vein was the most commonly inserted CVC among the patients (n = 12, 10.7%). Mean baseline serum albumin level was 23 g/L (SD: 7). The characteristics of the subjects are tabulated in Table 1.

RESULTS

A total of 112 patients were included in this study. More than half of the patients were male (n = 70, 62.5%) with a mean age and SD of 53.4 and 15.1. Mean BMI of patients is 23.08 kg/m^2 with SD of 5.14. The median PN duration was nine days (IQR = 5-19). Majority of the patients were from surgical ward (n = 61, 61.6%), followed by intensive care unit (n = 25, 22.3%). Hypertension was the most common underlying condition, which appeared in 41 patients (36.6%). Internal jugular vein was the most commonly inserted CVC among the patients (n = 12, 10.7%). Mean baseline serum albumin level was 23 g/L (SD: 7). The characteristics of the subjects are tabulated in Table 1.

Table 1. Characteristics of patients involved in the study.

Characteristic	n (%)	Mean ± SD	Median (IQR)
Age (years)		53.4 ± 15.1	
Gender			
Male	70 (62.5)		
Female	42 (37.5)		
Body Mass Index (kg/m2)		23.08 ± 5.14	
Duration of PN (days)			9 (5-19)
Ward			
Surgical	69 (61.6)		
Intensive Care Unit	25 (22.3)		
Medical	9 (8.0)		
Haematology	5 (4.5)		
Gastroenterology	3 (2.7)		
Burn Unit	1 (0.9)		
Underlying Conditions			
Hypertension	41 (36.6)		
Diabetes	20 (17.9)		
Dyslipidaemia	19 (17.0)		
Malignancy	17 (15.2)		
Cardiac conditions	14 (12.5)		
History of bowel operation	19 (17.0)		
Underlying GI conditions	25 (22.3)		
Central Venous Catheter (CVC) site#			
Internal jugular vein	12 (10.7)		
Subclavian vein	1 (0.9)		
Femoral vein	3 (2.7)		
Peripherally inserted Central Catheter	2 (1.8)		
Baseline serum albumin (g/L)		23 ±7	
Presence of CLABSI	25 (22.3%)		

Total number for CVC site was fewer than 112 due to missing data.

CLABSI was present in 25 patients, equivalent to a prevalence of 22.3%. In univariable analysis using simple logistic regression, age, BMI, haematology ward, CVC site at femoral vein, duration of PN and baseline serum albumin level had p-values less than 0.25, among which the duration of PN demonstrated statistically significant association with p-value < 0.05 (Table 2). When these variables were analysed with multiple logistic regression, only duration of PN showed statistically significant association, whereby each additional day of PN via CVC increased the odds of CLABSI by 1.08 times (adjusted odds ratio = 1.08; 95% CI = 1.03-1.13; p = 0.001) (Table 2). The logistic model had an area under receiver operating characteristics (ROC) curve of 0.6929, which fell between the ideal range of between 0.5 and 1. Interestingly, intensive care unit setting was not found to increase the odds of CLABSI in this study.

Table 2. Risk factors associated with CLABSI among adult patients on PN, univariable and multivariable analysis.

Risk Factor	Crude Odds Ratio (95% CI)	p-value	Adjusted Odds Ratio (95% CI)	p-value
Age	**0.98 (0.95-1.01)**	**0.106**	0.98	0.17
Gender *(male as reference)*	1.36 (0.53-3.50)	0.520	NS	NS
Body Mass Index	**0.93 (0.84-1.03)**	**0.144**	0.93	0.20
			Ward	
Surgical	Reference	N/A	N/A	N/A
Intensive Care Unit (ICU)	0.77 (0.25-2.35)	0.640	NS	NS
Haematology	**4.59 (0.71-29.80)**	**0.111**	N/A*	N/A*
Gastroenterology	1	N/A	N/A	N/A
Medical	1	N/A	N/A	N/A
Burn Unit	1	N/A	N/A	N/A
ICU *(non-ICU wards as reference)*	0.89 (0.28-2.52)	0.752	NS	NS
Duration of PN (days)	**1.07 (1.03-1.12)**	**<0.001**	1.08 (1.03-1.13)	0.001
			Underlying Conditions	
Hypertension	0.62 (0.23-1.65)	0.336	NS	NS
Diabetes	1.23 (0.40-3.81)	0.722	NS	NS
Dyslipidaemia	0.93 (0.28-3.13)	0.911	NS	NS
Any form of cancer	0.72 (0.10-2.76)	0.637	NS	NS
Cardiac conditions	0.55 (0.11-2.66)	0.46	NS	NS
History of bowel operation	0.93 (0.28-3.13)	0.911	NS	NS

Underlying GI condition	1.16 (0.40-3.33)	0.785	NS	NS
Central Venous Catheter (CVC) site				
Internal jugular vein	Reference	N/A	N/A	N/A
Subclavian vein	1	N/A	N/A	N/A
Femoral vein	**6 (0.39-92.28)**	**0.200**	N/A*	N/A*
Peripherally inserted Central Catheter	3 (0.14-64.26)	0.482	NS	NS
Baseline serum albumin	**0.93 (0.86-1.00)**	**0.051**	0.92	0.053

NS: Not significant; N/A: Not available.

Only variables showing p<0.25 in simple logistic regression (results in bold) were included in the multiple logistic regression.

* Excluded due to multicollinearity.

DISCUSSION

The prevalence of CLABSI among adult patients on PN at our local setting was found to be 22.3%, which is similar to the published literature. According to the findings by Opilla (2008), 1.3-26.2% receiving PN via CVC developed catheter-related BSI (10), whereas a local study conducted among the critically ill patients in Malaysia also reported a similar rate of 24% (8). Translating to real-world practice, almost 1 in every 4 patients receiving PN experienced BSI. When looking at the associated factors, only duration of PN was significantly associated with the occurrence of CLABSI in our study. This finding is in line with the study outcomes by Bretón et al. (2013), with at least double the odds of BSI among PN patients when duration of PN extended beyond 14 days (11). Longer duration of PN requires prolonged catheterisation, and this factor was also found to increase the odds of CLABSI by 1.08 times in the study done by Yilmaz et al. (2007), alongside other factors such as Acute Physiology and Chronic Health Evaluation (APACHE) II score and poor patient hygiene (12).

Pathogens can gain access to CVC device via the following routes: hematogenous colonisation from another source in the body; contamination of infusate, including medications and PN; extraluminal sources, whereby pathogens move along the external surface of catheter from entry site at skin; and intraluminal sources, including hub contamination, manipulation by patients and/or healthcare staff as well as pathogens migrating along internal surface of catheter (13,14). Of these possible routes, catheter hub is the major source of infection (13). Organisms from the catheter hub migrate down the inner surface of the catheter and form biofilm, which is relatively difficult to eradicate (15). Organisms on this adherent biofilm will enter the circulation along with the fluid introduced into the catheter and cause BSI (15). Without prompt treatment, it can progress rapidly to sepsis, multi-organ failure and death (16).

Understanding the possible mechanisms of CVC being contaminated, it is evident that the duration of PN is closely linked to CLABSI risk. Firstly, the longer the CVC is in place for PN administration, the greater the chance for bacteria to colonise the catheter and insertion site over time, possibly due to frequent manipulation of the catheter device and the compromised skin integrity around the insertion site (8). These increase the likelihood of pathogens entering the bloodstream, causing CLABSI. Biofilm development on the catheter surface is promoted simultaneously, which can serve as a continuous source of infection whenever there is a flow in the catheter (13). Apart from that, patients receiving

long-term PN may have underlying health issues that further increase their susceptibility to infections, such as immunosuppression, malnutrition, or chronic illnesses (8).

As a consequence of CLABSI, PN might need to be withheld or switched to peripheral route of administration. In the latter case, this may necessitate adjustment and oftentimes reduced PN composition due to the lower osmolarity permissible for peripheral line (3). Both situations would compromise the nutritional provision to the already ill patients. Besides, the development of infection may also delay interventional procedures, such as imaging procedures or surgeries which have been planned beforehand. Without solving the underlying issues, PN often must be continued, which in turn prolongs hospital stay and causes further complications.

To mitigate the risk of CLABSI, duration of PN needs to be minimised. This can be done with the collaborative effort from the hospital's Nutrition Therapy Team (NTT), which usually comprises medical prescribers, pharmacists, dietitians and nurses. It is recommended for NTT to review PN patients together at regular intervals to evaluate the needs to continue PN based on patients' clinical condition. The multidisciplinary effort enables formulation of the most optimum nutritional care plan for the patients, which may facilitate recovery and weaning from PN. It is also prudent to expedite any impending procedures for patients, as weaning off PN may only be attempted after resolving the underlying issues which necessitate PN in the first place. However, it can be practically difficult due to the overwhelming patient loads with limited resources at public hospitals.

Apart from that, strict infection control protocols need to be enforced from time to time, including regular site assessments, proper line maintenance, and using dedicated PN lines whenever possible. Monitoring for signs of infection is also critical for early detection and treatment. Hand antisepsis with an appropriate antiseptic solution during dressing changes is prudent to prevent contamination (17).

One of the limitations of our study is that data collection was done retrospectively from medical records, hence with likelihood of missing and inaccurate data. There could potentially be other contributing factors which were not captured in the past medical records, hence failed to be incorporated into this study. A prospective study would be able to overcome these limitations with more accurate and comprehensive data collection. Nevertheless, this study has provided an updated overview on the current practice and serves as a fundamental for future larger-scale study.

CONCLUSION

Approximately a quarter of patients in our study developed CLABSI, and increased PN duration was shown to increase its odds. Identifying the exact associated factors linking PN to CLABSI enables more specific approaches to tackle the issue. Relevant policy changes can be implemented, especially on the strict PN initiation criteria for those truly indicated and the subsequent close monitoring by NTT. If appropriate, switching from PN to enteral feeding should be done as early as possible to avoid unnecessary continuation of PN and complications.

Acknowledgement: The authors would like to express their gratitude to Dr. Mohd Zaki Zaili, the head of Microbiology Unit at Hospital Queen Elizabeth, for his expert input on the laboratory techniques used in diagnosing CLABSI.

Conflicts of Interest: The authors have no conflict of interest to declare.

Data Availability: Data for this study is not available for public as it was obtained from hospital medical records and online laboratory information system which are password protected.

Funding: The authors received no specific funding for this work.

CITATION

Fong PFF, Tan SL. Risk Factors of central-line associated bloodstream infections among adult patients on parenteral nutrition. International Medical Research Journal. 2025 May 1;11(1):112–20. https://doi.org/10.63719/imrj.2025.11.01.010

REFERENCES

1. British Association for Parenteral and Enteral Nutrition (BAPEN). Parenteral Nutrition [Internet]. [place unknown]: BAPEN; [updated 2023 Nov; cited 2025 May 9]. Available from: https://www.bapen.org.uk/education/nutrition-support/parenteral-nutrition/
2. Shao T, Verma HK, Pande B, Costanzo V, Ye W, Cai Y, et al. Physical activity and nutritional influence on immune function: An important strategy to improve immunity and health status. Frontiers in Physiology. 2021;12.
3. Mirtallo JM. Parenteral Nutrition. In: Feldman M, Friedman LS, Brandt LJ, editors. *Sleisenger and Fordtran's Gastrointestinal and Liver Disease: Pathophysiology, Diagnosis, Management*. 9th ed. Philadelphia: Saunders; 2010. p. 103–116.
4. Pittiruti M, Hamilton H, Biffi R, MacFie J, Pertkiewicz M. ESPEN guidelines on parenteral nutrition: central venous catheters (access, care, diagnosis and therapy of complications). Clinical nutrition. 2009 Aug 1;28(4):365-77.
5. Centres for Disease Control and Prevention. Bloodstream infection event (central line-associated bloodstream infection and non-central line-associated bloodstream infection). Device-associated Module BSI. 2017 Jun:1-38.
6. Fonseca G, Burgermaster M, Larson E, Seres DS. The relationship between parenteral nutrition and central line–associated bloodstream infections: 2009–2014. Journal of Parenteral and Enteral Nutrition. 2018 Jan;42(1):171-5.
7. Yazan H, Pavan A, Hariharan R. Central Line Associated Blood Stream Infections. Treasure Island, Florida: StatPearls Publishing; 2023.
8. Chan L, Ngeow YF, Parasakthi N. Bacterial infection of Central Venous Catheter in Short-Term Total Parenteral Nutrition. Medical Journal of Malaysia. 1998Mar;53(1):10–5.
9. Tan CC, Zanariah Y, Lim KI, Balan S. Central Venous Catheter-Related Blood Stream Infections: Incidence and an Analysis of Risk Factors. Medical Journal of Malaysia. 2007Dec;62(5):370–4.
10. Opilla M. Epidemiology of bloodstream infection associated with parenteral nutrition. American Journal of Infection Control. 2008;36(10).
11. Breton M, Martinez A, Navarro A, García B, Orna J. Risk Factors for Catheter-related Bloodstream Infection in Non-critical Patients with Total Parenteral Nutrition. Nutricion Hospitalaria. 2013:28(3):878-883.
12. Yilmaz G, Koksal I, Aydin K, Caylan R, Sucu N, Aksoy F. Risk factors of catheter-related bloodstream infections in parenteral nutrition catheterization. Journal of Parenteral and Enteral Nutrition. 2007;31(4):284–7.
13. Lal S. British Intestinal Failure Alliance (BIFA): Recommendation Management of Catheter Related Blood Stream Infections (CRBSIs). 2019 (2025 April 30). Available from: https://www.bapen.org.uk/pdfs/bifa/recommendations-on-management-of-crbsi.pdf

14. Ullman AJ. Routine care and maintenance of intravenous devices. UpToDate. 2022 (2025 Apr 30). Available from: https://www.uptodate.com/contents/routine-care-and-maintenance-of-intravenous-devices
15. Pagani J-L, Eggimann P. Management of catheter-related infection. Medscape. 2008 (2025 Apr 30). Available from: https://www.medscape.com/viewarticle/571265
16. Ostwald L. Central line bloodstream infections: CLABSI or CRBSI? Alliance for Vascular Access Teaching and Research. 2021 (2025 Apr 30). Available from: https://www.avatargroup.org.au/blog/central-line-bloodstream-infections--clabsi-or-crbsi-
17. Pironi L, Boeykens K, Bozzetti F, Joly F, Klek S, Lal S, et al. ESPEN guideline on home parenteral nutrition. Clin Nutr. 2020 Jun;39(6):1645–66.