Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Original article

Care of patients on home parenteral nutrition during the first year of the COVID-19 pandemic: Management of central line-associated bloodstream infections

Adriana Crivelli a, *, Marcela Fabeiro b, Marcelo Puga c, Natalia Dieguez c, Luciana Giunta c, Fabricio Pochettino c, Martín Balacco c, Gisela Merlo c, Verónica Garrido b, Humberto Fain c, Martín Buncu c, Andrés Martinuzzi c, M. Fernanda Cascarón c, Natalia Delgado c, Gabriela Capurro d, Víctor Bernardis e, Carolina Ghiglieri f, Amal Hassam c, Oscar Soria c, Diego Serra g, Lucas Morando g, Agustín Flores c, Horacio F. Gonzalez c, Adriana Fernandez b, RIANA (Red Interdisciplinaria de Atención Nutricional Ambulatoria, Argentina) 1

a Unidad de Soporte Nutricional y Enfermedades Malabsortivas, Hospital Interzonal General de Agudos “Gral. José de San Martín”, La Plata, Argentina
b Servicio de Nutrición y Dietética Del Hospital de Niños de La Plata, Argentina
c Nutri Home S.A, Argentina
d Servicio de Cuidados Intensivos Hospital Interzonal “Oscar Allende” de Mar Del Plata, Argentina
1 All the authors are members of the RIANA network (interdisciplinary network of outpatient nutritional care).

SUMMARY

Background and aim: The aim of this study was to analyze central line-associated bloodstream infections (CLABSI) in home parenteral nutrition (HPN) patients assisted by an interdisciplinary team during the first year of the COVID-19 pandemic in Argentina.

Methods: Longitudinal, retrospective and analytical study of patients on HPN for >90 days during 2020. Data collection included age (adults >18 years, pediatric <18 years), gender, diagnosis, type of catheter, number of lumens, venous access, days on HPN, infusion modality and number of CLABSI-associated events. In COVID-19 cases, number of patients, disease progression, mortality rate and microorganisms involved were analyzed.

Results: A total of 380 patients were included, 120 (31.6%) pediatric and 260 (68.4%) adult patients. Median age was 44.50 years (10; 62.25). Twelve patients (3.15% of the total) had COVID-19; of these, two pediatric and seven adult patients had no complications, and three adults died of COVID-19 pneumonia. The diagnoses observed were benign chronic intestinal failure (CIF, n = 311), grouped into short bowel (n = 214, 56.3%), intestinal dysmotility (n = 56, 14.7%), intestinal fistula (n = 20, 5.3%), and extensive small bowel mucosal disease (n = 21, 5.5%); malignant tumors (n = 52, 13.7%); other (n = 17, 4.4%). Total catheter days were 103,702. Median days of PN duration per patient were 366 (176.2, 366). The types of catheters used were tunneled (317 patients, 83.4%); peripherally inserted central (PICC) line (55 patients, 14.5%) and ports (8 patients; 2.1%). A total of 111 CLABSI was registered, with a prevalence of 1.09/1000 catheter days (adult, 0.86/1000 days; pediatric, 1.51/1000 days). The microorganisms identified in infectious events were Gram + bacteria (38, 34.5%); Gram-bacteria (36, 32%); mycotic (10, 9%); polymicrobial (4, 3.6%); negative culture and signs/symptoms of CLABSI (23, 20.3%). The odds ratio between pediatric and adult patients was 2.29 (1.35, 3.90).

Conclusion: The rate of CLABSI during the COVID-19 pandemic was within the ranges reported by international scientific societies. The risk of CLABSI was higher in pediatric patients, and mortality rate in COVID-19 infected patients was higher than in the general population.

© 2022 European Society for Clinical Nutrition and Metabolism. Published by Elsevier Ltd. All rights reserved.
1. Introduction

The care of patients on home parenteral nutrition (HPN) involves an interdisciplinary approach, which includes the participation of health care team members and the commitment of both patient and family.

After the outbreak of coronavirus disease 19 (COVID-19) in December 2019, the virus spread globally and was confirmed in Argentina in March 2020. On 19 March 2020, a mandatory nationwide lockdown was established in Argentina to curb the spread of COVID-19, locally known as Mandatory Preventive Social Isolation and Mandatory Preventive Social Distancing measures (ASPO and DISPO, respectively, by their Spanish acronyms). In December 2020, the official COVID-19 statistics published by the Ministry of Health of Argentina reported 1,531,374 cases, 44,672 deaths, 54.4% intensive care unit bed occupancy and 2.7% mortality rate of the total cases. By that date, 64,614 healthcare workers had been reported to have been infected with COVID-19 (4.2% of the total affected population) [1].

During the first year of the COVID-19 pandemic, telemedicine controls were implemented worldwide [2]. But the fear and distress inflicted by COVID-19 and the associated lockdown caused a growing feeling of distrust and insecurity among people, who were reluctant to let a stranger into their homes, thus affecting the quality of patient care delivery. In this context, the main international scientific societies, namely, the European Society for Clinical Nutrition and Metabolism (ESPEN) [3] and the American Society for Parenteral Enteral Nutrition (ASPEN) [4], published guidelines for the care of patients receiving home parenteral nutrition (HPN). Recommendations for HPN management included both children and adults [5].

Central line-associated bloodstream infection (CLABSI) is one of the main complications during HPN [6]. It greatly affects the patient quality of life because the costs of healthcare increase due to hospitalization, and may even lead to death. Considering these risks, rigorous and aseptic guidelines should be followed [7,8]. Compliance with these guidelines could help us assess the suitability of the care delivered by healthcare workers [9]. Accordingly, CLABSI development becomes one of the main indicators of the quality of HPN patient care [10,11]. However, the use of different criteria to define CLABSI, from clinical to strictly microbiological aspects, has resulted in the report of varied CLABSI rates [12].

In this work, we analyzed CLABSI in HPN patients cared by an interdisciplinary health team during the first year of the COVID-19 pandemic.

2. Methods

This longitudinal, retrospective and analytical study reviewed a database from a private health service company providing care to HPN patients during 90 days or more of the first year of the COVID-19 pandemic (January to December 2020). All protocols for HPN patient care were maintained, and monitoring was performed by telemedicine follow-up visits. Patient identifiable information was anonymized. The data collected included age (adult > 18 years, pediatric < 18 years), sex and diagnosis of benign chronic intestinal failure (CIF, including short bowel, intestinal dysmotility, intestinal fistula and extensive short bowel mucosal disease), malignant tumors and other. Additionally, we gathered information about type of catheter used (tunneled, port and peripherally inserted central catheter [PICC] line), number of catheter lumens, type of venous access, days on HPN, type of PN infusion (continuous, cyclic, nocturnal), and CLABSI-related infectious events. In the case of COVID-19 infection, number of patients, disease progression and mortality rate were analyzed.

Inclusion criteria for CLABSI were clinical symptoms (fever, shivering/chills, nonspecific feeling of being unwell in relation to infusion through the central venous catheter (CVC), and/or elevation of biochemical blood tests indicating infection (white blood cell count and/or C-reactive protein), and/or microbiological results (positive blood culture from the CVC and/or from a peripheral vein) [12]. According to the type of microorganism identified, CLABSI was classified as Gram-positive, Gram-negative, mycotic, polymicrobial and events with CLABSI-related clinical manifestations but negative culture. The number of infections per 1000 catheter-days was also estimated.

2.1. Statistical analysis

Data were analyzed using the R software, version 4.0.3. Qualitative data results are presented as frequencies and percentages. Age and catheter-days are informed as medians (Q1; Q3 interquartile range). Chi-square test or Fisher exact test were used to study the association between qualitative variables. The odd ratio (OR) with 95% confidence interval (CI) was adjusted by logistic regression. A p-value < 0.05 was considered statistically significant.

3. Results

A total of 380 HPN patients from the database complied with the inclusion criteria. Of these, 251 (66%) were on HPN before the study period (January—December 2020). The number of days on HPN per patient was 366,124, with a mean duration of 1538 ± 2181 days.

The median age of HPN patients was 44.50 years (10; 62.25); 120 patients (31.6%) were <18 years and 260 (68.4%) > 18 years. From the total number of cases, 52.4% were female. Table 1 shows the main characteristics of the patients.

Benign CIF was identified in 311 patients, who were grouped as follows: short bowel, n = 214 (56.3%); intestinal dysmotility, n = 56 (14.7%); intestinal fistula, n = 20 (5.3%); extensive short bowel mucosal disease, n = 21 (5.5%). The other diagnoses identified were malignant tumor (n = 52, 13.7%) and other (n = 17, 4.4%).

Twelve HPN patients (3.15%) were infected with COVID-19: two pediatric and seven adult patients did not have any complication, but three adults died as a result of COVID-19-associated pneumonia.

The total number of catheter days was 103,702, with a median PN duration of 366 days per patient (176.2; 366) during the study period. The types of catheters used were port (n = 8, 2.1%), tunneled (n = 317, 83.4%) and PICC line (n = 55, 14.53%). Venous access sites were as follows: 174 right subclavian vein (45.8%); 119 left subclavian vein (31.3%); 20 right axillary vein (5.3%); 23 right jugular vein (6.1%); 18 left jugular vein (4.7%); 16 left axillary vein (4.2%); 8 unconventional sites (2.1%); and 2 right femoral vein (0.5%).

The number of patients with single- and double-lumen catheters was 262 (68.9%) and 118 (31.1%), respectively. Concerning the type of infusion, 342 patients (90%) received nocturnal cyclic PN.

The number of infectious events registered was 111: one infectious event (17.1%) in 65 patients, two (2.9%) in 11 patients and three (2.1%) in 8 patients. This resulted in a prevalence of 1.05/1000 catheter-days during 2020 (adults, 0.86/1000; children 1.51/1000). From the total number of patients, 296 (77.9%) did not present any infectious event.

The microorganisms identified in infectious events were Gram + bacteria: 38 (34.5%), Gram-bacteria: 36 (32%), fungi: 10 (9%), polymicrobial communities: 4 (3.6%); negative culture: 23 (20.3%).
The OR between indicated, pediatric and adult patients receiving HPN was 2.29 (1.35; 3.90), suggesting that patients <18 years had a two-fold greater chance of developing at least one infectious event. Differences in the prevalence of infectious events between both groups were significant (Table 2). The analysis of patients from 2 up to 7 years of age by groups showed significant differences compared with patients >18 years: 2-year-olds, p < 0.002; 3 to 4-year-olds, p < 0.001; 5-year-olds, p < 0.004; 6-year-olds, p < 0.0001; 7-year-olds, p < 0.002). The number of children in the group >7 years was not enough to make a comparison.

The number of infectious events in HPN patients with benign CIF was higher than that recorded in patients with malignant tumors, but differences were not significant (p = 0.069; Table 3). Similarly, differences between HPN patients with benign CIF due to dysmotility and other causes were not significant (Table 4).

The association between number of CLABSI and number of catheter lumens was not significant. The low number of ports and PICC lines used did not allow to determine the risk of CLABSI in these groups of patients.

### Table 1
Characteristics of the patients on home parenteral nutrition for ≥90 days during 2020.

| Overall (n = 380) | Patients (%) |
|------------------|--------------|
| **Sex**          |              |
| Female           | 199 (52.4)   |
| Male             | 181 (47.6)   |
| **Age (median)** |              |
| > 18 years (adult) | 44.50 (10, 62.25) |
| < 18 years (pediatric) | 120 (31.6) |
| **Diagnosis**    |              |
| Malignant tumor  | 52 (13.7)    |
| Benign chronic intestinal failure | 214 (56.3) |
| Short bowel      | 56 (14.7)    |
| Intestinal dysmotility | 20 (5.3)    |
| Intestinal fistula | 21 (5.5)     |
| Extensive small bowel mucosal disease | 17 (4.4) |
| **Days on catheter (median)** | 366 (76.25, 366) |
| **Type of catheter** |              |
| Tunneled         | 317 (83.4)   |
| Peripherally inserted central catheter (PICC) line | 55 (14.5) |
| Port             | 8 (2.1)      |
| **Number of catheter lumens** |              |
| 1                | 262 (68.9)   |
| 2                | 118 (31.1)   |

### Table 2
Prevalence of infectious events in patients <18 and >18 years of age on home parenteral nutrition.

| Age              | Infectious events (1 or more) |
|------------------|------------------------------|
|                  | No (%)                       |
| <18 years        | 81 (67.5%)                   |
| >18 years        | 215 (82.7%)                  |
|                  | Yes (%)                      |
| <18 years        | 39 (32.5%) *                 |
| >18 years        | 45 (17.3%) *                 |

*p = 0.001.

### Table 3
Infectious events in patients on home parenteral nutrition according to diagnosis.

| Diagnosis                      | Infectious event (1 or more) |
|--------------------------------|------------------------------|
| Malignant tumor                | 46 (88.5%)                   |
| Benign chronic intestinal failure | 246 (76.6%)                |
|                                  | No (%)                       |
| Malignant tumor                | 6 (11.5%)                    |
| Benign chronic intestinal failure | 75 (23.4%)                |

*p = 0.069.

### 4. Discussion

The care of patients on HPN of this study during the COVID-19 pandemic complied with the guidelines issued by international scientific societies [3–5]. Our results showed that 3.15% of patients on HPN were infected with COVID-19 during the study period in Argentina; three of them were adults and died.

The use of different criteria to define CLABSI has resulted in the report of varied rates [15]. For instance, the Centers for Disease Control and Prevention (CDC) and ESPEN use microbiological criteria to define CLABSI [16,17]. On the other hand, based on the presence of clinical manifestations of infections, Tribler et al. [12] reported a CLABSI incidence of 1.95/1000 catheter-days; they also showed that only 47% of cases complied with the microbiological CDC/ESPEN criteria, and 53% were classified as probable infections. Accordingly, CLABSI incidence following the CDC/ESPEN criteria was 0.92/1000 days [12]. In the present study, using clinical and/or microbiological criteria, CLABSI rate was 1.09/1000 catheter-days, and 77.8% of HPN patients did not present any infectious event during the study period. The high rate of negative cultures and clinical manifestations of CLABSI currently found should be considered as a limitation to our study. In 2019, before the COVID-19 pandemic, the global CLABSI rate was similar to that observed during the pandemic (1/1000 catheter-days; 0.77/1000 and 1.4/1000 in adult and pediatric patients, respectively) (Nutrihome Quality Report, in accordance with ISO 9001 2015 Quality Management System).

A systematic epidemiological review of 39 studies on CLABSI in adult patients receiving HPN published in 2013 revealed that CLABSI rate ranged between 0.38 and 4.58 episodes/1000 catheter-days (median 1.31) [18]. The authors highlighted the variability in the definitions of CLABSI and reported that Gram + bacteria of human skin flora were responsible for more than half of infections [18]. In the present study, Gram + bacteria were the most frequently found, followed by Gram-ones.

A recent analysis of the ASPEN Sustain registry informed an incidence of 0.87 CLABSI episodes per 1000 PN days, reporting that such incidence was higher in children than adults (1.17/1000 vs 0.35/1000) [6]. In another study of 35 children on HPN, Mutalib et al. reported a 1.3 incidence of CLABSI per 1000 PN days, no infection in 16 children, and Staphylococcus as the microorganism most frequently found [19]. Another work found that CLABSI rate in adults and children was 0.35/1000 and 0.80/1000 PN days, respectively (p < 0.001) [20]. Our findings showed that CLABSI rate in patients <18 years was 1.51/1000 catheter-days (OR, 2.29).

Despite the use of tunneled and single-lumen catheters as recommended for patients on long-term HPN [17,21,22], the association between number of CLABSI and catheter lumens was not significant in our study, and the low number of patients using ports and/or PICC lines did not allow to perform a statistical analysis.

A retrospective study of 958 adult patients on HPN identified that radiation enteropathy, among other underlying etiologies, represented a three-fold risk of CLABSI as compared with surgical complications [23]. In our research, differences between patients with malignant tumors and ifor among the disorders included in the benign CIF group were not significant. These results are in...
Table 4
Infectious events in patients on home parenteral nutrition according to the cause of benign chronic intestinal failure.

| Infectious event (1 or more) | No | Yes |
|-----------------------------|----|-----|
| With intestinal dysmotility  | 43 (76.8%) | 13 (23.2%) |
| Without intestinal dysmotility | 203 (76.6%) | 62 (23.4%) |

*p < 1.

In contrast to those reported by the ASPEN registry, in which CLABSI were significantly more frequent in the short bowel group [6].

The most relevant limitation to our study was that it was a retrospective analysis of a database. On the other hand, its strength lied in the number of patients on HPN for more than 90 days receiving the same care delivered by an interdisciplinary group of healthcare workers who complied with guidelines suitable for the care of this type of patients and COVID-19 pandemic conditions.

5. Conclusion

During the COVID-19 pandemic, the rate of CLABSI was within the ranges reported by international scientific societies. This was particularly relevant, considering the higher risk of pediatric patients during that period. Mortality rate in COVID-19 infected patients was higher than in the general population.

Author contribution
AC, MF, MP, HFG and AF contributed to the conception and design of the research and the analysis of the data. ND, LC, FP, MB, GM, VG, HF, MB, AM, MFC, ND, GC, VG, CB, CG, AH, OS, DS, LM, and AF contributed to the acquisition of the information of the database. All authors drafted and critically revised the manuscript, agreed to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript.

Ethical approval
This study complies with the basic principles of secondary data analyses. Patient personal data were anonymised and further protected by incorporating them into a new database with new identifiers. Data collection was not invasive and performed in accordance with the Declaration of Helsinki and amendments as well as regulations and laws involving human subjects’ rights and protection.

Financial disclosure
The authors received no financial support for this study. Nutrihome® provided the database information but neither funded nor participated in manuscript writing or revision.

Declaration of competing interest
All authors are involved in the follow-up of Nutrihome® patients.

Acknowledgments
The authors are grateful to Clerici V, Quirós C, Bogado M, Escoda R, Scharlovsky H, Cabrera A, Moretti D, Sposito M.V., Duarte R, Blanco V, Stanazú Y, Lopez N, Rosales M, Rivero S, Aravena S, Duje L, Zilli L, Gaitán M, and Vega R. for patient data provision.

References
[1] https://www.argentina.gob.ar/coronavirus/informes-diarios/sala-de-situacion/diciembre-2020
[2] Cloutier A, Bond A, Taylor M, Ablett J, Teubner A, Farrer K, et al. Successful implementation of remote video consultations for patients receiving home parenteral nutrition in a national UK Centre. Frontline Gastroenterol 2020;11:704–7.
[3] Lal S, Van Gossum A, Joly F, Boffetti F, Cuerda C, Lamprech G, et al. Home artificial nutrition & chronic intestinal failure special interest group of the European society for clinical nutrition and metabolism (ESPEN). Considerations for the management of home parenteral nutrition during SARS-CoV-2 pandemic: a position paper from the home artificial nutrition and chronic intestinal failure special interest group of ESPEN. Clin Nutr 2020;39(7):1988–91.
[4] Wells Mulberin D, Walker R, Holcombe B, Guenter P. ASPEN report on nutrition support practice processes with COVID-19: the first response. Nutr Clin Pract 2020;35(5):783–91.
[5] Barclay AR, McCuekin C, Hill S, Protheroe S, Batta A. Exit strategies from the COVID-19 lockdown for children and young people receiving home parenteral nutrition (HPN): lessons from the BSPCHAN Intestinal Failure Working Group experience. Frontline Gastroenterol 2021;12(4):348–53.
[6] Ross VM, Guenter P, Corrigan ML, Kovacevich D, Winkler MF, Resnick HE, et al. Central venous catheter infections in home parenteral nutrition patients: outcomes from Sustain: American society for parenteral and enteral nutrition’s national patient registry for nutrition care. Am J Infect Control 2016;44(12):1462–8.
[7] Kocak C, Punts JVL, Hojsak I. ESPGHAN/ESPEN/ESPR/CSPEN working group on pediatric parenteral nutrition. ESPGHAN/ESPEN/ESPR/CSPEN guidelines on pediatric parenteral nutrition: venous access. Clin Nutr 2018;37(6 Pt B):2379–91.
[8] Bond A, Chadwick P, Smith TR, Nightingale JMD, Lal S. Diagnosis and management of catheter-related bloodstream infections in patients on home parenteral nutrition. Frontline Gastroenterol 2020;11(1):48–54.
[9] O’Grady NP, Alexander M, Burns L, Dellingler EP, Garland J, Heard SO, et al. Guidelines for the prevention of intravascular catheter-related infections. Clin Infect Dis 2011;52(9):e162–93.
[10] Dreesen M, Portin L, Wauters G, Herbots L, Van den Berghe G, et al. Outcome indicators for home parenteral nutrition (HPN) care: point of view from adult patients with benign disease. JPEN - J Parenter Enter Nutr 2015;39(7):828–36.
[11] Dibb MJ, Abraham A, Chadwick PR, Shaffer JL, Teubner A, Carlson GL, et al. Central venous catheter salvage in home parenteral nutrition catheter-related bloodstream infections: long-term safety and efficacy data. JPEN - J Parenter Enter Nutr 2016;40(5):699–704.
[12] Trübner S, Brandt CF, Hvistendahl M, Staun M, Brabech P, Moser CE, et al. Catheter-related bloodstream infections in adults receiving home parenteral nutrition: substantial differences in incidence comparing a strict microbiologically to a clinically based diagnosis. JPEN - J Parenter Enter Nutr 2018;42(2):393–402.
[13] Santarpia L, Buonomo A, Pagano MC, Alfonsi L, Foggia M, Mottola M, et al. Central venous catheter related bloodstream infections in adult patients on home parenteral nutrition: prevalence, predictive factors, therapeutic outcome. Clin Nutr 2016;35(6):1394–8.
[14] Rodgers SL, Mundi MS, Hurt RT, Salonen BR. To pull or not to pull: salvaging central line catheters in home parenteral nutrition. Curr Nutr Rep 2018;7(4):324–8.
[15] Pfitzner M, Hamilton H, Biffi R, MacFie J, Perktiewicz M, ESPEN. ESPEN Guidelines on Parenteral Nutrition: central venous catheters (access, care, diagnosis and therapy of complications). Clin Nutr 2009;28(4):365–77.
[16] Dreesen M, Foulon V, Spreit L, Goossens GA, Hiele M, De Pourcq L, et al. Epidemiology of catheter-related infections in adult patients receiving home parenteral nutrition: a systematic review. Clin Nutr 2013;32(1):16–26.
[17] Mutalib M, Evans V, Hill S. Aseptic non-touch technique and catheter-related bloodstream infection in children receiving parenteral nutrition at home. United European Gastroenterol J 2015;3(4):393–8.
[18] Buchanan AL, Opilia M, Kwasyon D, Amantadonis TG, Okamoto R. Risk factors for the development of catheter-related bloodstream infections in patients receiving home parenteral nutrition. JPEN - J Parenter Ent Nutr 2014;38(6):744–9.
[19] Bech LF, Drustrup L, Nygaard L, Skorupski T, Christensen LD, Vinter-Jensen L, et al. Environmental risk factors for developing catheter-related bloodstream infection in home parenteral nutrition patients: a 6-year follow-up study. JPEN - J Parenter Enter Nutr 2016;40(7):989–94.
[20] Kovacevich DS, Corrigan M, Ross VM, McKeever L, Hall AM, Braunschweig C, American society for parenteral and enteral nutrition guidelines for the selection and care of central venous access devices for adult home parenteral nutrition administration. JPEN - J Parenter Enter Nutr 2019;43(1):15–31.
[21] Ole S, Nightingale J, Donnelly S, Naghibi M, Willsmore J, Lloyd D, et al. Outcome of adult patients receiving parental support at home: 36 years’ experience at a tertiary referral centre. Clin Nutr 2021;40(11):5639–47.