

# The Frequency, Severity, and Risk Factors of Hickman Catheter-Related Complications in Pediatric Cancer Patients: A Single-Center Experience from Bosnia and Herzegovina

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## What is already known on this topic?

- Using Hickman central venous catheters (CVCs) for long-term venous access in infusional chemotherapy for pediatric cancer patients is generally safe but is associated with significant morbidity, including mechanical, infectious, or thrombotic complications. In addition to the fact that these complications can prolong hospital stays and increase care costs, some are potentially life threatening.

## What this study adds to this topic?

- Our study confirms frequent Hickman catheter-related complications in pediatric cancer patients. These complications do not necessarily represent medical errors since they are not always preventable, even with optimal care. However, strict adherence to aseptic technique, personnel education, and competencies are required in appropriately managing Hickman CVCs.

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Received: August 14, 2023

Revision Requested: September 12, 2023

Last Revision Received: November 24, 2023

Accepted: November 26, 2023

Publication Date: January 12, 2024

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## ABSTRACT

**Objective:** This study aimed to identify the frequency, severity, and risk factors associated with Hickman catheter-related complications in children with hemato-oncological malignancies at the largest pediatric tertiary care unit in Bosnia and Herzegovina.

**Materials and Methods:** A cross-sectional study was conducted on a cohort of pediatric cancer patients who underwent Hickman central venous catheters (CVCs) between January 2019 and December 2022. Mechanical, infectious, and thrombotic Hickman catheter-related complications were evaluated and analyzed. We also investigated possible risk factors associated with these complications.

**Results:** Seventy-one Hickman CVCs were inserted in 68 children (44 boys and 24 girls) at a mean age of  $6.9 \pm 4.6$ . Forty (58.8%) children had hematological malignancies and 28 (41.2%) solid cancers. The median follow-up after Hickman CVC insertion was 190 days (95% CI [160–212]) for 12 644 catheter days. During follow-up, 10 (14.1%) mechanical, 7 (9.9%) infectious, and 1 (1.4%) thrombotic complications were recorded (0.8, 0.48, and 0.08 per mechanical, infectious, and thrombotic complications per 1000 catheter days, respectively). A slightly higher incidence of complications was recorded in children with hematological malignancies (1.59 per 1000 catheter days) compared with children with solid cancers (1.22 complications per 1000 catheter days).

**Conclusion:** Using Hickman CVCs for long-term venous access in infusional chemotherapy for pediatric cancer patients is safe but is associated with significant morbidity.

**Keywords:** Children, Hickman catheter-related complications, pediatric cancers

## INTRODUCTION

The survival of pediatric patients with cancer has substantially improved over the last several decades.<sup>1</sup> Chemotherapy is pivotal in treating most pediatric cancers and contributes to improved clinical outcomes.<sup>2</sup> Children with hemato-oncological malignancies frequently undergo the insertion of tunneled central vascular access devices (CVADs) using tunneled external lines (TELs) such as Hickman central venous catheters (CVCs) to allow delivery of chemotherapy. In addition, Hickman CVCs are frequently used to infuse antibiotics or other medications and nutritional supplements into the pediatric population. Although Hickman CVCs have significantly improved the care of pediatric cancer patients,<sup>3</sup> their

**Cite this article as:** Zvezdic Z, Zaimovic E, Milisic E, Jonuzi A, Glamoclija U, Vranic S. The frequency, severity, and risk factors of hickman catheter-related complications in pediatric cancer patients: A single-center experience from Bosnia and Herzegovina. *Turk Arch Pediatr.* 2024. [epub ahead of print]

use is burdened with a significant incidence of mechanical, infectious, or thrombotic complications,<sup>4</sup> affecting 14–36% of patients within 2 years from the placement of CVCs.<sup>5</sup> In addition to the fact that these complications can prolong hospital stays and increase care costs, some are potentially life threatening.<sup>4</sup> Therefore, risk stratification is vital to optimizing care pathways that have been shown to reduce the risk of premature CVAD removal and the occurrence of the mentioned complications.<sup>4,6</sup>

Studies on the adult population have shown that left-sided insertion, male sex, and obesity are associated with an increased risk of Hickman catheter-related complications.<sup>7</sup> Other studies have found that risk factors include neutropenia, multiple lumen catheters, male sex, and obesity<sup>8,9</sup> as well as the duration of CVC use, length of hospitalization time, insertion of CVCs in the intensive care unit, nonoperative cardiovascular disease, parenteral nutrition, and administration of blood products.<sup>10</sup> Studies on CVC-related complications in pediatric cancer patients are relatively rare in the literature and usually involve a few patients.<sup>11–16</sup>

There is a complete lack of studies on this topic in Bosnia and Herzegovina and neighboring countries; therefore, the study aimed to identify the frequency and severity of Hickman catheter-related complications in pediatric cancer patients in Bosnia and Herzegovina. We also investigated the possible risk factors associated with these complications and the clinical outcomes of pediatric patients.

## MATERIALS AND METHODS

### Study Design and Population

The cross-sectional study was conducted at the Clinical Center University of Sarajevo and comprised medical records of pediatric cancer patients hospitalized and treated for 4 years (from January 2019 through December 2022).

Data were collected from all patients referred to our pediatric surgery department for surgical insertion of Hickman catheters under general anesthesia. Three possible complications were defined as mechanical, thrombotic, and infectious. Collected data from medical records included demographic patient information [age, sex, body mass index (BMI), underlying malignancy, type of cancer, catheter lumen (single or dual lumen), and French sizes on Hickman catheters], location of insertion, duration of insertion, the occurrence of complications, microbiological findings, number of Hickman catheter insertions, and causes of removal.

### Hickman Central Venous Catheter Placement

The anesthesia protocol was the same for all patients and comprised sevoflurane for the induction and maintenance of general anesthesia. The same team performed the procedure on all patients. The procedure consisted of the surgical placement of the Hickman catheter in the internal jugular vein under aseptic conditions. After implantation, a radiological assessment of the Hickman CVC's position was mandatory. All Hickman CVC attempts were successful. Trained pediatric nurses handled standard routine CVC care. It included regular dressing changes with chlorhexidine, flushing the CVC with 3 mL of heparinized solution (heparin, 200 IU/mL) at least twice

a week and dressing the skin at the Hickman CVC exit site with a sterile gauze dressing.

### Central Venous Catheters Related Complications and Outcome

Catheter-related bloodstream infection (CRBSI) is a laboratory-confirmed bloodstream infection originating from an intravenous catheter and not related to an infection at another site.

Catheter-related local infection (CRLI) presents as swelling, redness, and feelings of pain or soreness in the area within 2 cm of where the catheter exits the body. Catheter-related thrombotic complications are defined as venous thromboembolism (VTE) associated with using a Hickman CVC.

The incidence of CVC-related complications was calculated as a number of complications  $\times$  1000/number of catheter days after calculating the incidence for every patient category.

The primary outcomes were the frequency and severity of complications (mechanical, thrombotic, and infectious) and the duration of Hickman CVC use, defined as the duration between insertions and removal. The secondary outcomes included the identification of risk factors for Hickman catheter-related complications.

### Ethics Committee Approval

All medical records were pseudo-anonymized for the current study. Institutional Review Board of Clinical Center University of Sarajevo approved the study (Approval Number: 16-103/2023). The study was carried out according to the Declaration of Helsinki. The patients' parents consented to publish the data in the study.

### Statistical Analysis

All statistical assays were performed using the Statistical Package for the Social Sciences software, version 26 (UNICOM Systems, Inc., Mission Hills, CA, USA). Mean and median were used to measure central tendency, while SD and range were used as measures of dispersion for continuous variables. The values of categorical variables were presented as numbers or percentages. The evaluation of the z-score for skewness and kurtosis, histograms, bargraphs, and Q–Q plots, together with Kolmogorov–Smirnov test, were used for the evaluation of data distribution normality for each variable. Confidence intervals at the 95% limits and *P*-values were calculated for each risk factor analyzed.

## RESULTS

### Clinical Characteristics of the Cohort

During the study period, 71 Hickman CVCs were placed in 68 newly diagnosed pediatric cancer patients. There were 44 (64.7%) males and 24 (35.3%) females, with a male/female ratio of 1.83:1. The mean age at catheter placement time of the entire cohort was  $6.9 \pm 4.6$  years. The mean age for males was  $6.9 \pm 4.4$  years and for females was  $7.34 \pm 5.1$  years. There were 36 (52.9%) children under 6 and 32 (47.1%) older than 6. The mean age of children in the age group below 6 years was  $3.30 \pm 2.3$  years, while the mean age of children in the age group 6 and older was  $11.1 \pm 5.2$  years. In total, 40 (58.8%)

children had hematological malignancies and 28 (41.2%) solid cancers. The median follow-up for the entire cohort was 190 days (95% CI, 160–212) for 12 644 catheter days. Among the 68 patients, 65 (95.6%) had only 1 Hickman CVC inserted in the right internal jugular vein during the study period. A second Hickman CVC was inserted in the left internal jugular vein in 3 (4.4%) patients.

### The Frequency and Characteristics of Central Venous Catheter-Related Complications

Out of a total of 71 Hickman CVCs inserted (68 primary inserted and 3 reinserted), 49 catheters (69.0%) were successfully removed at the end of therapy (catheters no longer required), 4 catheters (5.6%) were removed due to the death of patients, and 18 (25%) Hickman catheters were removed early due to complications, implying an overall incidence of 1.42 per 1000 catheter days for the development of a complication. During follow-up, 10 (14.1%) mechanical, 7 (9.9%) infectious, and 1 (1.4%) thrombotic complications were recorded (0.8, 0.48, and 0.08 for mechanical, infectious, and thrombotic complications per 1000 catheter days, respectively). Among mechanical complications, Hickman CVC obstruction occurred in 6 children (8.5%), translocation of the Hickman CVC was recorded in 3 (4.2%) children, and accidental removal of the CVC affected 1 (1.4%) child. Seven episodes of infections resulted in the removal of the Hickman CVC. Four (5.6%) were systemic, and 3 (4.2%) were local infections. A single bacteria was isolated in 3 (75%) positive cultures in children with systemic infections, while more than 1 bacteria (2) was recorded in 1 case of systemic infection (25%) (Table 1). We recorded only 1 (1.4%) thrombotic complication during the study period: intrinsic thrombosis related to the catheter (intraluminal thrombosis).

According to the age and complications related to Hickman CVC, children younger than 6 years of age had a higher incidence of all complications (1.69 complications per 1000 catheter days) as well as a higher incidence of mechanical complications (0.92 complications per 1000 catheter days) and infectious complications (0.77 complications per 1000 catheter days). There were no thrombotic complications in this age group. Children aged 6 years and older had an incidence of total complications of 1.14 per 1000 catheter days, i.e., 0.65 mechanical complications per 1000 catheter days, infectious complications of 0.33 complications per 1000 catheter days, and thrombotic complications of 0.16 complications per 1000 catheter days.

Females developed a higher incidence of total complications than males (1.91 complications per 1000 catheter days vs. 1.18 complications per 1000 catheter days). According to

the type of complications, females had a higher incidence of mechanical complications than males (1.43 complications per 1000 catheter days vs. 0.47 complications per 1000 catheter days). In contrast, males developed a higher incidence of infectious complications than females (0.71 complications per 1000 catheter days vs. 0.24 complications per 1000 catheter days).

Concerning the type of underlying malignancy, a slightly higher incidence of complications was recorded in children with hematological malignancies at 1.59 per 1000 catheter days compared with children with solid cancers, with 1.22 complications per 1000 catheter days. According to the type of underlying malignancy, children with hematological malignancies had a higher incidence of infectious and thrombotic complications (0.72 per 1000 catheter days and 0.15 per 1000 catheter days, respectively), while children with solid cancers developed a higher incidence of mechanical complications (0.87 per 1000 catheter days). The incidence of all Hickman-related CVC complications according to the patient's age, sex, and underlying malignancy is fully summarized in Table 2.

In children with no complications, the median BMI value was 18 (95% CI, 14.6–19.2), and the median BMI category was 50% (95% CI, 15–95). In contrast, median BMI and BMI percentile values in children with mechanical complications were 14.6 (95% CI, 13.3–23.7) and 32 (95% CI, 4–94), respectively.

## DISCUSSION

This study analyzed the use of Hickman CVCs in pediatric cancer patients, emphasizing that this method can be burdened with significant complications or premature catheter removal in addition to the apparent advantages of use. The failure and complications of CVCs result in interrupted medical treatment, morbidity, and even mortality for pediatric patients. Children with CVCs are already vulnerable to complications and disability due to their underlying health conditions.<sup>17</sup> Data from this study showed that complications resulted in premature device removal in 25% of cases, even by adopting approved Hickman CVC management procedures. This finding is similar to a recent study by Zhang et al.<sup>18</sup> Van den Bosch et al.<sup>19</sup> reported that ~37% of Hickman CVCs in pediatric cancer patients were prematurely removed owing to complications. However, a lower percentage of the overall complications of ~10% that led to the premature removal of the Hickman CVC was reported by Perdikaris et al.<sup>17</sup> The overall complications recorded per 1000 catheter days for Hickman lines in our study of 1.42/1000 catheter days are lower compared with 2 retrospective studies on adults for this type of CVC,<sup>20,21</sup> but similar or higher than in other studies with pediatric cancer patients.<sup>12,17,22</sup> Such a difference in complication rates between the studies mentioned above probably originates from different study designs, primarily in defining the type of complication and its outcome, either in the resolution and continuation of CVC function or its premature removal. In the present study, we analyzed only those complications that resulted in the premature removal of Hickman CVC. This mainly pertains to infectious complications, considered as such only if they could not be resolved with conservative measures. Accordingly, the percentage and number of complications per 1000 catheter days in our study of 9.9% and 0.8 were lower than those in other studies.<sup>12,13,17,22,23</sup>

**Table 1.** Etiology of Systemic Infections

Pathogens	Number (Percentage)	Incidence
<i>Citrobacter braakii</i>	1 (20%)	0.079/1000 catheter days
<i>Enterobacter cloacae</i>	1 (20%)	0.079/1000 catheter days
<i>Stenotrophomonas maltophilia</i>	1 (20%)	0.079/1000 catheter days
<i>Serratia marcescens</i>	1 (20%)	0.079/1000 catheter days
<i>Pseudomonas spp.</i>	1 (20%)	0.079/1000 catheter days

**Table 2.** The Type and Incidence of Hickman CVC Complications According to the Patient's Age, Sex, and Underlying Malignancy

Variables		Incidence of Complications per 1000 Catheter Days			
		All Complications (n = 18)	Mechanical Complications (n = 10)	Infective Complications (n = 7)	Thrombotic Complications (n = 1)
Total		1.42	0.79	0.55	0.08
Sex	Males	1.18	0.47	0.71	—
	Females	1.91	1.43	0.24	0.24
Age (years)	<6	1.69	0.92	0.77	—
	≥6	1.14	0.65	0.33	0.16
Underlying malignancy	Hematological malignancies	1.59	0.72	0.7	0.15
	Solid cancers	1.22	0.87	0.35	—

Additionally, in contrast to these studies, in which infectious complications were more frequent,<sup>12,13,17,22,23</sup> mechanical complications most often caused premature removal of Hickman CVC in our study. Our study identified an overall incidence of mechanical complications after insertion of 14%, which falls within the previously reported range of published data.<sup>12,13,24</sup> Interestingly, we found that younger age (<6 years) was associated with a higher incidence of mechanical complications. This observation is consistent with previously published studies.<sup>24,25</sup> The possible reason for this finding may be that Hickman lines in young children will likely be subjected to accidental rotational and tractional forces that might damage the line, making it prone to mechanical obstruction.

We had only 1 patient with symptomatic CVC-related thrombosis. The incidence of thrombotic complications related to Hickman CVC in our study of ~1% of all complications and 0.16 complications per 1000 catheter days is lower compared with other pediatric studies.<sup>22,26,27</sup> It is important to note that only the clinically symptomatic CVC-related thrombosis was an endpoint of this study, knowing from the literature that the incidence is higher if clinically asymptomatic thrombosis is also considered.

As in the Pardikaris et al study,<sup>17</sup> our study also revealed that males developed catheter-related infections that led to catheter removal more frequently than females. Pardakaris et al postulated that the reasons for the higher occurrence of infectious complications in males may lie in the fact that males do not follow the standards for Hickman CVC care and infection prevention as well as that males are more active and do not follow the instructions or guidance as females do.<sup>17</sup> However, females had a higher prevalence of mechanical complications.

In line with previous studies,<sup>13,28</sup> the present study showed that children under 6 more frequently developed Hickman catheter-related complications than older children. Because young children are not able to understand the utility and the necessity of the Hickman CVC and ignore the guidelines for the prevention of catheter-related infections as a consequence of cognitive immaturity during that period of life, the active participation of their parents is of crucial importance in the recommended measures of proper care of the Hickman CVC.<sup>17</sup>

Our finding that children with hematological malignancies are more likely to develop complications related to Hickman CVCs

than those with solid tumors aligns with the results of similar studies.<sup>13,29</sup> The reasons for this difference in the frequency of complications are uncertain. However, they may be attributable to the type of disease, intensity of therapy, frequency with which devices are accessed, or duration of neutropenia.

Although obesity is a well-recognized risk factor for deep venous thrombosis (DVT) and CVC-related thrombosis in adult patients with cancer,<sup>30</sup> as well as for CRBSIs,<sup>31</sup> this study found no association of an overweight condition with a higher risk for CVC-related thrombosis or CRBSI in children with solid cancers. Part of this observation is based on the findings of Abate et al,<sup>22</sup> who suggest that there is no reason to consider overweight children or adolescent cancer patients at higher risk for DVT, which is different from what is generally stated for adult cancer patients. The finding of the recent study that underweight children had slightly more complications compared to other BMI categories is in contrast to the study conducted by Wang et al, who observed no association between underweight and Hickman-related complications, particularly with CRBSI.<sup>31</sup> A proposed mechanism underlying this underweight paradox is that pediatric malignancy results in a malnourished state, manifested as weight loss accompanied by deficits in immune system function, tissue maintenance, and other processes potentially responsible for Hickman-related complications. This finding could also be explained by the fact that clustering is a normal phenomenon in small random and pseudo-random data samples. However, the obtained pattern is often interpreted as significant in random events. Further research is necessary to determine whether extreme BMI (in our case, very low) in children increases the risk of Hickman-related complications.

This study has several limitations. First, due to the study's retrospective nature, further clinical information regarding complications was not collected after patients were discharged. Therefore, our results may have discrepancies from the accurate complication rates. Second, the study involved a small sample size, meaning its findings do not necessarily represent the general pediatric cancer population. Third, the present study analyzed only complications that resulted in premature removal of Hickman CVCs, leaving the overall complication rate unknown. Fourth, data were collected from a single unit of a pediatric hospital. Therefore, these results cannot be generalized to a national level.



In conclusion, using Hickman CVCs for long-term venous access in infusional chemotherapy for pediatric cancer patients is generally safe but is associated with significant morbidity. Strict adherence to aseptic technique, personnel education, and competencies are required in appropriately managing Hickman CVCs.

**Ethics Committee Approval:** All medical records were pseudo-anonymized for the current study. Institutional Review Board of Clinical Center University of Sarajevo approved the study (Approval Number: 16-103/2023). The study was carried out according to the Declaration of Helsinki.

**Informed Consent:** The patients' parents consented to publish the data in the study.

**Peer-review:** Externally peer-reviewed.

**Author contributions:** Conception – Z.Z., S.V.; Design – Z.Z., S.V.; Supervision – S.V.; Funding – none; Materials – Z.Z., S.V.; Data Collection and/or Processing – Z.Z., E.Z., E.M., A.J., U.G., S.V.; Analysis and/or Interpretation – Z.Z., E.Z., E.M., A.J., U.G., S.V.; Literature Review – Z.Z., S.V.; Writing – Z.Z., S.V.; Critical Review – Z.Z., E.Z., E.M., A.J., U.G., S.V.

**Declaration of Interests:** Una Glamoclija is the employee of Bosnalijek d.d., Sarajevo. Other authors don't have conflict of interest to declare.

**Funding:** This study received no funding.

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