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1 **The Hidden Cost of Catheter Related Blood Stream Infections in Patients on**
2 **Parenteral Nutrition**

3

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17

18 **Abstract**

19

20 **Background & Aims**

21 Parenteral nutrition (PN) is a valuable and life-saving treatment for patients with

22 intestinal failure. While its use is increasing, it has been demonstrated to be a risk

23 factor for intravenous catheter-related blood stream infection (CRBSI) - a significant,

24 serious and potentially fatal complication of PN use. CRBSI can have serious

25 secondary consequences for patients, though, there is a paucity of literature

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26 describing these. The aim of this study is to audit the incidence of, and evaluate the
27 consequences of, complications associated with CRBSI

28

29 Methods

30 Medical records were examined for all parenterally fed patients diagnosed with a
31 CRBSI from 01/01/16 to 31/12/17 in a UK tertiary referral centre for patients requiring
32 intravenous nutritional support. Patients were identified prospectively; data relating to
33 the infection and complications was collected retrospectively.

34

35 Results

36 114 episodes of CRBSI were recorded in 80 patients. 57 occurred during an inpatient
37 admission, 57 occurred in the community and resulted in admission. 21 different
38 adverse events occurred as a result of the CRBSI. The complications identified were
39 varied with the most common being acute kidney injury, deranged electrolytes and
40 urinary tract infections. Other significant complications included DVT, pulmonary
41 abscess and infective endocarditis. 35% of episodes resulted in delayed discharge
42 and 12% required escalation to a critical care bed. The financial impact is estimated
43 at over £800,000 per annum.

44

45 Conclusions

46 The findings demonstrate a plethora of complications which can arise following
47 CRBSI, which pose a significant health risk to parenterally fed patients who already
48 have reduced physiological reserve. Moreover, these findings represent additional
49 financial and resource burden to the health service. The adverse events resulting
50 from CRBSIs should, therefore, be audited to improve outcomes: well-resourced
51 specialist centres are best placed to provide this service.

52

53 **Introduction**

54 Parenteral nutrition (PN) is a valuable and life-saving treatment for patients with
55 intestinal failure and its use is increasing with the advances in home PN services(1).
56 PN is an independent risk factor for intravenous catheter-related blood stream
57 infection (CRBSI)(2), whilst also being a risk factor for many other adverse physical,
58 social and psychological conditions(3,4).

59

60 Despite efforts to reduce CRBSI associated with PN use, and a target of <1 episodes
61 per 1000 catheter days(5), infections are still an important clinical problem. Inpatient
62 rates are reported between 1.5-10.0 episodes per 1,000 parenteral nutrition days and
63 home PN rates between 0.38-4.58 episodes per 1000 catheter days(6-8).

64 Inconsistency in the descriptive terms used in the literature can create difficulty in
65 comparison but it remains that, although there is variability in the reported rates of
66 CRBSI, it is a significant, serious and potentially fatal complication of PN use.

67

68 CRBSI can have serious secondary consequences for the individual patient. In
69 critical care, CRBSI has been shown to increase length of ICU stay and length of
70 ventilation when compared to similar patients with central lines who did not develop a
71 catheter related infection(9). An observational study of patients on home PN reports
72 infective endocarditis, pneumonia, septic shock and venous thrombosis as
73 complications of CRBSI(10). Complications of CRBSI also lead to a significant
74 increased cost¹⁰. Reported excess healthcare costs associated with CRBSI vary(9,
75 11) and it is unclear whether the reported costs include the treatment of
76 complications resulting from the CRBSI or just the treatment of the CRBSI alone.

77

78 **Aim**

79 The aim of this study is to audit the incidence of, describe and evaluate the cost of
80 complications associated with CRBSI in patients on PN at Leeds Teaching Hospitals.

81

82 **Methods**

83 All patients on PN with confirmed CRBSI at Leeds Teaching Hospitals between
84 01/01/16 - 31/12/17 were studied. At Leeds Teaching Hospitals a CRBSI is
85 diagnosed using paired blood cultures with a differential time to positivity of ≤ 2 hours.
86 The nutrition team record all CRBSIs in the Trust prospectively. Subsequently,
87 electronic medical notes of all episodes were examined, and relevant data were
88 extracted retrospectively. A complication of a CRBSI was defined as an adverse
89 medical event which occurred within 90 days after diagnosis, investigation or
90 management of the infection or at any time during an admission for a CRBSI.
91 Complications were excluded if any other reasonable cause was demonstrated. All
92 patients who developed a CRBSI as an outpatient were admitted for management.
93 Subsequently, all events relating to the admission for these patients were considered
94 to be a consequence of the infection. An estimate of the financial burden of CRBSI's
95 was made using data on cost of beds per day, and costs of the treatment of the
96 complications, provided by the financial department of the hospital trust.

97

98 **Results**

99 114 episodes of CRBSI were recorded in 80 patients with a median of 1 episode per
100 patient (IQR: 1-2). The mean age of patients at diagnosis of CRBSI was 54 (21-83)
101 years old. 59/114 (51.8%) of the patients were male. 57 CRBSIs were developed as
102 an outpatient and 57 were developed during an inpatient admission. For an
103 outpatient admitted because of a CRBSI the median length of admission was 18
104 days (IQR: 13-25). The line was removed in 66% of the 114 episodes, of these 43%
105 were PICC lines and a new line(s) was inserted in 75% of cases. There were 21
106 different adverse events identified as a complication of the CRBSI. These occurred a
107 total of 101 times (table 1). 69% of CRBSI episodes resulted in the patient missing
108 PN for an average of 6.5 days (IQR:2-13) while 12% of infections lead to cessation of

Commented [DB1]: Use mean, rather than average. Put in an age and the entire range e.g. 54 (range 46-80) years.

Commented [DB2]: Rather than 54.52%, use the number of patients with % to one decimal place e.g. 44 (54.5%)

109 the PN regime. When the CRBSI was developed during an admission 35% had
110 evidence of resultant delayed discharge.

112 **Table 1. Adverse events occurring as a result of CRBSI in adult patients on PN.**

113 *MRSA – Methicillin-Resistant Staphylococcus Aureus, VRE – Vancomycin-Resistant*
114 *Enterococci, ESBL – Extended Spectrum Beta-Lactamase.*

115 Financial implications

116 A standard ward bed costs £220 per day and with a total of 1979 admission days, the
117 cost amounts to £435,380. A high dependency bed costs £1459 per day, with a total
118 of 23 days, this amounts to £33,557. An intensive care bed costs £1820 per day, with
119 a total of 50 days, this amounts to £91,000. The estimated total cost of treatment of
120 complications (excluding bed costs) is £275,469. The total incurred cost of treating
121 the complications resulting from 114 CRBSI's, over the 2 years, is therefore
122 £835,406. This equates to an average of £7,328 being incurred, per CRBSI episode,
123 as a result of the complications alone.

124

125 Causative Organisms

126 The most common cultured organisms causing the CRBSI were a mixed culture
127 (23/114), coagulase negative Staphylococcus (21/114), Klebsiella sp. (16/114),
128 Escherichia Coli (9/114), Enterobacter sp. (6/114), Methicillin Sensitive
129 Staphylococcus aureus (MSSA) (6/114), Candida sp. (5/114), Staphylococcus
130 Epidermidis (5/114) and the remaining 28 included 14 other species including MRSA
131 and Pseudomonas.

132

133 **Discussion**

134 The findings demonstrate a plethora of adverse events occurring with CRBSIs, many
135 of which incur significant risk to the patient.

136

137 The documented adverse events can be categorised into four different groups
138 dependent on whether they were caused by the infection itself, by the treatment of
139 the infection, due to hospital admission for the infection or as a result of missing PN.
140 Here we will discuss these categories separately.

141

142 Adverse Events Associated with the Infection and Septic State

143 Acute kidney injury (AKI) occurred in over one fifth of patients with a CRBSI in this
144 study. AKI is a common problem throughout hospitalised patients affecting 13-18% of
145 all admissions in developed countries(12) and has been demonstrated to increase
146 morbidity and mortality(13) highlighting a significant health risk to these patients. AKI
147 increases the risk of chronic kidney disease (CKD) and end-stage renal failure
148 (ESRF)(14) and, hence, development of AKI is a significant complication in
149 parenterally fed patients who are already at increased risk of impaired renal
150 function(15,16).

151

152 Deep seated infections resulting from CRBSIs such as candida endophthalmitis and
153 infective endocarditis had a significant harmful outcome for the patients. A case of
154 endocarditis resulted in development of a pulmonary abscess, whilst the patient who
155 developed endophthalmitis consequently had permanently reduced visual acuity.
156 Previously reported complications that can occur as a result of such deep-seated
157 infections include death, heart failure and blindness(17,18).

158

159 Other complications occurring as a result of the CRBSI included new onset atrial
160 fibrillation, a tonic-clonic seizure, transient deterioration of polymyositis resulting in
161 dysphagia and subsequently aspiration pneumonia. These highlight examples of the
162 effect CRBSIs can have on pre-existing chronic and intermittent conditions, in an
163 increasingly co-morbid population this demonstrates the potential synergistic impact
164 CRBSIs can have on patient health.

165

166 Intensive care admission was required for seven (6%) patients and high dependency
167 unit for four (4%) patients providing cardiovascular or respiratory support or both.

168 This demonstrates the potentially life-threatening nature of CRBSIs, whilst
169 representing extra cost in the treatment of these patients. With ICU beds in the trust
170 costing eight times and HDU beds six times that of a normal ward bed, the excess
171 cost of critical care beds over a two-year period equates to £108,000.

172

173 Adverse Events Associated with Hospital Admission

174 The results suggest that CRBSIs often resulted in delayed discharge for patients who
175 contracted their infection during a hospital admission with estimated delays ranging
176 from two days to six months. Aside from the obvious additional costs of prolonged
177 hospital stay this also puts the patient at increased risk of contracting further hospital
178 acquired infections. Five patients in this study were found to have contracted a
179 multidrug-resistant bacterial colonisation during their admission. These include
180 MRSA, VRE and ESBL producing bacteria.

181

182 Adverse Events Associated with Treatment of CRBSI

183 66% of patients had their infected line removed with the remaining being successfully
184 salvaged. 75% of patients required another line either as replacement for their
185 previous or for concurrent treatment and PN whilst salvaging the infected one. With
186 recurrent line insertions come associated procedural risks of up to 20% in central
187 lines(19). In this series seven deep vein thromboses occurred secondary to midlines
188 and one patient developed a subclavian aneurysm as a result of a failed insertion of
189 a central line. Although no further morbidity or mortality occurred as a result of these
190 complications, they all required continued anti-coagulation for between three and six
191 months.

192

193 Further complications related to treatment of the CRBSI include clostridium difficile
194 infection likely resulting from antibiotic use and two Vancomycin prescribing errors
195 resulting in stage 3 acute kidney injury.

196

197 Adverse Events Associated with Missed PN

198 A significant proportion of patients missed at least one day of PN; this poses a risk of
199 dehydration and malnutrition, particularly in the septic patient. In the short term this
200 may contribute to the acute kidney injury and electrolyte disturbances observed. In
201 patients with longer periods without PN they risk malnutrition, including the risk of
202 refeeding syndrome and the complications related to this such as impaired wound
203 healing and hospital acquired infection(21).

204

205 A salutary example of the consequences of a CRBSI was a patient who was
206 receiving PN to improve nutritional status prior to chemotherapy. A CRBSI resulted in
207 cessation of PN and subsequent deterioration of nutritional status to the point where
208 they were unable to receive cancer treatment. Before PN could be reinstated the
209 patient deteriorated, with the cancer as their cause of death. Although this was an
210 isolated incident, this case highlights the grave potential result of missing PN at a
211 critical point.

212

213 Although the risk of CRBSI with parenteral nutrition is well recognised, data on the
214 consequences of CRBSI development are scarce. Our study builds on the findings
215 from previous studies which have described some complications resulting from
216 CRBSIs (9,10). Centres that treat patients with parenteral nutrition need to have
217 facilities to deal with the serious consequences of a CRBSI. There is no prior
218 literature to compare the cost of complications resulting from CRBSIs; these findings
219 highlight the need to consider the cost of complications of CRBSIs in service
220 development for patients who depend on parenteral nutrition.

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Limitations

As data were collected retrospectively this study is limited by the documentation of the clinical teams at the time of entry. Hence, some minor complications may have been omitted. As a descriptive study, conclusions could not be drawn regarding risk factors for developing complications. A further prospective, analytic study could explore this.

Conclusion

These findings demonstrate a plethora of complications which can arise following CRBSI. Many of the described complications pose a significant health risk to parenterally fed patients who already have reduced physiological reserve. Moreover, these findings represent additional financial and resource burden to the health service. The adverse events resulting from CRBSIs should, therefore, be audited to improve outcomes: well-resourced specialist centres are best placed to provide this service.

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