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Clostridium difficile infection in general surgery patients; identification of high-risk populations

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ABSTRACT

Background: Risk factors associated with *Clostridium difficile* infection (CDI) in general surgical patients are poorly characterised. This study aimed to characterise the incidence and associations of *C. difficile* positivity (CDP) in general surgical inpatients to aid in the design of future policies regarding focused screening and risk-stratification mechanisms in this patient subpopulation.

Materials and methods: Discharge, laboratory and coding data from all general surgery inpatients admitted to a large tertiary referral general surgical unit, between March 2005 and May 2007, were examined.

Results: 21,371 patient records were interrogated. 101 (0.47%) CDP cases were identified from laboratory records and compared with non-CDP controls for age, gender, length of stay (LOS), admission to intensive care unit or high dependency unit (ICU/HDU), co-morbidities and surgical procedures. Univariate analysis identified a range of risk factors associated with positivity.

Multivariate analysis identified malignancy, gastrointestinal disease, anaemia, respiratory disease, circulatory disease, diabetes mellitus, those undergoing gastrointestinal surgery and increasing age to be independently associated with CDP status.

Conclusions: This study identifies incidence and risk factor associations of those who tested CDP in a large contemporary general surgery inpatient population. Focused screening programmes based on high-risk populations may provide information on further risk factors and allow risk-stratification.

Further healthcare worker education regarding risk factors may reduce the clinical impact of CDI by encouraging increased vigilance and therefore earlier detection.

1. Introduction

Recent studies show that whilst the incidence and severity of methicillin-resistant *Staphylococcus aureus* infection is decreasing, the incidence of *Clostridium difficile* infection (CDI) is continuing to escalate[1,2] with increasing resistance to medical therapy.[3]

CDI can cause a spectrum of disease from asymptomatic colonisation to enteric illnesses including fulminant pseudomembranous colitis.[4] The consequences of CDI can be important to both the individual and healthcare institution, including an increased risk of mortality (up to 25% in elderly patients),[2] higher risk of additional infections, longer length of stay (LOS) and ward closures in order to control outbreaks.[5,6] CDI increases the cost of managing a patient by 54%,[7,8] with estimates suggesting CDI costs an average-sized district general hospital £400,000 with more than 2000 lost bed days annually.[9]

Despite a myriad of infection control measures, such as hand hygiene, environmental cleaning and prudent antibiotic stewardship, introduced throughout the UK to tackle the growing CDI problem, the increasing incidence of CDI[10] suggests that these measures are only partially effective. Whilst general measures such as effective infection control programmes have been shown to reduce infection trends,[11] such measures may be more successful if they are targeted towards high-risk inpatient populations, providing a more focused approach to primary prevention.

In addition, screening patients for *C. difficile* status may also provide an alternative approach. Prompt identification of CDI can

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potentially improve outcomes by allowing early administration of treatment[11] and rapid isolation of infected patients can reduce environmental contamination, helping control the transmission of *C. difficile*.[12] Furthermore, as asymptomatic carriers of *C. difficile* are a potential source for transmission,[4,13] identifying and treating these patients may help reduce the spread of CDI, although results from such studies are conflicting.[14–16] However, as faecal carriage of *C. difficile* does not correlate with CDI,[13] screening all patients could lead to over-excessive or unnecessary treatment and paradoxically increase the patients' risks of developing CDI.[17] Therefore any screening programme should be targeted to patients with the highest risk of developing CDI and more work on the effectiveness of this modality as an intervention to reduce CDI incidence is required.

Whilst much work has concentrated on risk factor associations in medical patients,[17] there are few studies specifically examining rates of infection within the general surgical inpatient populations. CDI rates of 4.2% in colorectal patients and 5% of liver transplant recipients have been reported,[18,19] but recent epidemiology of CDI may be changing in view of outbreaks caused by hyper-virulent strains of *C. difficile*, with up to 53% mortality and a 23% rate of colectomy.[20] As such, there is a need for accurate contemporary data on the incidence of CDI and a means to potentially identify those patient populations at increased risk. This provides a method to risk stratify those patients for increased surveillance.

Here we examine a large general surgical inpatient population, in order to quantify both the impact of infection on outcome and the factors associated with infection within this specific inpatient population.

2. Methods

Discharge summaries relating to all hospitalised general surgery inpatients at the Royal Infirmary of Edinburgh (RIE), UK, results of all *C. difficile* cytotoxin assays from the RIE Microbiology Database and complete data from the Discharge Coding Database at the RIE, between March 2005 and May 2007, was examined retrospectively.

Patient demographics included date of birth, gender, dates of admission and discharge, mortality, ICU/HDU admission, patient co-morbidities (ICD-10 codes), and surgical procedures performed (OPSC4 codes). *C. difficile* positive (CDP) status was ascertained from positive stool samples recorded by the microbiology database which recorded those samples that had been taken by clinical staff when clinically indicated. Stool samples were either tested on the day of collection for the presence of *C. difficile* toxin A or B (*C. difficile* TOX A/B II™, TECHLAB, USA), or if delayed, were stored at 4 °C and tested within 24 h. Positive assay for *C. difficile* toxin A and/or toxin B in those who had clinically-indicated testing defined CDP status. Only the first CDP episode during the study period for each case was recorded as a positive result, subsequent episodes were excluded from the analysis ($n = 17$).

21,270 general surgical inpatient admissions who were admitted during the study period and who did not prove CDP status positive during their admission were used as a comparison population. Only the first admissions during the study period for patients in the comparison population were used, 2097 subsequent inpatient episodes within the study period were therefore excluded from analysis.

19/103 (18.4%) of the CDP cases had missing data from the discharge coding database. Medical case notes for these 19 cases were therefore sought from medical records, with data subsequently obtained for 17. 8327/29,597 (28.1%) of the control population had missing data fields from the discharge coding database and were excluded from analysis. General surgical patients admitted to the general surgical department but who did not stay in the general surgery wards, or those who stayed in general surgical wards but were not general surgical inpatients were also excluded from the data analysis.

2.1. Statistical analysis

Shapiro–Wilks tests were performed to assess the normality of the data. To examine demographical differences in CDP status, two-sample *t*-tests have been used for continuous data, with chi-square tests or Fishers exact tests as appropriate used for categorical data. LOS, and time between admission, CDP status and discharge, data follows a non-normal distribution and in these cases a Mann–Whitney *U* test has been used. As a number of factors were found to be related to CDP status, a multivariable logistic regression was performed on those felt to be most clinically relevant [age, diabetes, respiratory disease, anaemia, circulatory disease, malignancy, gastrointestinal disease, renal failure and gastrointestinal surgery].

Permissions for this study were sought from the University of Edinburgh prior to the study.

3. Results

3.1. Patient population

31,814 surgical admissions involving 29,700 general surgical patients were analysed. 101 cases were identified as CDP and compared with 21,270 non-CDP patients. 2 CDP cases (1.98%) and 8327 non-CDP patients (28.1%) were excluded due to missing data. The incidence of patients with a CDP status was 4.73 per 1000 admissions.

3.2. Demographics

CDP patients were significantly older than non-CDP patients [mean (SD) 65.3 (17.6) vs. 51.1 (20.1), $p < 0.001$]. Age was independently associated with a positive result for *C. difficile* (OR = 1.02, 95% CI (1.01, 1.04)], $p < 0.001$; where the odds ratio gives the corresponding increase in odds for an increase in age of a single year). Gender was not associated with CDP status. Within the CDP population 52 (51.5%) CDP cases were male, whilst in the control group 9793 (46.0%) were male ($p = 0.274$).

3.3. Co-morbidities

Patient variables, including co-existing pathology and surgical interventions, were examined for an association with CDP status. Univariate analysis identified a number of co-pathologies which were significantly associated with CDP status (Table 1.).

Multivariate analysis was therefore subsequently performed on the eight univariate analysis variables felt to be most clinically relevant. This demonstrated that the following factors were independently associated with positive *C. difficile* status: Age ($p < 0.001$), gastrointestinal disease ($p < 0.001$), malignancy ($p < 0.001$), respiratory disease ($p < 0.001$), circulatory disease ($p < 0.001$), diabetes mellitus ($p < 0.05$), anaemia ($p < 0.05$) and gastrointestinal surgery ($p < 0.05$) (c-index = 0.788) (Table 2).

3.4. Outcomes

The median LOS for CDP cases was significantly longer than non-CDP controls (16 days [interquartile range (IQR) 8–33] versus 2 days [IQR 1–5], $p < 0.001$). For cases, the median number of days from admission to the surgery wards until CDP status and from CDP status until discharge were both significantly longer than the total