The impact of the COVID-19 pandemic on antimicrobial prescribing at a specialist paediatric hospital- an observational study

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Abstract

Introduction

The COVID-19 pandemic has severely impacted healthcare delivery and there are growing concerns that the pandemic will accelerate antimicrobial resistance.

Methods

Data on patient characteristics and antimicrobial administrations for inpatients treated between 29 April 2019 and Sunday 28 March 2021 were extracted from the electronic health record at a specialist children's hospital in London, UK. Interrupted time series analysis was used to evaluate antibiotic days of therapy (DOT) and the proportion of prescribed antibiotics from the WHO 'Access' classification.

Results

A total of 23,292 inpatient admissions were included. Prior to the pandemic there were an average 262 admissions per week compared to 212 during the pandemic period. Patient demographics were similar in the two periods but there was a shift in the specialities that patients had been admitted to. During the pandemic, there was a crude increase in antibiotic DOTs, from 801 weekly DOT before the pandemic to 846. The proportion of Access antibiotics decreased from 44% to 42%. However, after controlling for changes in patient characteristics, there was no evidence for the pandemic having an impact on antibiotic prescribing.

Conclusion

The patient population in a specialist children's hospital was affected by the COVID-19 pandemic, but after adjusting for such changes there was no evidence that antibiotic prescribing was significantly affected by the pandemic. This highlights both the value of routine, high-quality EHR data and importance of appropriate statistical methods that can adjust for underlying changes to populations when evaluating impact of the pandemic on healthcare.

Background

There is growing concern that the COVID-19 pandemic will accelerate antimicrobial resistance (AMR) - an existing global health threat. High rates of antibiotic use in COVID-19 patients have been reported despite low rates of bacterial co-infections. [1] But perhaps more relevant to children who are generally mildly affected by the disease, are behavioural and structural changes in society and in healthcare settings that might impact how antibiotics are being used. A survey of hospitals and healthcare networks from June 2020 found that 65% of respondents thought that the pandemic had had a negative impact on antimicrobial stewardship (AMS) activities.[2] Factors such as increased pressure on healthcare workers, less opportunity for isolation of infectious patients and increased rates of empirical antimicrobial use for patients with respiratory symptoms could lead to increased antibiotic use; however, increased focus on hand hygiene in hospitals could lead to reductions in the spread of AMR and social distancing in society might lead to reductions in patients presenting at hospital with respiratory illnesses.[3] Understanding the impact of the pandemic on antimicrobial use can inform AMS policies and the response to future pandemics.

This study aimed to evaluate the impact of the COVID-19 pandemic on antibiotic prescribing in a tertiary paediatric hospital in London, UK. The changes to the patient population and to the use of all types of antimicrobials were described and multivariable regression models were used to estimate the effect on antibiotic.

Methods

Setting

The UK implemented restrictions to limit the spread of COVID-19. A first nationwide lockdown was implemented on 23 March 2020 and schools had moved online on 20 March 2020. This was followed by a month-long second national lockdown in November 2020 and a third lockdown in January 2021.[4]

Great Ormond Street Hospital (GOSH) is a paediatric tertiary care hospital in London with an established AMS team.[5] The AMS team comprises an antimicrobial pharmacist, an infectious disease consultant and a microbiology consultant and their work include a weekly hand over and ward rounds on four days of the week. AMS activities continued at the same level compared to pre-pandemic, however, the face-to-face stewardship rounds transitioned to a virtual format using the comprehensive electronic patient record. As part of a systems response to the pandemic, most complex paediatric inpatients in North Central London CCG were cared for at GOSH from April 2020, instead of their local hospital. Working patterns were also affected with more staff working remotely, being off sick or being deployed to other hospitals.

Data

This study used routinely collected deidentified hospital data from inpatients at GOSH between 29 April 2019 and 28 March 2021 and who spent at least one night in hospital (ethical approval (17/LO/0008)). Admissions data was linked to data on treatment speciality, surgical encounters and medication prescribing data. Patients older than 25 years of age when admitted were excluded from the study (<1% of admissions) but no other exclusion criteria were applied.

Descriptive statistics of patient characteristics were derived from information recorded at admission (see Table S1 for definitions).

Administration of any antimicrobial on a calendar day, regardless of the number of administrations, represented one day of therapy (DOT). The number of patient days, including the day of discharge, was used as the denominator to calculate DOTs per 1000 patient days. Antibiotics administered were then grouped into Access, Watch and Reserve groups as developed by the WHO[6] and the proportion of Access antibiotics was calculated. All analysis was carried out using R version 4.0.3.[7]

Interrupted time series model

Interrupted time series models were used to compare counts of weekly antibiotic DOTs and the percent of Access antibiotics before the pandemic with the first year of the pandemic. The hypothesis was that the pandemic would cause an immediate and constant shift in antimicrobial consumption, commonly referred to as a level change with no lag. A negative binomial model with the number of patients days (logged) included as an offset was used for antibiotic DOTs and a binomial model was used to model the percent of Access antibiotics. See Table S5 for full list of variables tested for inclusion in the model. Model residuals were checked for signs of autocorrelation and tested for using the Breusch-Godfrey test and the final model was selected using the Akaike Information Criterion.

Results

There were 23,292 inpatient admissions (14,449 individual patients). There were 46 weeks included in the pre-COVID-19 period and 54 weeks in the COVID-19 period with each week contributing a minimum of 1,450 patient days. During the pre-COVID-19 period 44% of antibiotic DOTs were from the Access group compared to 42% during the pandemic.

There was no meaningful difference in the median age between patients admitted before and during the pandemic but those admitted in the COVID period more likely to get at least one antibiotic, antiviral or antifungal during their stay during the pandemic (Table 1). A positive COVID-19 test was found for 134 admissions. Median weekly patient days by speciality before and during the pandemic and variation over time can be found in Table S3 and Figure S1.

There was an increase in crude antibiotic and antiviral DOTs between the period before and during the pandemic (Table S4). Antibiotic DOTs by AWaRe group can be found in Table S5.

There was considerable variation in antibiotic DOTs per 1000 patient days between specialities but no speciality experienced a substantial change during the pandemic period (Figure 1a). There was substantial variation in the proportion of Access DOTs between specialities and the two specialities with highest antibiotic DOTs saw a decrease in the percent of Access DOTs (Figure 1b).

No statistically significant difference in antibiotic consumption could be detected for either antibiotic DOTs (incidence rate ratio 1.01 (95% confidence interval: 0.95, 1.08) or percent of Access antibiotics (odds ratio 0.83, (95% confidence interval: 0.04, 16.1))(Table S6). There was no evidence of autocorrelation - residual plots and autocorrelation tests can be found in supplementary materials (Figures S1 and S2). Table S2 shows the variables included in the final model for both outcomes.

Discussion

We found an increase in crude antibiotic DOTs per 1000 patient days but after adjusting for changes to the patient population using statistical modelling, there was no evidence of significant changes to antibiotic use during the first year of the pandemic.

The variation in changes in patient bed days between specialities explains most of the crude increase in antibiotic DOTs as there is substantial variation in antibiotic DOTs between specialities (Figure 1a). The large increases in intensive care patients during the COVID-19 pandemic are likely the result of transfers from other hospitals, as is the increase in number of cancer patients. These are patient groups with intrinsically greater use of antimicrobials. For specialities such as paediatric respiratory medicine, the reduction in bed days is likely a consequence of a decrease in demand due to behavioural changes during lockdown. The increase in the proportion of emergency admissions and the decrease in surgeries will have also accounted for some of the crude differences.

Antimicrobial use in patients with COVID-19 have been widely reported but far less is known about the wider impact on antibiotic prescribing for all patients.[8] Multiple studies have examined the pandemic impact on antibiotic prescribing in primary care in England and report a decrease in GP prescribing but an increase in dental prescribing.[9–11] There is more limited data regarding secondary care but there was a 4.8% increase in total prescribing rate between 2019 and 2020 in England but the patient population was vastly different to previous years[12]. This study provides new insights on the pandemic impact on inpatient antimicrobial use in children whilst considering the complex changes to patient population. It also highlights the value of a dedicated AMS team.

All data in this study was routinely collected and digitally extracted from a database. This study demonstrates how hospital EHR data can be used to evaluate important system changes and antimicrobial use monitoring. The value of EHR data featured heavily in the UK's five year National Action Plan to tackle antimicrobial resistance.[13] Despite this, a recent systematic review found that few antimicrobial use studies used solely digitally extracted data.[14]

A study strength is the use of a large routinely collected, comprehensive patient-level dataset. We used two different antibiotic use metrics which captured both volume changes as well as the antibiotic type. The rich data and metric choice provide a more accurate overview of the changes to antimicrobial use and their appropriateness. Interrupted time series models were used which allowed controlling for the substantial 1. Hughes, S., Troise, O., Donaldson, H., Mughal, N. & Moore, L. S. P. Bacterial and fungal coinfection among hospitalized patients with COVID-19: a retrospective cohort study in a UK secondary-care setting. *Clin. Microbiol. Infect.* **26**, 1395–1399 (2020).

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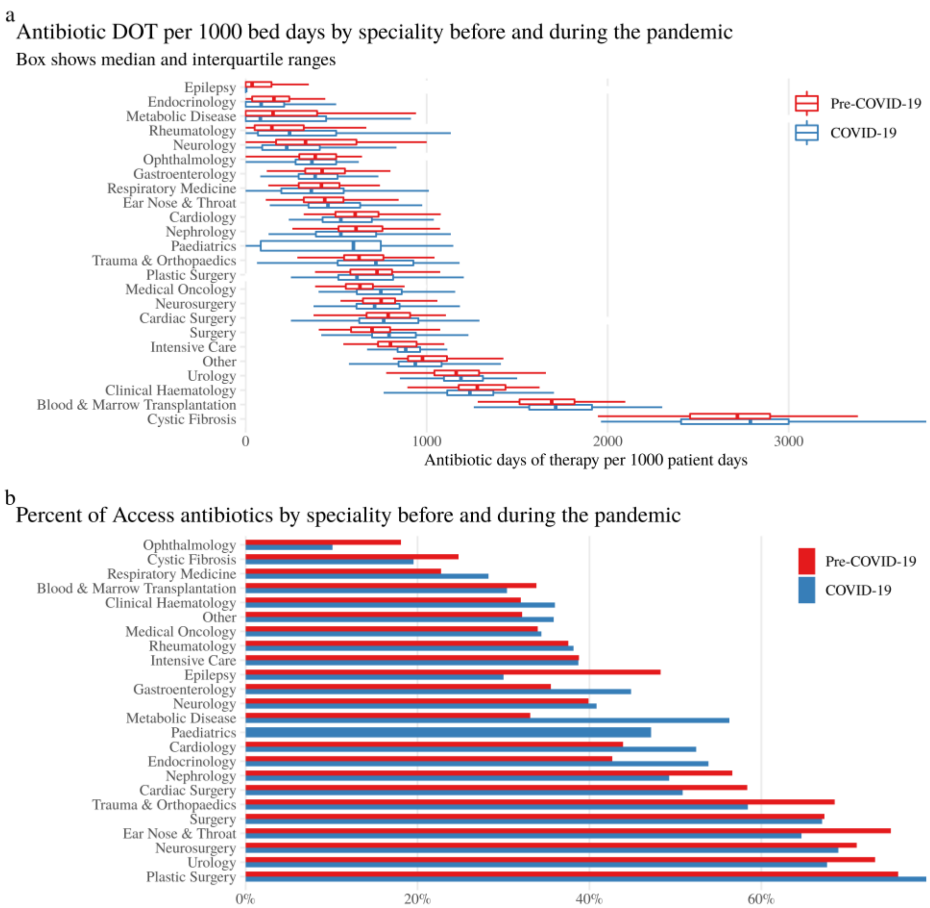
Table 1: Patient level characteristics before and during the COVID period

Characteristic	Pre-COVID-19, N = 26,531	COVID-19, N = 22,545	p-value[a]
Age (years)	5.3 (1.8, 10.7)	5.2 (1.4, 11.2)	0.14
Male	6,449 (55%)	6,375 (56%)	0.3
Any theatre encounter	5,577 (48%)	5,023 (44%)	<0.001
Admission type			<0.001
Elective	9,802 (84%)	8,404 (74%)	
Emergency	690 (5.9%)	1,185 (10%)	
Other	27 (0.2%)	46 (0.4%)	
Transfer	1,203 (10%)	1,798 (16%)	
Antibiotics during stay	5,925 (51%)	6,324 (55%)	<0.001
Antifungals during stay	945 (8.1%)	1,153 (10%)	<0.001
Antivirals during stay	475 (4.1%)	605 (5.3%)	<0.001
Antiprotozoal during stay	99 (0.8%)	117 (1.0%)	0.2
Immunosuppressants during stay	413 (3.5%)	445 (3.9%)	0.14

[1]Median (IQR); n (%)

[a]Wilcoxon rank sum test; Pearson's Chi-squared test

Figure 1


a
Antibiotic DOT per 1000 bed days by speciality before and during the pandemic
Box shows median and interquartile ranges
Epilepsy
Endocrinology
Metabolic Disease
Rheumatology
Neurology
Ophthalmology
Gastroenterology
Respiratory Medicine
Ear Nose & Throat
Cardiology
Nephrology
Paediatrics
Trauma & Orthopaedics
Plastic Surgery
Medical Oncology
Neurosurgery
Cardiac Surgery
Surgery
Intensive Care
Other
Urology
Clinical Haematology
Blood & Marrow Transplantation
Cystic Fibrosis
0
1000
2000
3000
Antibiotic days of therapy per 1000 patient days
Pre-COVID-19
COVID-19
b
Percent of Access antibiotics by speciality before and during the pandemic
Ophthalmology
Cystic Fibrosis
Respiratory Medicine
Blood & Marrow Transplantation
Clinical Haematology
Other
Medical Oncology
Rheumatology
Intensive Care
Epilepsy
Gastroenterology
Neurology
Metabolic Disease
Paediatrics
Cardiology
Endocrinology
Nephrology
Cardiac Surgery
Trauma & Orthopaedics
Surgery
Ear Nose & Throat
Neurosurgery
Urology
Plastic Surgery
0%
20%
40%
60%
Pre-COVID-19
COVID-19