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Original Contribution

Changing epidemiology and management of infectious diseases in US EDs[☆]



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ABSTRACT

Background: The rise of antibiotic-resistant pathogens is believed to have influenced the emergency department (ED) epidemiology and management of infectious diseases (IDs) since 2000.

Methods: Data from the National Hospital Ambulatory Medical Care Survey from 2000 to 2010 were used to examine temporal trends in the incidence of IDs presenting to EDs. Outcome measures included national visit rates, visit proportions, and antimicrobial prescriptions for all ID primary diagnoses, as well as for specific organ systems of interest (respiratory tract, skin/soft tissue, and urinary tract).

Results: An ID-related primary diagnosis was given in 18.3% (95% confidence interval, 17.9%-18.8%) of all ED visits during the study period. The hospitalization rate for these conditions is 7.8% (95% confidence interval, 7.3%-8.3%). The share of macrolide prescriptions for upper respiratory tract infections and lower respiratory tract infections increased by 34% and 46%, respectively, and that of quinolone prescription for lower respiratory tract infections doubled from 9% to 18.4% during the study period. Management of skin and soft tissue infections shifted from predominant use of cephalosporins to sulfonamides. For UTIs, quinolones were most commonly prescribed, with an increasing use of third-generation cephalosporins. Antibiotics were more frequently prescribed to patients who are white compared with (white: 60%, black: 57%, other races: 52%, P < .05).

Conclusion: The changing epidemiology of IDs diagnosed in US EDs reflects national trends in emerging pathogens and drug resistance. Broad-spectrum antibiotics are being prescribed at increasing rates. There are significant demographic disparities in nationwide antibiotic prescription practices.

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1. Introduction

Emergency departments (EDs) are an important venue to study trends in infectious disease (ID) epidemiology and management [1,2]. EDs have previously been shown to carry a disproportionate burden of infectious complaints and are often the first venue to identify and manage emerging outbreaks [1]. Among ID complaints in US EDs, the most common categories are upper respiratory tract infections (URIs), lower respiratory tract infections (LRIs), skin and soft tissue infections (SSTIs), and urinary tract infections (UTIs) [3].

The management of these infections has substantially changed over the past 15 years. For example, bacterial causes of respiratory infections have shown emerging resistance to first-line antibiotics [4]; meanwhile,

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viral respiratory infections have resulted in numerous major outbreaks, including the 2003 SARS epidemic and the 2009 H1N1 influenza pandemic. Similarly, the epidemiology and management of SSTIs are believed to have changed since the rise of community-associated methicillin-resistant Staphylococcus aureus (CA-MRSA) in the first decade of this century [5–8]. New resistance patterns have also been noted in UTIs, particularly with regards to β -lactams and fluoroquinolones [9,10].

In the wake of increasing resistance, health care settings, including EDs, have adopted strategies of antibiotic stewardship, such as formulary restrictions, policies of prior approval, and provider education [11]. These efforts take into account local resistance patterns because, both globally and within the United States, there are significant regional variations in antibiotic resistance [12]. There are also regional variations in provider prescription practices for common infections [3]. However, few studies have examined individual demographic disparities in prescription practices for commonly treated infections.

The primary objective of this study is to characterize the temporal trend of ED visits from 2000 to 2010 for all ID-related diagnoses, with an added focus on the most common organ systems of infections (URIs, LRIs, SSTIs, and UTIs). A secondary objective is to characterize antimicrobial prescription practices for each of these classes and relate them to the described epidemiology. Finally, we aimed to explore

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whether demographic and regional disparities accounted for variability in antibiotic prescriptions.

2. Methods

2.1. Study design

This study examines a cohort of ED visits from 2000 to 2010 using the National Hospital Medical Care Survey (NHAMCS). For each year, we evaluated the total number of ED visits, the number of infection-related ED visits, as well as the basic demographics and antibiotic prescribing practices associated with each visit. This study was granted exempt status for human subjects research by Johns Hopkins University School of Medicine Institutional Review Board.

2.2. Study setting

The National Hospital Medical Care Survey is a nationally representative survey conducted by the Centers for Disease Control and Prevention and the National Center for Health Statistics (NCHS) [13]. It uses probability sampling of ED visits in 50 states and District of Columbia, excluding federal, military, and Veterans Administration hospitals. Basic ED visit information, including demographic (eg, age, sex, race) and clinical information (eg, reason for visit, prescriptions, ED diagnoses, and disposition) of sampled ED visits, was recorded in a standardized patient record form by trained staff.

Before 2006, antimicrobials were coded based on the drug "as entered" on the NHAMCS patient record form using NCHS-developed "drug entry code" and "generic code" classification as well as the FDA's National Drug Code Directory (NDCD) [14]. After 2006, drugs were coded using the "drug entry code" described above and coded based on their generic components and therapeutic classes using Multum Lexicon Drug Database. Multum classification categorized drugs into 3 therapeutic class schemes. Antimicrobials were coded as "anti-infectives" at level 1 with 20 second-level codes for major antimicrobial drug class (eg. cephalosporins) and 36 third-level codes for subcategory class (eg, third-generation cephalosporins). NCHS has provided guidance to transform NDCD before 2006 to the corresponding codes in the Multum Database to compare the drug prescription trend before and after the drug coding system change [15]. Data regarding ED diagnoses are coded according to the International Classification of Disease, Ninth Revision (ICD-9). We classified the primary ED diagnosis of each ED visit as infectious or noninfectious based on a previously described protocol (eTable 1 in the Supplement) which was restricted to those diagnoses that are always or almost always caused by infectious agents [16]. Thus, codes for sepsis and severe sepsis are not included because they have less specificity as to the cause or organ system involved and can include terms of noninfectious diagnoses [17].

2.3. Statistical analysis

Adjusted sample weights, strata, and primary sampling unit design variables provided by NHAMCS were included in all analyses using the SAS 9.3 SURVEYFREQ procedure (SAS Institute Inc, Cary, NC) which accounted for the 4-stage probability sampling scheme. These provided an unbiased national estimate of US ED visits if it was based on more than 30 cases in the sample data or if the relative standard error was greater than 30%. Results are reported as weighted frequencies, percentages, and 95% confidence intervals (CIs) for individual characteristics of interest. The visit rate per 1000 US civilian noninstitutionalized persons, which describes the amount of infectious diagnoses in the general population, could serve as a surrogate for the incidence of ID complaints among EDs throughout the United States. US population estimates of the civilian noninstitutionalized population used in computing annual visit rates for NHAMCS by selected demographics were provided by NCHS based on US Bureau of the Census estimates. We also reported

the visit proportion, which reflects the contribution of these visits relative to the other diseases. The visit proportion is valuable because it is independent of global changes in ED volume and utilization.

The national annual overall visit rates as well as sex-, age-, race-, and region-specific rates for IDs per 1000 US civilian, noninstitutionalized population were estimated using procedures for multistage survey data and US census data provided in NHAMCS documentation for public users of the NHMACS. The significance of differences in the ID-related ED visit rates or antibiotics prescription rate by specific demographic group in the data set was assessed using the χ^2 test. All percentages presented are weighted percentages. A multivariate logistic regression was performed to determine whether demographic characteristics (age group, sex, race, ethnicity, payment type, year of visit) of an ED visit or ED characteristics (geographical region, metropolitan statistical area, and type of hospital ownership) were associated with receipt of an antibiotic prescription for each ED diagnosis of interest after controlling for covariates. P < .05 was considered statistically significant.

3. Results

Among 1,290,774,445 total ED visits from 2000 to 2010 (95% CI, 1,174,165,294-1,407,383,596), IDs accounted for the primary ED diagnosis in 236,291,402 visits (95% CI, 213,269,698-259,313,106), corresponding to 18.3% (95% CI, 17.9%-18.8%) of all ED visits or 74 (95% CI, 67-81) ED visits per 1000 US civilian persons. As a group, 18.5 million (95% CI, 16.7-20.2 million) of these patient visits were admitted to hospital, which correspond to a hospitalization rate of 7.8% (95% CI, 7.3%-8.3%). Hospitalizations differed based on infection type: 19.1% of LRIs, 12.6% of UTIs, 11.1% of SSTIs, and 1.1% of URIs (P < .001). As compared with the Northeast, patients presenting to the South region were more likely to be hospitalized for URIs (OR, 2.02; 95% CI, 1.31-3.12) and LRIs (OR, 1.63; 95% CI, 1.34-1.99). White race was found to be a predictor in hospitalizations only for SSTIs (OR, 0.74; 95% CI, 0.60-0.93) when compared with other races.

Upper respiratory tract infections, LRIs, SSTIs, and UTIs together accounted 71.8% of all IDs visits (95% CI, 71.1%-72.5%). Visit rates per 1000 US civilian persons stratified by age, sex, race, ethnicity, and region are shown in Table 1, and proportions of ID-related US ED visits per 1000 ED visits by these demographics are shown in eTable 2 in the Supplement. Female patients had a significantly higher rate and proportion of ID-related visits than male patients (both P < .05). Black patients experienced a significantly higher share of diagnoses in US civilian population and in all ED visits compared with white patients (both P < .05). Visit rates also significantly varied by geographical region.

Overall ED visits increased from 108 million in 2000 to 130 million in 2010. The annual visit rate for all ID-related diagnoses remained stable between 71 and 77 per 1000 civilian population from 2000 to 2008; however, the rate increased by almost 20% to 88 per 1000 persons in 2009 before decreasing back to 77 per 1000 persons during 2010. As a proportion of all ED visits, ID-related complaints were stable between 17.2% and 18.7% for most years of the study period. The 2 years with higher ID-related visit proportions were in 2003 (19.2%) and 2009 (19.5%). Temporal trends are shown for each of the ID categories of interest in Fig. 1. During 2009, URIs and LRIs increased by 17% and 21%, respectively. The rate of ED visits for SSTIs also shows an increase during the past decade, with a higher rate of increase between 2000 and 2004 (80%; from 6.4 to 11.5 per 1000 persons) compared with 2005-2010 (18%; from 11.4 to 13.5 per 1000 persons).

Trends of antimicrobial prescriptions in EDs for each of the infectious categories of interest are shown in Fig. 2A-D. Patients with URIs were most commonly prescribed penicillins, and patients with LRIs were most commonly prescribed macrolide antibiotics. The use of macrolides for URIs and LRIs increased by 34% and 46%, respectively, during the study period. The use of quinolone antibiotics for LRIs doubled during the study period (from 9.0% to 18.4%). A total of 1.58 million (95% CI, 1.08-2.09 million) ED visits for LRIs were prescribed antivirals, which

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