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Assessment of Ambulatory Antibiotic Prescribing Trends for Urinary Tract Infections in Infants and Children

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Abstract

Objective: The aim of this research was to study the prescribing trends of antibiotics for adherence to the guidelines issued by the American Academy of Paediatrics by utilizing the National Ambulatory Medical Survey (NAMCS) 2016 database.

Methods: This was a retrospective, secondary database analysis research exploring the antibiotic prescribing patterns for Urinary Tract Infections (UTI) in infants and children aged 2 to 24 months for the year of 2016 using National Ambulatory Medical Care Survey data. This database was based on a sample of visits to non-federally employed office-based physicians who are engaged in direct patient care and community health centers. Patient sex, race, as well as the source of payment, and the provider type were among the demographic variables studied for adherence to the guidelines.

Results: The total number of ambulatory care visits was 316. Of those, 144 (45.6%) patient were prescribed inappropriate antibiotics. Nurse practitioners and physician assistants (48), general/family practitioners (31) and internists (28) were responsible for the majority of inappropriate prescriptions. African American patients (79) received inappropriate prescriptions in most of the cases.

Conclusion: Antibiotic resistance is a public health problem of increasing magnitude, and finding effective solutions to address this problem is critical. Antibiotic resistance is also an economic burden on healthcare. Adherence to guidelines minimizes antibiotic resistance and promotes patients and public health.

Keywords

Antibiotics; National Ambulatory Medical Survey; Urinary Tract Infections

Introduction

The United States Centres for Disease Control and Prevention (CDC) estimates that the infections caused by antibiotic-resistant bacteria result in about 2 million cases of illness and 23,000 deaths in the U.S. annually [1]. The European Centre for Disease Prevention and Control produces similar numbers, estimating that antibiotic-resistant bacteria kill approximately 33,000 Europeans every year [2]. Prevalence of Urinary Tract Infections (UTI) in the US is about 7 per cent in patients aged infants and children 2 to 24 months [3]. It is estimated that Paediatric Urinary Tract Infection (UTI) costs the healthcare system upwards of 180 million dollars annually, and accounts for over 1.5 million clinician visits per year [4]. UTIs account for 1.8% of all paediatric hospitalizations. At the beginning of the last decade, the hospital costs for UTIs were $2,585 per hospitalization and rose to $3,838 by 2006. UTIs account for mean hospital charge increase from $6,279 to $10,489 per admission. That same pharmacoeconomic analysis study reports that aggregate hospital charges associated with UTIs exceeded $520 million in the last decade [5].

As we can see, UTIs present not only an increased in healthcare costs directly and decreased quality of life for the children, but also in indirect costs, such as lost wages resulting from parents missing work due to need for caring for the sick child. Identifying antibiotic prescribing patterns for pediatric UTIs is important in terms of recognizing whether there is antibiotic overuse or misuse, increased mediation costs and, most importantly, increased antibiotic resistance. The Urinary Tract is the most common site of occult and serious bacterial infections. Most of the time there is no identified source of infection [6]. Studies support that delays in appropriate treatment of pyelonephritis increase the risk of renal damage. The epidemiology of Urinary Tract Infections (UTIs) in children often varies by age, gender and other factors [7]. About 8% of girls and 2% of boys experience at least one UTI before the age of 7. UTI may lead to transient renal failure in 40% and permanent renal damage in 5% of patients [8]. The incidence of UTIs is the highest in the first year of life for all children but will often decrease among boys after infancy [7]. Rising health care costs, overutilization of health care resources, medication errors and inappropriate prescribing are challenging issues facing the health care researchers. According to Centre for Disease Control and Prevention (CDC), antibiotic resistance has risen in the last decade. Current antibiotics in the market are losing their effects at an alarming rate, while the development of new agents isn't keeping pace with it.

Despite the *"National Action Plan for Combating Antibiotic-Resistant Bacteria"* goal of reducing inappropriate outpatient antibiotic use by 50% by 2020, but the extent of in appropriate prescribing remains large [9]. When combing diagnosis and ages, 30% of the prescriptions prescribed from 2010 to 2011 in ambulatory care settings throughout the US were inappropriate. The "Clinical Practice Guidelines for the Diagnosis and Management of the Initial UTI in Febrile Infants and Children 2 to 24 Months", issued by the American Academy of Paediatrics indicate that the first-line antibiotics for the treatment of paediatric UTI should be cephalosporin, amoxicillin plus clavulanic acid, or trimethoprim-sulfamethoxazole. Adherence to American Academy of Paediatrics (AAP) guidelines for management of pediatric urinary tract infections (UTIs) can decrease the risk of bacteria developing resistance and translate into better clinical outcomes. Inappropriate antibiotics can contribute to antimicrobial resistance and may increase the risk of UTI [10]. When it comes to presentation it can present in many ways, it may present as asymptomatic bacteriuria as well as complicated or uncomplicated infections in the upper and lower urinary system. The goal of therapy is to provide the patient with symptomatic relief and to prevent the progression of renal damage. Antibiotic selection in this case depends on identification of dominant uropathogens, severity of symptoms, patient follow up, pharmacokinetics, drug toxicity, cost, antibiotic resistance as well as community resistance patterns [8].

The guidelines prefer oral therapy over parenteral for empiric antibiotic selection, such as amoxicillin/clavulanate, trimethoprim/sulfamethoxazole, and oral cephalosporin's, such as cefixime, cefpodoxime, cefprozil, cefuroxime axetil and cephalexin based on mg/kg dosing. In case the patient experiences adverse drug reactions to oral agents or are unable to retain oral intake, the clinicians can switch to parenteral agents. Preferred intravenous choices are ceftriaxone, cefotaxime, ceftazidime, piperacillin, and aminoglycosides. When it comes to the duration of therapy for this patient population, the American Academy of Paediatrics recommends a seven to 14-day course for all children two months to two years old [10].

The aim of this research was to study prescribing patterns of antibiotics for adherence to the guidelines by the type of prescriber, prescriber and patient location, patient's age race, sex and other variables using NAMCS 2016 database. The research attempted to study whether prescribers are adherent to the guidelines. Appropriate prescribing of antibiotics is one of the most important tools to minimize antibiotic resistance and promote patients and public health.

Literature Review

UTIs (Urinary Tract Infections) represent common bacterial infections in children. UTIs are among the most common pediatric admission diagnoses. Younger children and females are more likely to be hospitalized. This infection has increased hospital charges disproportionately to hospital costs. The socioeconomic burden of pediatric UTI exceeds $520 million and is increasing at a rapid rate. For this reason, more children with UTI diagnosis depend on public insurance agencies for healthcare coverage [11].

Up to 20% of young children with renal damage diagnosed after UTI are at risk of recurrent UTIs, renal deterioration and renal scarring [12]. Renal scarring is most likely to occur in young children and delayed treatment is often an additional risk factor for scarring. A study by Copp et al. looking at national ambulatory antibiotic prescribing patterns for pediatric UTIs form the years 1998 to 2007, noted that third-generation cephalosporins are among the most commonly prescribed agents by ambulatory care physicians for paediatric UTIs, especially for febrile infants, who are more likely to experience complications [13]. Third-generation cephalosporin use has more than doubled from 1998 to 2007 [14].

Continuous prescribing of antibiotics, such as cephalosporin and carbapenems without any etiological diagnosis can lead to development of ESBL (Extended-Spectrum Beta-Lactamase) and CRE (Carbapenem-Resistant Enterobacteriaceae)-producing microbes. This resistance can lead to biofilm production by the bacteria and further result in recurrent pyelonephritis and renal scarring. The empiric use of antibiotics has to be taken into consideration with local epidemiology and antibiotic susceptibility [15].

Urine culture is a good diagnostic tool to tailor broad-spectrum therapy and avoid unnecessary empiric therapy [16]. In fact, about a third of children younger than 2 years of age don't have any urine testing performed before being prescribed an antibiotic for a UTI. A questionnaire completed by 82 general practitioners showed that only 14% regularly send urine from febrile infants and toddlers [17]. Sixty-three per cent sent urine from only up to 10% of patients, while 26% were unable to collect urine at all. Consulting local antibiogram for assistance with empiric antibiotic therapy selection can help reduce the empiric use of antimicrobials. Antibiotic susceptibility results from bacteria isolated in prior urine cultures should always be performed before selecting empiric UTI therapy. Lastly, one should consider empiric treatment only for those at highest risk for UTI and with the greatest likelihood of clinical benefit from prophylaxis [18]. The study conducted by Lutter et. al concluded that children who receive prophylactic antibiotics and are admitted to the hospital for UTIs are often infected with an organism that is resistant to third-generation cephalosporin [19].

According to a study by Antoon et. al, despite susceptibility of infants and young children to empiric antibiotics being about 87%, it can result in resistance and increased the length of hospital stay, especially among those who are afebrile, admitted to intensive care unit and those with *E. coli* infection. This highlights the importance of continued surveillance of such patients in this age group [20]. A cohort by Dore-Bergeron et al. showed that treatment with intravenous antibiotics can have a success rate of about 86%. This includes normalization of temperature within 48 hours, negative control urine and blood culture results, given the cultures were performed, as well as absence of hospitalization [21].

There has been a decline from 50% to 19% in the practice of intravenous antibiotic prescription of longer than 4 days for UTI in infants less than 60 days old from 2005 to 2015 without an increase in hospital readmissions. This emphasizes the appropriateness of short-course intravenous antimicrobial therapy for pediatric UTI [22]. A large cohort study has also shown that young infants with UTIs can be successfully treated with a short 3-day course of intravenous antibiotics without any treatment failure. Only severe illness and known abnormalities of genitourinary tract are predictors of treatment failure, in which case a longer course of treatment is recommended [23].

When it comes to demographic variables having a role in antibiotic prescribing patterns for UTI, children less than 2 years of age are 3.7 times more likely to be prescribed a broad-spectrum antibiotic compared to children 13 to 18 years of age. As of 2007, age less than 2 years, female gender, and the presence of temperature of 100 [4]. F or greater were predictors of receiving a broad-spectrum antimicrobial agent, while most pediatric UTIs are susceptible to narrower-spectrum agents [14]. There is evidence suggesting that a fluoroquinolone and the probiotic combination can decrease the frequency of recurrent UTIs, decrease antibiotic course and healthcare costs in paediatric population [24].

Methodology

In this retrospective, secondary database analysis research, antibiotic prescribing patterns for UTIs in febrile infants in children aged 2 to 24 months for the year of 2016 were studied using National Ambulatory Medical Care Survey data. This database was based on a sample of visits to non-federally employed office-based physicians who are engaged in direct patient care and community health centres. Patients with a primary diagnosis of UTIs were extracted from the data using NAMCS ICD-10 code "N 39.0". After selecting the cases, the data was analysed to see whether the antibiotics prescribed were first-line and compliant with American Academy of Paediatrics 2011 guidelines. According to these guidelines, cephalosporin, amoxicillin plus clavulanic acid, or trimethoprim-sulfamethoxazole is first-line therapies [10]. Oral empiric therapy, such as amoxicillin/clavulanate, trimethoprim/sulfamethoxazole, and oral cephalosporins, such as cefixime, cefpodoxime, cefprozil, cefuroxime axetil and cephalexin, is preferred over parenteral, which, for the purposes of this study, were considered appropriate first-line therapies.

Patient sex, race, as well as the source of payment, and the provider type were among the operational factors used in data analysis. Sources of payment were defined as coverage through private insurance, Medicaid, Medicare, or other state-based programs, self-pay, workers compensation, and charity. All variables were categorized into "patient" or "physician" factors. Data analysis was performed using Statistical Package for Social Sciences (SPSS) software for descriptive data analyses and statistical coding. For descriptive analysis, we used means, standard deviations, and chi-square test to explore the relationship between various demographic variables to adherence to the guidelines. The extracted data set was checked for integrity, equality, and distribution of number of records in every phase of analysis. The hypothesis focused on whether the number of non-first-line antibiotics prescribed was related to physician specialty, geographic region and various patient-specific demographics, such as gender, race or payment type.

Results

The majority of the sample were males (60%), black (34.5%), followed by white (32.9%) and Hispanic (19%) population. Outpatient visits mostly occurred in the South (35.1%), followed by North (22.8%). The majority of the patient visits were paid by state/county charity programs (41.1%), followed by Medicaid (31.3%) and private insurances (15.8%). Most of the patients were seen by a nurse practitioner or physician assistant (40.2%), followed by a general/family practitioner (23.4%) and a urologist (18.4%) (Table 1).

Demographics	Frequency	Per cent
Gender		
Female	126	40
Male	190	60
Race		
White	104	32.9
African American	109	34.5
Asian	38	12
Hispanic	60	19
Other	5	1.6
Insurance type		
Self-pay	12	3.8
Private insurance	50	15.8
Medicaid	99	31.3
State/county charity programs	130	41.1
Other	25	7.9
Region		
North	72	22.8
South	111	35.1
East	69	21.8
West	64	20.3
Provider type		
General/Family	74	23.4
Internist	35	11.1
Pediatrician	22	7
Urologist	58	18.4
Nurse Practitioner/Physician Assistant	127	40.2

Table 1: Samples.

Prescribing Pattern Based on Demographic Variables	Appropriate prescribing	Inappropriate prescribing	Chi-square
Gender			0.818
Female	70	56	
Male	102	88	
Race			0.000
White	77	27	
African American	30	79	
Asian	20	18	
Hispanic	44	16	
Other	1	4	
Insurance type			0.038
Self-pay	5	7	
Private insurance	24	26	
Medicaid	63	36	
State/county charity programs	72	58	
Other	8	17	
Region			0.000
North	42	30	
South	35	76	
East	46	23	
West	49	15	
Provider type			0.000
General/Family	43	31	
Internist	7	28	
Paediatrician	6	16	
Urologist	37	21	
Nurse Practitioner/Physician Assistant	79	48	

Table 2: Significant factor in prescribing practices.

The total number of ambulatory care visits was 316. In 172 (54.4%) of the cases, first-line or appropriate agents were chosen. This means inappropriate agents were prescribed at the end of 144 (45.6%) patient visits.

Nurse practitioners and physician assistants (48), general/family practitioners (31) and internists (28) were responsible for the majority of inappropriate prescriptions with internists having the biggest discrepancies between appropriate (7) and inappropriate (28) prescribing practices. This was also the case with paediatricians with appropriate agents given in 6 cases and inappropriate medications given in 16 cases. The prescribing pattern based on the provider type was found to be significant (χ^2=0.000). Antibiotics deemed inappropriate were often prescribed in South and North regions with prescribing practice being statistically significant in terms of geographic area (χ^2=0.000).

African American patients (79) received inappropriate prescriptions in most of the cases (χ^2=0.000). Most inappropriate prescriptions were given to patients whose visits were paid by state/county charity programs (58), Medicaid (36) and private insurances (26) (χ^2=0.038). As we can see, race, provider type and geographical area were related with prescribing patterns, while gender was not found to a significant factor in prescribing practices (Table 2).

Discussion and Conclusion

The analysis showed that the majority of inappropriate prescriptions were given to African Americans during the visits occurring in the South regions. This corresponds with data from other studies about South being one of the geographical areas with poor health and wellness [25], while African American population being amongst underserved populations As for the insurance type, the vast majority of the patients were members of state or county charity programs and Medicaid, which also corresponds to available data [11]. The frequency of the visits may suggest that the caregivers of those patients are more likely to utilize the resources available to them at no cost. However, the frequency of inappropriate prescribing being covered by those programs are proof of pediatric UTI representing a big socioeconomic burden.

Nurse practitioners and physician assistants accounted for most appropriate and inappropriate prescriptions possibly due to representing the majority of the sample. While this was also the case with general/family practitioners and urologists, the discrepancies between appropriate and inappropriate agents prescribed by internists were note-worthy. This can be explained by the lack of practice of internists in the paediatric population, as opposed to adults. While general/family practitioners and urologists among those responsible for most inappropriate prescriptions, they were also the ones prescribing most appropriate agents. This might be related to the assumption that they are more experience with paediatric population than internal medicine specialists. A surprising finding was that paediatricians, despite being the primary provider type caring for paediatric population, were as responsible for inappropriate prescribing practices as much as internal medicine specialists.

This study showed that in over 40% of the cases, inappropriate antibiotic agents were prescribed. These results are in line with the available data on appropriate prescriptions in paediatric populations ranging from 30% to as high as 67% [25,26].

It is no surprise that the treatment of UTIs has been a challenge to many providers when it comes to paediatrics. Among factors making its management challenging is diagnostic uncertainty. Because clinical presentation can be very non-specific in infants and reliable urine specimens for culture can only be obtained through invasive methods, such as urethral catheterization or suprapubic aspiration, diagnosis can be challenging and can result in treatment delay [10].

The present study was retrospective in nature and relied on the latest reported NAMCS data. It only includes outpatient visits for the period of 2015-2016. The data doesn't include all other visits not recorded by providers leading to non-response bias. We did not have access to medical patient medical records, thus we were not able to exclude those already receiving antibiotic or with recurrent UTIs. Another limitation was that we relied on provider's diagnosis of the condition and assumed the antibiotic agent was for the UTI rather than for other diagnoses.

For the cases using non-first-line agents, we were not able to verify whether the selection was due to allergy to first-line agents or merely the prescriber's choice.

Antibiotic resistance is a public health problem of increasing magnitude, and finding effective solutions to address this problem is critical. There are nonclinical factors influencing the use of antibiotics prescribing practices [27].

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