# Comparative Sensitivity Testing Of Escherichia Coli And Pseudomonas Aeruginosa Isolates From El Paso, Texas, USA And Ciudad Juarez, Mexico.

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**Citation**

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**Abstract**

Background: The U.S./Mexico border is more than 2,000 miles long and stretches 62.5 miles wide on each side. With more than 2 million residents, El Paso, Texas and Ciudad Juarez, Mexico comprise the largest U.S-Mexico border population. Every month, more than 4 million Americans and Mexicans cross the border to work, shop, visit, and seek medical care. It is hypothesized that factors stemming from uncontrolled and easy access to antibiotics in Ciudad Juarez, together with the enormous flow of traffic across the border, make this a prime area for the development of bacterial resistance.Objective: To compare the bacterial sensitivity patterns of Escherichia coli and Pseudomonas aeruginosa isolates from two U.S.-Mexico border cities.Methods: Isolates were collected from patients seen and treated at two hospitals in El Paso and two in Ciudad Juarez. The organisms were tested at a reference laboratory in El Paso according to NCCLS standards. Statistical analyses were performed using SAS to compare proportions of susceptible organisms between El Paso and Juarez.Results: A total of 364 Escherichia coli and 285 Pseudomonas aeruginosa isolates were identified and tested. Escherichia coli isolates in Juarez were more frequently resistant to aztreonam, cefazolin, cefepime, cefotaxime, ceftriaxone, ciprofloxacin, and gentamicin ($p<.05$) as compared to those in El Paso. Extended spectrum betalactamases (ESBL)-producing Escherichia coli were more prevalent in Juarez as compared to El Paso. Pseudomonas aeruginosa isolates in Juarez were more frequently resistant to amikacin, aztreonam, ceftazidime, ciprofloxacin, gentamicin, piperacillin/tazobactam, and tobramycin as compared to those in El Paso ($p<.05$).Conclusion: We documented significant differences in bacterial resistance between the two cities for Escherichia coli and Pseudomonas aeruginosa isolates. Although we encountered some variations, these differences supported that antimicrobial resistance is more prevalent in Juarez, Mexico than in El Paso, Texas for these two organisms.

## INTRODUCTION

This study was conducted in Ciudad Juarez, Chihuahua, Mexico and neighboring El Paso, Texas, USA which are within walking distance of each other. With a combined border population exceeding 2 million, Ciudad Juarez and El Paso, Texas comprise the largest population on the U.S.-Mexico border. Ciudad Juarez is more than twice the size of its sister city in the U.S. and is the fourth largest city in Mexico. It is estimated that 32 million[1] people cross the northbound border legally each year, many of them crossing the border daily (more than 90 000) to work, shop, attend school, seek medical care, or to visit family and friends. Although exact figures are not available, it is known that many El Pasoans cross the southbound border for similar reasons, many of them seeking to purchase medications that are more accessible and less expensive. In a recent study[2], approximately 35% of the El Paso population reported having purchased medications in Ciudad Juarez in the previous twelve month period. Because many prescription medicines including antibiotics are available without a prescription in Mexico, it has been speculated that overuse of these over-the-counter antibiotics could increase resistance patterns in this area.

In 1997, the World Health Organization (WHO) provided recommendations regarding how to best combat the escalation of bacterial resistance in developing countries.[3] These recommendations clearly point out the important role that antibiotic misuse plays in the development of antibiotic resistance. Surveillance of these patterns is essential to

evaluate the extent and impact of antibiotic use and misuse.

Although very few studies have looked at bacterial resistance patterns in Latin America, the SENTRY studies have produced some important findings. The SENTRY Antimicrobial Surveillance Program is a prospective, longitudinal, multinational study aimed at tracking the emergence of antimicrobial resistance worldwide.[4] In some of the early reports, Staphylococcus aureus and Escherichia coli were ranked one and two respectively as the organisms most frequently associated with bloodstream infections. Streptococcus pneumonia and Pseudomonas aeruginosa were ranked sixth and seventh. Significant differences were noted between the susceptibility patterns in the U.S. and Canada for S. aureus, Enterococcus spp., and Enterobacter spp.. In the U.S., 73.8% of Staphylococcus aureus was susceptible to oxacillin compared to 97.3% in Canada. The authors speculated that even though the reason for this is unclear it may be due to differences in antibiotic utilization practices.

The SENTRY study group also reported results from a number of studies that evaluated antimicrobial susceptibility patterns for bacterial isolates from Latin America. In one study of patients with pneumonia,[5] Pseudomonas aeruginosa and Staphylococcus aureus were the two most common organisms isolated. The most active antibiotic against Pseudomonas aeruginosa was meropenem ($MIC_{50}$, 1 g/mL; 71.6% susceptible) followed by amikacin ($MIC_{50}$, 4 g/mL; 70.4% susceptible). In another SENTRY study in Latin America, Andrade[6] reported increased resistance to first line agents among urinary tract pathogens. The SENTRY group has conducted the most comprehensive studies of this type and has carried out surveillance studies in many different U.S. cities and countries around the world.

MYSTIC is another global surveillance program that monitors resistance patterns in many medical centers around the world.[7] This program evaluates and compares susceptibility patterns of meropenem against many gram negative and gram positive organisms and has produced large amounts of data. While antibiotic surveillance studies are seen as essential in monitoring bacterial resistance, neither of these two large groups has conducted any type of surveillance in cities along the U.S.-Mexico border, an area that possesses unique factors that make resistance an issue of increasing concern. To our knowledge, our group is the only one that has begun to evaluate antibiotic resistance patterns in this setting.

## METHODS

Specimens for bacterial culture were collected from patients seen and treated for infections at two hospitals in El Paso and two hospitals in Ciudad Juarez over a period of two years. Comparable hospitals were chosen on each side of the border (one county and one private hospital, each with a similar number of beds). Institutional Review Board approval was obtained at each of the four hospitals selected as well as at The University of Texas at El Paso. All organisms were batched and stored under appropriate conditions and were collected on a regular basis. All isolates obtained from participating hospitals were coded in a way such that only the investigators could know the hospital of origin.

Cultures of the organisms obtained from hospitals in Ciudad Juarez were transported according to CDC-approved guidelines for the transportation of biological samples.[8] Importation permits were obtained from the CDC and USDA. A customs broker was used to manage the logistics of U.S. and Mexican Customs. The isolates were packaged and labeled to expedite clearance through the U.S. Public Health Service of Quarantine and release by U.S. Customs. They were also packaged to withstand breakage and leakage of the contents and labeled accordingly as specified in the following federal regulations: USPHS 42 CFR Part 72 – Interstate Shipment of Etiologic Agents and DOT 49 CFR Part 173 – Transportation of Etiologic Agents. All samples collected were identified by a hospital code, date of collection, body site, inpatient or outpatient status, and zip code. No patient identifiers were obtained with the samples.

Organisms were transported frozen in Microbank® vials on dry ice. Samples were transported to a reference microbiology laboratory in El Paso for microbial identification and antimicrobial susceptibility of Escherichia coli and Pseudomonas aeruginosa strains. Upon arrival, the isolates were sub-cultured onto appropriate agar media to assess for viability and purity. Once correctly identified, isolates were stored at -70C until antimicrobial susceptibility testing was performed. These analyses were performed by using the Microscan® System according to the National Committee for Clinical Laboratory Standards (NCCLS) (NCCLS 1999).[9] Statistical analyses (Fisher's Exact Tests, SAS Version 9.1) were performed to compare proportions of resistant organisms in El Paso and Ciudad Juarez. The antimicrobials used for testing were selected from standard recommended panels for these organisms.

## RESULTS

A total of 356 Escherichia coli isolates were tested (181 from El Paso hospitals and 175 isolates from Ciudad Juarez hospitals). Statistically significant differences with a $p<0.05$ were noted in susceptibility to aztreonam, cefazolin, cefepime, cefotaxime, ceftriaxone, ciprofloxacin, and gentamicin. ESBL-producing Escherichia coli was more prevalent in Ciudad Juarez hospitals (15% and 14%) than in El Paso hospitals (2% and 6%).

A total of 290 Pseudomonas aeruginosa isolates were tested (196 from El Paso hospitals and 94 from Ciudad Juarez hospitals). Statistically significant differences with a $p<0.05$ were noted in susceptibility to amikacin, aztreonam, ceftazidime, ciprofloxacin, gentamicin, piperacillin/tazobactam, and tobramycin. Tables 1 and 2 provide a complete description of susceptibility results in both cities. Multidrug resistant Pseudomonas aeruginosa (resistant to ceftazidime, ciprofloxacin, and tobramycin) was found in 19.1%, 0%, 1%, and 3.1% of the isolates in Ciudad Juarez hospitals (A and B) and El Paso hospitals (A and B), respectively.

### Figure 1

Table 1. Percent of susceptible isolates

| Antibiotic | Juarez (n=85) Hosp A | Juarez (n=88) Hosp B | El Paso (n=96) Hosp A | El Paso (n=95) Hosp B | p-value |
|---|---|---|---|---|---|
| Amikacin | 99 | 99 | 99 | 99 | 1.0 |
| Amox-clav | 96 | 99 | 89* | 93 | <0.05 |
| Aztreonam | 85 | 84* | 97 | 94 | <0.01 |
| Ceftriaxone | 85 | 84* | 98 | 94 | <0.01 |
| Cefotaxime | 85* | 86 | 98 | 94 | <0.01 |
| Cefoxitin | 95 | 98 | 94* | 98 | 0.42 |
| Cefazolin | 82 | 81* | 88 | 85 | 0.60 |
| Amp-sulb | 35 | 35 | 43 | 32* | 0.45 |
| Ciprofloxacin | 60 | 55* | 75 | 62 | <0.05 |
| Tobramycin | 79 | 56* | 91 | 86 | <0.01 |
| Cefepime | 85* | 86 | 98 | 94 | <0.01 |
| Gentamicin | 80 | 72* | 91 | 86 | <0.01 |
| Imipenem | 99* | 99* | 100 | 100 | 0.36 |
| Levofloxacin | 61 | 56* | 74 | 64 | 0.07 |
| Pip-tazo | 97 | 97 | 94 | 93* | 0.57 |
| TMP-SMX | 33* | 49 | 55 | 43 | <0.05 |

Amox-clav=amoxicillin plus clavulanate; Amp-sulb=ampicillin plus sulbactam; Pip-tazo=piperacillin plus tazobactam; TMP-SMX=trimethoprim plus sulfamethozaxole

*Hospital with the lowest susceptibility to antibiotic

**Figure 2**

Table 2. Percent of susceptible isolates

| Antibiotic | Juarez (n=68) Hosp A | Juarez (n=21) Hosp B | El Paso (n=98) Hosp A | El Paso (n=98) Hosp B | p-value |
|---|---|---|---|---|---|
| Amikacin | 79* | 100 | 88 | 94 | 0.01 |
| Aztreonam | 82 | 95 | 81 | 63* | <0.01 |
| Ceftazidime | 60* | 95 | 94 | 82 | <0.01 |
| Ciprofloxacin | 68 | 61* | 82 | 68 | 0.06 |
| Tobramycin | 63* | 67 | 88 | 78 | <0.01 |
| Cefepime | 66* | 95 | 88 | 75 | <0.01 |
| Gentamicin | 59* | 67 | 81 | 65 | 0.01 |
| Imipenem | 84* | 86 | 90 | 89 | 0.64 |
| Levofloxacin | 69 | 71 | 80 | 68* | 0.28 |
| Pip-tazo | 99 | 100 | 98 | 88* | <0.01 |
| Piperacillin | 93 | 91 | 98 | 83* | <0.01 |

Pip-tazo=piperacillin plus tazobactam

*Hospital with the lowest susceptibility to antibiotic

## DISCUSSION

The short term implication associated with the observed difference in susceptibility relates to the empirical selection of antibiotics. Guidelines recently published by The Medical Letter, May 2007,[11] recommended cefotaxime, ceftriaxone, cefepime, or ceftazidime as the empiric drug of choice for Escherichia coli infections . All of these drugs had susceptibility percentages >85% in both Juarez hospitals and >94% in both El Paso hospitals. Alternative empiric treatment options for Escherichia coli that are recommended by The Medical Letter are ampicillin and gentamicin, other aminoglycosides, amoxicillin/clavulanate, piperacillin/tazobactam, imipenem, aztreonam and fluoroquinolones. Ampicillin tested in this study had 74% and 78% resistance rates in Ciudad Juarez hospitals and 66% and 77% in El Paso hospitals. Although recommended by The Medical Letter as one of the alternative treatments, ampicillin plus sulbactam showed low susceptibility rates on both sides of the border (35% in Ciudad Juarez and 43% and 32% in El Paso). For acute uncomplicated urinary tract infections The Medical Letter recommends trimethoprim/sulfamethoxazole, but resistance to these two agents was as high as 67% in Ciudad Juarez and 57% in El Paso. The two fluoroquinolones tested in this study, ciprofloxacin and levofloxacin, showed relatively low susceptibility patterns against Escherichia coli (range of 55% to 75% for all hospitals). Piperacillin/tazobactam had susceptibilities of 97% in Juarez hospitals and >93% in both El Paso hospitals. Imipenem has susceptibility percentages of 99% in both Juarez hospitals and 100% in El Paso hospitals.

Overall, empirical treatment of systemic Escherichia coli infections with first line drugs recommended by The Medical Letter would seem to be appropriate. On the other hand, recommended alternative treatments may not always provide sufficient coverage. However, based on our findings, it appears that piperacillin/tazobactam, imipenem, and aztreonam may serve as options if for any reason the drugs of choice cannot be used. Although our study did not specifically evaluate the treatment of urinary tract infections, documented susceptibility rates suggest that trimethoprim/sulfamethoxazole may not be appropriate as a drug of choice for the treatment of acute uncomplicated urinary tract infections. An additional observation is that when examining the antibiotics with the lowest susceptibility patterns, eleven of these were linked to organisms tested from Ciudad Juarez while only four of these were linked to organisms from the four El Paso hospitals. Table 1 provides a complete list of antibiotics tested and their respective susceptibility rates.

Guidelines recently published by The Medical Letter, 2007, recommend piperacillin/tazobactam plus or minus an aminoglycoside as the drug of choice for empirical therapy against Pseudomonas aeruginosa systemic infections. In our study, piperacillin/tazobactam had 99% and 100% susceptibilities in both Ciudad Juarez hospitals and 98% and 88% in El Paso hospitals against this organism, indicating that this would be an appropriate first line agent. Alternative drugs of choice options for empiric therapy include ceftazidime, ciprofloxacin, imipemen, aztreonam, cefepime, plus or minus an aminoglycoside. Of the pathogens tested in this study, 60% were susceptible to ceftazidime at the Ciudad Juarez public hospital, indicating that this agent may not be a good choice for the treatment of infections caused by this organism. In both El Paso hospitals, ceftazidime showed susceptibilities higher than 80% which supports the use of this agent. On the other hand, only 64% of the organisms tested at the El Paso private hospital were susceptible to aztreonam, which is of some concern. The aminoglycoside, amikacin, had 79% susceptibility at the Ciudad Juarez public hospital and 100% susceptibility at Ciudad Juarez public hospital. Two other aminoglycosides,

tobramycin and gentamicin, had similar susceptibility percentages at public and private hospitals in both cities (63% and 67% susceptibility at the Ciudad Juarez hospitals and 87% and 78% susceptibility at the El Paso hospitals). Based on these findings, empirical treatment with first line drugs recommended by The Medical Letter seem appropriate for treating systemic Pseudomonas aeruginosa infections. However, in the Ciudad Juarez private hospital, it appears that gentamicin and tobramycin (susceptibility of 67%) may not be appropriate choices for use in combination therapy when compared to amikacin (100% susceptibility). In addition, alternative treatments recommended by The Medical Letter may not always be appropriate based on the observed variations in susceptibility patterns in this area. Similar to what was seen with Escherichia coli, the antibiotics with the worst susceptibility profiles for Pseudomonas aeruginosa were more commonly linked to Ciudad Juarez isolates as compared to El Paso (seven in Juarez vs. three in El Paso). Table 2 highlights hospitals with the lowest susceptibilities for each antibiotic tested. Finally, the incidence of multidrug resistant Pseudomonas aeruginosa was 19.1% in one of the hospitals in Ciudad Juarez, which is a much higher rate than that published in a recent report of U.S. hospitals (9.3%).[12]

The rates of antimicrobial resistance associated with the two gram-negative organisms tested in the present study stand in contrast to findings from a previous study where we reported higher incidence of methicillin-resistant Staphylococcus aureus (MRSA) in El Paso as compared to Ciudad Juarez.[13] In that study, 44.3% of isolates were MRSA in El Paso as compared to 7.8% MRSA in Ciudad Juarez. It seems apparent to us that resistance patterns are organism-specific and are influenced by the common antibiotics prescribed in the area.

We acknowledge that there are some important limitations to our study. Due to the complexity of this study, in terms of dealing with numerous institutions, logistics of border crossings in transporting isolates, and bi-national standards related to the practice of medicine, clinical and epidemiologic data was not collected. This type of data may have allowed for a more in depth examination of prescribed antibiotics, usage patterns, related indications and patient outcomes. Additionally, there were fewer cultures from Ciudad Juarez because routine cultures are not always obtained in Juarez hospitals. A greater number of samples may have allowed us to draw more robust conclusions from our data.

## CONCLUSIONS

We documented significant differences in prevalence of antimicrobial resistance in Ciudad Juarez hospitals as compared to El Paso hospitals for both Escherichia coli and Pseudomonas aeruginosa isolates. In general, these differences supported our hypothesis that antimicrobial resistance is more prevalent in Ciudad Juarez, Mexico than in El Paso, Texas for these two organisms. Our results demonstrate the importance of monitoring hospital-specific bacterial susceptibility patterns in achieving optimal antibiotic selection. Finally, antibiotics recommended as first line agents by The Medical Letter appear to be appropriate in most cases with the possible exception of Escherichia coli in acute uncomplicated urinary tract infections. On the other hand, recommended alternative agents may produce more variable results.

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## CONFLICT OF INTEREST

All authors have no conflicts of interest with the study. There are no financial nor personal relationships with other people or organizations that could inappropriately influence or bias our work.

This study was approved by the University of Texas at El Paso Institutional Review Board.

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