Prevalence of Ceftriaxone Susceptible, Piperacillin-tazobactam Non-susceptible *Escherichia coli* Bacteremia in Patients with Hematologic Malignancy

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BACKGROUND

- Piperacillin-tazobactam (TZP) is commonly used in the treatment of proven or suspected bacteremia in patients with hematologic malignancy
- Hyperproduction of *bla*TEM and *bla*SHV and the presence of inhibitor resistant TEMs have been found to contribute to TZP resistance
- TZP resistance is common in ceftriaxone (CRO) resistant *Escherichia coli* (*E. coli*) isolates
- The prevalence of CRO susceptible, TZP nonsusceptible *E. coli* bloodstream infections is unknown in patients with hematologic malignancy

OBJECTIVES

- Primary: To determine the prevalence of CRO susceptible, TZP non-susceptible *E. coli* bacteremia in patients with hematologic malignancy
- Secondary: 28-day mortality and microbiological recurrence within 90 days

METHODS

- Retrospective cohort study of adult (age ≥ 18) patients with *E. coli* bacteremia on either the leukemia or stem cell transplant (SCT) services at The University of Texas MD Anderson Cancer Center between 8/2016 and 7/2019
- Isolates were categorized according to current CLSI resistance breakpoints and identified through review of microbiology lab reports in the EMR
- A first isolate was defined as the first positive blood culture
- Subsequent episodes of *E. coli* bacteremia were defined as any isolate obtained at least 24 hours after the first negative blood culture
- Stata software version 13.0 was used for data analysis

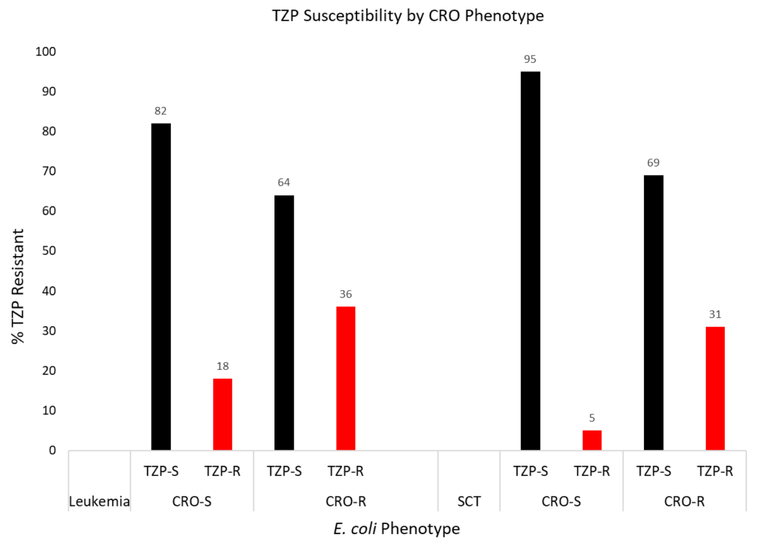
RESULTS

Table 1. Distribution of MICs

	CRO	TZP
MIC_{50} (ug/ml)	0.094	4
MIC_{90} (ug/ml)	≥64	128
Range (ug/ml)	0.094 to ≥64	3 to ≥256
Susceptible (%)	54	74
Intermediate (%)	1	8
Resistant (%)	45	16

Table 1. CRO and TZP MIC distributions of 404 *E.* coli bloodstream isolates

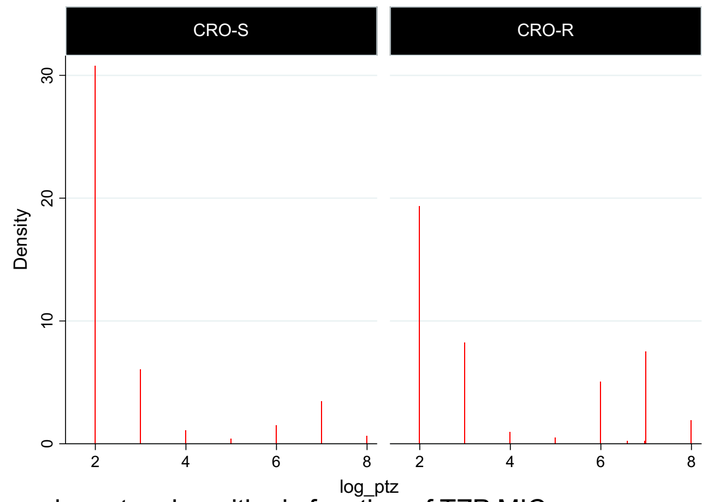
Figure 2. TZP Susceptibility by CRO Phenotype



CRO-S = CRO susceptible
CRO-R = CRO non-susceptible
TZP-S = TZP susceptible
TZP-R = TZP non-susceptible

Figure 2. Prevalence of TZP susceptibility by CRO resistance based upon service. The over all prevalence of CRO susceptible, TZP nonsusceptible *E. coli* was seen in 9.8% and 2.5% of leukemia and post SCT patients

Figure 1. TZP MIC by CRO Susceptibility



log_ptz = logarithmic function of TZP MIC

Figure 1. Logarithmic function of TZP MIC distribution based upon CRO sensitivity

- Higher prevalence of CRO resistant *E. coli* compared to CRO susceptible in TZP non-susceptible isolates (34.9% vs 14.2%, $p < 0.01$)
- 91% of CRO resistant isolates were extended-spectrum beta-lactamase (ESBL) producers
- The TZP MIC_{50} and MIC_{90} in CRO sensitive isolates were 4ug/ml and 64ug/ml, respectively
- TZP MIC_{50} and MIC_{90} in CRO resistant isolates were 8ug/ml and 128ug/ml, respectively
- TZP nonsusceptibility was more common in subsequent episodes of bacteremia compared to the first (39.4% vs 20.1%, p <0.01)
- The 28-day mortality rate of CRO susceptible, TZP non-susceptible *E. coli* bloodstream isolates was 22.6% (7 out of 31 patients)
- Compared to CRO susceptible, TZP susceptible *E. coli,* there was an increased likelihood of 90-day microbiological recurrence in the CRO susceptible, TZP non-susceptible group (OR 3.90; CI 1.42-10.75, p<0.01)

CONCLUSIONS

- The prevalence of TZP non-susceptible, CRO susceptible *E. coli* from patients with hematologic malignancy was 7.7% and had an increased likelihood of 90-day microbiological recurrence
- TZP nonsusceptibility became more common with subsequent episodes of bacteremia compared to the first
- TZP nonsusceptibility is common in patients with hematologic malignancy and *E. coli* bacteremia with significant variations by CRO resistance phenotype
- The clinical implications and genetic cause of this phenotype is currently unknown and warrants further investigation