



Letter to the Editor

Worrisome high frequency of extended-spectrum beta-lactamase-producing *Escherichia coli* in community-acquired urinary tract infections: A case–control study; methodological issues



We read with interest the valuable article by Castillo-Tokumori and colleagues published in the *International Journal of Infectious Diseases* (Castillo-Tokumori et al., 2017). The authors aimed to describe community-acquired urinary tract infections (CA-UTI) caused by extended-spectrum beta-lactamase (ESBL)-producing *Escherichia coli* and its risk factors. They conducted a case–control study involving 67 patients with ESBL and 105 patients with non-ESBL *E. coli* CA-UTI. The authors found that chronic corticosteroid use was significantly associated with ESBL CA-UTI, which is problematic.

The authors reported (in their Table 2) that there was a statistically significant association between chronic corticosteroid use and ESBL CA-UTI (crude odds ratio (OR) 8.39, 95% confidence interval (CI) 0.96–73.45; $p=0.023$). However, there are issues regarding the CI and p -value. In a statistically significant association, the CI should not cross unity (1) and the P -value should be less than 0.05 (Rothman et al., 2008). In the aforementioned association, the CI has crossed 1, whereas the reported P -value is less than 0.05. We examined this association and found it to be non-significant (correct P -value = 0.06) (Table 1).

Furthermore, the authors reported a large OR with a wide CI for the association between chronic corticosteroid use and ESBL CA-UTI in the univariate (OR 8.39, 95% CI 0.96–73.45) and multivariate models (OR 24.32, 95% CI 2.39–246.92), which is questionable. The researchers indicated that the large effect estimates and wide CIs resulted from the sparse data, as there were insufficient numbers of observations in the different strata of the independent and dependent variables (Greenland et al., 2016; Greenland and Mansournia, 2015). The sparseness of the data would have been severe in the multivariate models, since the

Table 1

Univariate association between chronic corticosteroid use and ESBL CA-UTI using ordinary and penalized logistic regression.

	ESBL	Non-ESBL
Corticosteroid use		
Yes	5	1
No	62	104
Estimated OR (95% CI)		
Ordinary logistic regression	8.38 (0.95–73.45)	
Penalized logistic regression	4.42 (0.86–22.46)	

ESBL, extended-spectrum beta-lactamase; CA-UTI, community-acquired urinary tract infection; OR, odds ratio; CI, confidence interval.

number of strata is increased in these models (Greenland et al., 2016).

The data provided by Castillo-Tokumori et al., on the association between chronic corticosteroid use and ESBL CA-UTI, are clarified in Table 1. The sparseness of the data was confirmed, as the number of observations was low and the adjusted OR and 95% CI were larger and wider, respectively, compared to the corresponding univariate OR and 95% CI. Hence, the bias due to sparse data should be removed using appropriate and efficient statistical methods, such as penalization via data augmentation (Greenland et al., 2016; Ayubi and Safiri, 2017). We re-analyzed the crude OR using the penalization method with log- f (2,2) prior distribution, and the estimations improved remarkably (Table 1). The adjusted OR could also be corrected using this method, but the individual data would be needed. Hence, we propose that Castillo-Tokumori et al. re-analyze their adjusted estimates using the method introduced herein, in order to obtain unbiased and valid estimates. It is expected that the adjusted unbiased association between chronic corticosteroid use and ESBL CA-UTI would be diluted and non-significant.

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Conflicts of interest

None of the authors has a conflict of interest to disclose.

Author contributions

EA and SS designed the study. EA and SS drafted the manuscript. Critical revision was done by EA and SS.

References

- Ayubi E, Safiri S. "Predictors of failure after single faecal microbiota transplantation in patients with recurrent *Clostridium difficile* infection: results from a three-year cohort study"; methodological issues. *Clin Microbiol Infect* 2017;23:890.
- Castillo-Tokumori F, Irey-Salgado C, Málaga G. Worrisome high frequency of extended-spectrum beta-lactamase-producing *Escherichia coli* in community-acquired urinary tract infections: a case–control study. *Int J Infect Dis* 2017;55:16–9.
- Greenland S, Mansournia MA. Penalization, bias reduction, and default priors in logistic and related categorical and survival regressions. *Stat Med* 2015;34:3133–43.
- Greenland S, Mansournia MA, Altman DG. Sparse data bias: a problem hiding in plain sight. *BMJ* 2016;352:i1981.
- Rothman KJ, Greenland S, Lash TL. *Modern epidemiology*. Lippincott Williams & Wilkins; 2008.

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