

Letter to the Editor

**Alarming increase in carbapenemase-producing *Klebsiella* spp causing bloodstream infections in pediatric population in India**

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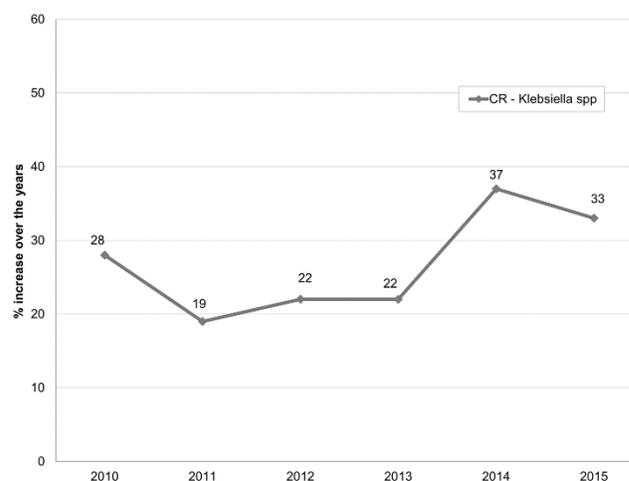
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Dear Editor,

Carbapenemases are a versatile group of  $\beta$ -lactamases characterized by their resistance to virtually all  $\beta$ -lactam antibiotics, including cephalosporins and carbapenems. This retrospective study was conducted to monitor the change in the trend of carbapenem-resistant (CR) *Klebsiella* spp causing bloodstream infections (BSI) in patients  $\leq 15$  years of age during January 2010 to November 2015 at Christian Medical College, Vellore, South India. Antimicrobial susceptibility testing was done by disk diffusion method as per CLSI guidelines, and isolates that were resistant to both imipenem and meropenem were included in the analysis. All the CR-*Klebsiella* spp were characterized by both phenotypic and molecular methods for carbapenem resistance. The total of *Klebsiella* spp isolated from BSIs over a five year period were as follows: 29 (2010), 77 (2011), 49 (2012), 45 (2013), 78 (2014) and 27 (2015). Of these, CR rates were found to be 28% (n = 8/29), 19% (n = 15/77), 22% (n = 11/49), 22% (n = 10/45), 37% (n = 29/78) and 33% (n = 9/27) in 2010 to 2015, respectively. Most of the CR *Klebsiella* spp exhibited co-resistance to penicillins, cephalosporins and other classes of drugs, except colistin and tigecycline. Among the CR *Klebsiella* spp, 39 isolates were randomly chosen and screened for the carbapenemases genes *bla*<sub>NDM</sub>, *bla*<sub>SPM</sub>, *bla*<sub>IMP</sub>, *bla*<sub>VIM</sub> and *bla*<sub>Oxa-48</sub> like [1]. Of the 39 isolates tested, 27, 3, 4 and 1 isolates were positive for *bla*<sub>NDM</sub>, *bla*<sub>Oxa-48</sub>-like, *bla*<sub>NDM+Oxa-48</sub>-like and *bla*<sub>NDM+VIM</sub> genes, respectively. Four isolates were negative for all the five genes tested. Notably, sequencing of two each of *bla*<sub>NDM</sub> and *bla*<sub>Oxa-</sub>

48-like positives revealed that all sequenced isolates contained *bla*<sub>NDM-1</sub> and *bla*<sub>Oxa-181</sub> gene variants, respectively. A similar observation was seen in the adult population as well (unpublished data), which points towards a local transmission of these gene variants within the hospital. Such local dissemination of resistant genes in the hospital and community increases the CR *Enterobacteriaceae* rates over the years. Among the isolates tested, *bla*<sub>NDM</sub> gene was found to be the most prevalent, followed by *bla*<sub>Oxa-48</sub>-like genes among the pediatric population. Moreover, the rates of CR *Klebsiella* spp were increased from 28% in 2010 to 33% in 2015 (Figure 1). This issue was addressed in our previous study where 22% of the *Klebsiella* spp exhibited resistance to carbapenems [2]. In recent years,

**Figure 1.** Trend line analysis of carbapenem resistant *Klebsiella* spp between 2010 and 2015.



similar observations were noted in various studies, this includes a retrospective analysis by Datta *et al.*, where in over ten years they had found that carbapenem resistance has increased from 2.1% in 2002 to 52% in 2009 in *Klebsiella* spp [3]; Gupta *et al.*, have reported 7% of carbapenem resistance in *Klebsiella* spp and 4% in *Escherichia coli* [4]; Datta *et al.*, have reported 12% resistance rates in *Klebsiella* spp and 3.5 % in *E.coli* [5]; Porwal *et al.*, reported 44% of CR *Klebsiella* spp among the ICU patients, indicating the risk for high mortality rates [6]. Remarkably, in our experience, among the ESKAPE pathogens, the rate of carbapenem resistance is rapidly rising in *Klebsiella* spp. To conclude, it is important to monitor the changes in the trends, burden and the outcome of carbapenemase producing *Klebsiella* spp in India among the pediatric group, to help in guiding effective empirical therapy

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