

Title: *Bordetella pertussis* Antibiotic Resistance in Southern Brazil: A 3-Year Surveillance Study

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Pertussis is a serious infectious disease of the human respiratory tract caused by *Bordetella pertussis*. The increased incidence of this disease in the last years has surprised the world. Antibiotics recommended for treatment or chemoprophylaxis belongs to the class of macrolides. The first erythromycin resistant strain was described in Arizona (1994), but rare reports of resistance have been described. Some studies have associated erythromycin resistance with the mutation in 23s rRNA gene with an A-to-G transition mutation at position 2047. Methods to verify the susceptibility of *B. pertussis* are not fully standardized, for this reason, are not routinely used by clinical laboratories. The antimicrobial susceptibility profile of three antimicrobials (erythromycin, ceftriaxone and levofloxacin) was performed in a collection of 250 isolated of *B. pertussis* identified in the state of the Paraná, during 2012 to 2014. The susceptibility was determined by disk diffusion and Epsilometer test (E-Test) in Regan-Lowe agar without cephalixin. The plates were incubated at 35°C in humid atmosphere. Zone size and MICs were read on the 3rd, 5th and 7th day of incubation. *B. pertussis* analyzed showed high antimicrobial susceptibility to the antimicrobials tested, presenting zone of inhibition (among the susceptible strains) of 36-66 mm, 46-70 mm and 22-40 mm and MIC₅₀/MIC₉₀ of 0.047/0.19, 0.094/0.19 and 0.50/0.75 to erythromycin, ceftriaxone and levofloxacin respectively. Only one isolate of *B. pertussis* (0.4%) showed hetero resistance to erythromycin and ceftriaxone, with the MIC range of 0.25-6 µg/ml and 1.5 - >256 µg/ml, respectively. The first strain of *B. pertussis* that exhibits a heterogeneous phenotype was reported in 2002, in Atlanta, presenting a MIC >256 µg/ml. Studies conducted in the USA have shown that the rate of erythromycin resistant strains was of 0.1 to 7%. However, higher rates (23%) were found in France. The strains analyzed in our study required higher concentrations of levofloxacin to inhibit the growth than those described in the literature. The resurgence of pertussis highlights the importance of monitoring resistance to erythromycin and other antibiotics of clinical use, offering an alternative treatment, especially in cases of pneumonia, major complication associated with death in newborns caused by this disease.

Keywords: *Bordetella pertussis*, antimicrobials resistance, heterogeneous phenotype, erythromycin.