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CLINICAL MICROBIOLOGY - SHORT COMMUNICATION

Streptococcus agalactiae strains isolated from cancer patients in Rio de Janeiro, Brazil

Glenda de Figueiredo Sanches[1,2] · Pamella Silva Lannes-Costa[1] · Melissa Coimbra Cristoforêto[1] · Kelly S. Doran[2] · Ana Luíza Mattos-Guaraldi[3] · Prescilla Emy Nagao[1]

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Abstract

Streptococcus agalactiae is a recognized pathogen associated with infections in neonates, elderly, and immunocompromised adults, particularly those with cancer. In the present investigation, clinical-epidemiological features, multidrug resistance profiles, and virulence genes of *S. agalactiae* strains isolated from cancer patients were investigated. *S. agalactiae* capsular distribution assays demonstrated that Ia (43.6%) and V (23.6%) types were predominantly detected among 55 clinical isolates tested; only one strain (GBS1428) was capsular type III/ST-17. The *fbsB* and *hylB* genes were detected in all isolates, while the *iag*, *lmb*, and *fbsA* genes were detected in 94.5%, 91%, and 91% of oncological isolates, respectively. The combination of PI-1 and PI-2a was the most common (60%) among *S. agalactiae* strains isolated from oncologic patients. *S. agalactiae* strains were resistant to tetracycline (85.5%), erythromycin (9%), and clindamycin (5.5%). Norfloxacin non-susceptible was detected in 7.3% of *S. agalactiae* strains. Our findings reinforce the need for *S. agalactiae* control measures in Brazil, including cancer patients.

Keywords *Streptococcus agalactiae* · Serotypes · Adults · Cancer · Virulence factors · Antimicrobial susceptibility

Introduction

Streptococcus agalactiae (group B *Streptococcus*) is a major cause of infectious disease and significant morbidity in neonates, pregnant women, elderly, and immunocompromised adult patients, particularly those with underlying diseases, including neoplasia [1, 2]. In Brazil, a previous study demonstrated several cases of different types of infections, mostly detected among adult patients with solid tumors and/or making use of indwelling medical devices [3].

The wide spectrum of clinical manifestations of patients reflects an efficient virulence mechanism and consequent *S. agalactiae* pathogenic potential. Previous studies have described the presence of genes coding for several virulence factors among *S. agalactiae* strains, including surface proteins, toxins, and hydrolytic enzymes that mediate bacterial interaction to host cells, penetration of epithelial/endothelial barriers, and evasion from the innate immune system [4, 5]. Capsular polysaccharide (CPS) plays a relevant role in the evasion of host defense mechanisms and has also been used during epidemiological typing of *S. agalactiae* strains (Ia, Ib, and II to IX). Epidemiological studies have demonstrated an association of type III strains with meningitis [6]. Multilocus sequence typing (MLST) revealed that a particular *S. agalactiae* clone of capsular type III designated the hypervirulent clonal complex (CC)-17 clone is responsible for the vast majority of infections and is strongly associated with meningitis [7, 8]. The ST-17-specific surface-expressed protein Gbs2018C (hereafter named HvgA for hypervirulent *S. agalactiae* adhesin) may contribute to neonatal intestinal colonization and crossing blood-brain barriers, leading to meningitis [9]. Surface protein adhesins, including fibrinogen-binding proteins (*fbs*A and *fbs*B), laminin-binding protein (*lmb*), and three structurally distinct types of

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✉ Prescilla Emy Nagao
pnagao@uol.com.br; pnagao@uerj.br

[1] Laboratório de Biologia Molecular e Fisiologia de Estreptococos, Instituto de Biologia Roberto Alcantara Gomes, Rio de Janeiro State University, Rua São Francisco Xavier, 524 - PHLC 5º andar sala 501B-Maracanã, Rio de Janeiro, RJ CEP 20550-013, Brazil

[2] Department of Immunology and Microbiology, University of Colorado School of Medicine, Aurora, CO, USA

[3] Faculdade de Ciências Médicas, Rio de Janeiro State University (UERJ), Rio de Janeiro, RJ, Brazil

pili (*PI-1*, *PI-2a*, and *PI-2b*) are considered essential molecules in promoting *S. agalactiae* invasive disease [4]. In addition, hyaluronidase (*hylB*) and glycosyltransferase (*iag)* activities may also favor *S. agalactiae* dissemination through host tissues [4, 10].

The dissemination of resistant clones may reflect the impact of long-term use of antimicrobial agents during the prevention and treatment of *S. agalactiae* disease. Penicillin and other beta-lactams are generally recommended for time-dependent therapy of *S. agalactiae* infections, including nonpregnant patients: 10 days of therapy—generally acceptable for bacteremia, pneumonia, pyelonephritis, and skin/soft tissue infections; 14 days minimum—meningitis; and minimum 4 weeks—osteomyelitis, endocarditis, and ventriculitis. The addition of gentamicin for the initial 2 weeks of therapy is recommended for endocarditis [11, 12]. Cases of reduced penicillin susceptibility associated with mutations in the penicillin-binding proteins (PBPs) have been reported [5, 13]. Alternative antibiotics, including macrolides and lincosamide, may be utilized for penicillin-allergic patients, although the use of vancomycin should be reserved for penicillin-allergic cases with a high risk of anaphylaxis [5, 12]. However, in cases of neonatal and adult infections, an increasing rate of clindamycin resistance among erythromycin-resistant clinical isolates has been reported worldwide [13–15].

Accordingly, further epidemiological and microbiological investigations remain necessary in order to support the implementation of prevention and treatment strategies of *S. agalactiae* infections. Only a few studies involving epidemiological aspects of *S. agalactiae* infections in cancer patients were previously reported [2, 3, 16]

In this research, clinical-epidemiological features, multidrug resistance (MDR) profiles, and virulence mechanisms of *S. agalactiae* strains related to different types of infections in adult cancer patients were evaluated by phenotypic and genotypic methods.

Material and methods

Study setting and patients

S. agalactiae strains (n = 55), obtained from the culture collection of our laboratory, were previously isolated from different clinical sites of cancer inpatients, during a 3-year period (2013–2015)—Instituto Nacional do Cancer (INCA), Rio de Janeiro metropolitan area, a Brazilian reference center coordinated by the Ministry of Health (MS/CONPREV).

Respiratory tract infections were defined with the presence of progressive pulmonary infiltrates, consolidation, or cavitary lesion, observed after the assessment of thoracic radiographs. Tracheal secretions in intubated patients, sputum, or tracheal aspirations in non-intubated patients were considered as positive if they were associated with clinical or radiological signs that indicated an infection. Age groups were designed based on the World Health Organization (WHO): 16 to 29 years old (y.o), 30 to 59 y.o, and ≥ 60 y.o. Data collected for epidemiologic analysis included age, sex, and year of presentation. Cancer types included genitourinary (ovarian, bladder, prostate, and colon cancer); gastrointestinal (rectum, anal, and intestine cancer); head and neck (maxilar, parotid gland, cavum, and thyroid cancer); respiratory (lung, rhinopharynx, and oropharynx cancer); and hematological (lymphoma, multiple myeloma).

S. agalactiae were selected for further identification when they were grown in any quantity from normally sterile body fluid or when they were isolated in significant numbers or in pure culture from other specimens obtained at clinical sites in which infection was suspected. Blood cultures were always obtained in pairs. All clinical samples yielding more than three organisms were regarded as contaminated and discarded. A positive urinary culture was considered as significant independently of the bacterial count in the presence of local (dysuria, polyuria) or systemic signs. *S. agalactiae* was considered to be a potential pathogen when the growth was > 10^4 CFU/mL as the only isolate or > 10^5 CFU/mL as the predominant isolate; > 10^3 CFU/mL, in cases of nephropathies, was also considered a potential pathogen. *S. agalactiae* strains were screened by hemolysis on blood agar plates, Gram stain, catalase, CAMP, and hippurate hydrolysis tests. Microorganisms were grouped by streptococcal grouping (DR0584A Oxoid, Brazil) following the recommendation of kit provided for identification of *S. agalactiae* (Lancefield group B). *S. agalactiae* strains were cultured in Brain Heart Infusion medium (BHI; Difco) at 37 °C and stored at − 80 °C with BHI liquid media supplemented with 20% glycerol [3].

PCR assays for the detection of virulence and antimicrobial resistance genes

S. agalactiae strains were cultivated in BHI broth at 37 °C overnight, until an optical density (OD) of 0.4 at = 570 nm. Bacterial DNA samples were obtained by using the Quiagen Kit DNA following the manufactory instruction and stored at − 20 °C [17]. The detection of nine *S. agalactiae* capsular polysaccharides (Ia, Ib, II-VIII) was investigated by a multiplex PCR assay based on the method previously described [17].

The gene coding for the following virulence factors and macrolide resistance was investigated by PCR assay: laminin-binding protein (*lmb* gene); hyaluronidase (*hylB* gene); fibrinogen-binding proteins A (*fbsA* gene); fibrinogen-binding proteins B (*fbsB* gene); invasion-associated gene (*iag* gene); pili island encoding PI-1, PI-2a, and PI-2b; macrolide resistance (*mefA/E* gene); and hypervirulent GBS adhesin (*hvgA* gene) [18, 19]

Antimicrobial susceptibility profiles

Antimicrobial susceptibility testing was performed by the disk diffusion method and the results were interpreted according to Clinical Laboratory Standards Institute (CLSI) guidelines [20]. The following antimicrobial drugs were tested: penicillin G (10 μg), ceftriaxone (30 μg), chloramphenicol (30 μg), levofloxacin (5 μg), linezolid (30 μg), vancomycin (30 μg), tetracycline (30 μg), azithromycin (15 μg), erythromycin (15 μg), and clindamycin (2 μg).

Multidrug resistance (MDR) profiles were considered when *S. agalactiae* strains were found resistant to antimicrobial agents belonging to three or more different antibiotic classes [21]. Minimum inhibitory concentration (MIC) of ampicillin, benzylpenicillin, clindamycin, linezolid, vancomycin, ciprofloxacin, moxifloxacin, and norfloxacin was determined using the Etest® strip (bioMérieux, Marcy l'Etoile, France). Breakpoints for *Staphylococcus aureus* and *Enterococcus spp* were considered for ciprofloxacin, moxifloxacin, and norfloxacin.

Macrolide–lincosamide–streptogramin (MLS) resistance phenotypes were evaluated by erythromycin-clindamycin double-disk assays (*D* test) and defined as follows: M phenotype—erythromycin resistant and clindamycin susceptible with no inducible resistance visible in the overlap zone; L phenotype—only clindamycin resistant; MLS-inducible (iMLS) phenotype erythromycin resistant and clindamycin susceptible with a blunted D-shaped zone of inhibition; MLS-constitutive (cMLS) phenotype—resistant to both erythromycin and clindamycin [22].

Results and discussion

In the present investigation varied clinical-epidemiological features, multidrug resistance (MDR) profiles and virulence mechanisms of *S. agalactiae* strains related to different types of infections were evaluated in 55 adult cancer patients attended in a Reference National Cancer Institute-INCA located in the metropolitan area of Rio de Janeiro, Brazil.

S. agalactiae infections were observed among patients with solid tumors (72.7%) and hematologic disorders (5.5%) as follows: genitourinary (n = 23; 41.8%), gastrointestinal (n = 7; 12.7%), head and neck (n = 5; 9.1%), respiratory (n = 5; 9.1%), and hematologic (n = 3; 5.5%). *S. agalactiae* infections occurred in most of the cancer patients (n = 43) presenting comorbidities, including systemic arterial hypertension and diabetes. *S. agalactiae* infections were mostly (54.6%; n = 30) observed among elderly cancer patients (≥ 60 years old) (Table 1).

The microbiological analysis demonstrated *S. agalactiae* strains recovered from different clinical sites, such as urine (67.3%), blood (14.6%), tracheal aspirates (5.5%), skin lesion (3.6%), lung, biliary secretion, and cervical secretion (1.8% each). In most of the cases, *S. agalactiae* strains were isolated in pure cultures (83.6%) and all positive urinary cultures presenting ≥ 10^5 CFU/mL. Laboratory diagnosis of clinical samples found *S. agalactiae* strains associated with the following species: (i) urine (n = 5)—*Providencia rettgeri*, *Escherichia coli*, *Pseudomonas aeruginosa*, or *Klebsiella pneumoniae*; (ii) tracheal aspirates (n = 3)—*K. pneumoniae*, *Moraxella* (*Branhamella*) *catarrhalis*, *Enterococcus faecalis*, *Serratia marcescens*, and/or *P. aeruginosa*; (iii) skin lesion (n = 1)—*Staphylococcus aureus* (Table 1).

S. agalactiae capsular distribution assays showed that Ia (43.6%) and V (23.6%) types were predominantly detected

Table 1 Clinical and microbiological features of 55 cancer patients with *Streptococcus agalactiae* infections

Characteristic	Patients, *n* (%)
Gender	
Female	28 (51%)
Male	27 (49%)
Age, years	
16–29	2 (3.6%)
30–59	19 (34.5%)
≥ 60	30 (54.6%)
Unknown	4 (7.3%)
Clinical samples	
Urine	37 (67.3%)
Blood	8 (14.6%)
Tracheal aspirates	3 (5.5%)
Skin lesion	2 (3.6%)
Lung	1 (1.8%)
Biliary secretion	1 (1.8%)
Cervical secretion	1 (1.8%)
Unknown	2 (3.6%)
Neoplastic disorder	
Genitourinary	23 (41.8%)
Gastrointestinal	7 (12.7%)
Head and neck	5 (9.1%)
Respiratory	5 (9.1%)
Hematologic	3 (5.5%)
Unknown	12 (21.8%)
Comorbidities	
Systemic arterial hypertension	21 (38.2%)
Smoke	12 (21.8%)
Alcohol abuse	5 (9.1%)
Diabetes mellitus	4 (7.3%)
Cirrhosis	1 (1.8%)
Unknown	12 (21.8%)

16.4% *S. agalactiae* strains were concomitantly found with *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Serratia marcescens*, *Escherichia coli*, *Moraxella* (*Branhamella*) *catarrhalis*, *Enterococcus faecalis*, and/or *Providencia rettgeri*

among the 55 clinical isolates tested, followed by types II (14.6%), III (11%), IV (3.6%), VI (1.8%), and VII (1.8%). Capsular types Ib and VIII were not detected in this study (Table 2). A correlation between *S. agalactiae* capsular types and neoplastic disorders was not currently identified (Table 2). Moreover, capsular type IX was not presently investigated due to the fact that it has been reported in patients from Asia and Oceania [23, 24].

Previous studies have shown variations in *S. agalactiae* capsular type distribution depends on factors such as geographical region, ethnicity, and other characteristics of the examined population [25]. In Brazil, a high incidence of type Ia recovered from colonized and symptomatic pregnant women has been reported [26–28]. During 2010–2014, *S. agalactiae* capsular type V strains were frequently (25%) related to cases of invasive bone joint infections among patients from France [29].

Although several works reported the prevalence of *S. agalactiae* capsular type Ib in Brazil, no strains were identified in cancer patients for a 3-year period [26–28, 30]. *S. agalactiae* strains belonging to capsular type III were identified in 11% of cancer patients from INCA, a higher prevalence compared to colonized women (6.6%) and non-pregnant (3%) adults of Southeast and South regions from Brazil, respectively [26, 30]. Moreover, capsular type IV was currently detected in 4% of oncologic strains. Previous studies indicated the emergence of invasive capsular type IV strains in neonates and adults [31, 32]. Capsular type IV was detected in 13.1% of *S. agalactiae* isolates in outpatient and inpatient populations from Curitiba city, Paraná State [30]. Only one *S. agalactiae* strain belonging to capsular type VII was identified in cancer patients from INCA. The occurrence of capsular types VI-IX is more common in Asia and countries of Oceania, including Australia and New Zealand [23, 24].

Heterogeneity of virulence and invasive potential of *S. agalactiae* strains isolated from cancer patients was demonstrated by detection of genes coding for surface proteins, adhesins, and enzymes related to host-pathogen interactions: fibrinogen-binding proteins (*fbs*A and *fbs*B genes), laminin-binding protein (*lmb* gene), pili (*PI-1*, *PI-2a* and *PI-2b* genes), hyaluronidase (*hylB* gene), glycosyltransferase (*iag* gene), and hypervirulence clone ST-17 (*hvgA* gene) (Table 2) [4, 9, 10]. Data showed that 100% *S. agalactiae* strains isolated from cancer patients presented *fbs*B and *hylB* genes, while the *iag* gene was detected in 94.5% of oncological isolates. The genes *lmb* and *fbsA* responsible for extracellular matrix proteins adherence were observed in 90% *S. agalactiae* strains. In Brazil, the presence of *lmb* gene was previously verified in all strains isolated from groups of colonized and symptomatic adult patients [26]. In Argentina, a study performed with the pregnant woman showed frequency for the virulence gene *lmb* in 94.3% and *hylB* 79.5%, confirming their presence in most human isolates [33].

Table 2 General characteristics and capsular type of 55 *S. agalactiae* strains

Characteristic	Capsular type						
	Ia	II	III	IV	V	VI	VII
Type of infection							
Invasive	5	4	1	0	3	0	1
Non-invasive	19	4	5	1	9	1	0
No documented	0	0	0	1	1	0	0
Age							
16–29 y.o	0	1	1	0	0	0	0
30–59 y.o	11	1	2	0	4	0	1
≥ 60 y.o	11	6	3	1	8	1	0
Unknown	2	0	0	1	1	0	0
Clinical samples							
Urine	18	3	5	1	9	1	0
Blood	3	2	1	0	2	0	0
Tracheal aspirates	1	1	0	0	1	0	0
Skin lesion	1	1	0	0	0	0	0
Lung	1	1	0	0	0	0	0
Biliary secretion	0	0	0	0	0	0	1
Cervical secretion	0	0	0	0	0	0	0
Unknown	0	0	0	1	1	0	0
Neoplastic disorders							
Genitourinary	13	2	2	2	4	0	0
Gastrointestinal	2	2	2	0	1	0	0
Head and Neck	1	1	0	0	2	0	1
Respiratory	1	2	0	0	2	0	0
Hematologic	2	0	0	0	1	0	0
Unknown	6	1	1	0	3	1	0
Antimicrobial resistance							
Penicillin G	0	0	0	0	0	0	0
Ceftriaxone	0	0	0	0	0	0	0
Levofloxacin	0	0	0	0	0	0	0
Chloramphenicol	0	0	0	0	0	0	0
Vancomycin	0	0	0	0	0	0	0
Linezolid	0	0	0	0	0	0	0
Tetracycline	23	6	5	3	9	0	1
Clindamycin	0	2	0	1	0	0	0
Azithromycin	2	1	0	1	1	0	0
Erythromycin	1	1	0	1	2	0	0
Virulence factors genes							
Lmb	23	8	5	2	11	0	1
Hylb	24	8	6	2	13	1	1
fbsA	24	6	4	2	12	1	1
fbsB	24	8	6	2	13	1	1
Iag	23	8	6	2	12	0	1
PI-1 + PI-2a	11	5	5	1	10	0	1
PI-1 + PI-2b	7	2	0	0	1	0	0
PI-2a	2	1	1	1	2	1	0
PI-2b	4	0	0	0	0	0	0

Table 2 (continued)

Characteristic	Capsular type						
	Ia	II	III	IV	V	VI	VII
hvgA	0	0	1	0	0	0	0

y.o, years old. Blank control reactions without any DNA template were carried out simultaneously in PCR assays

S. agalactiae strains from cancer patients presented at least one of three pilus islands, either alone or in combination (Table 2). The most frequently identified pilus island was the combination of PI-1 and PI-2a (60%), indicating an uneven distribution of pilus islands among *S. agalactiae* types, as previously reported in a study with infected neonates and mothers in China [34]. The highest frequency of PI-1 + PI-2a pilus islands was currently detected among capsular types Ia and V *S. agalactiae* isolated from cancer patients with urinary infections (57.5%).

S. agalactiae ST-17 was recognized as a hypervirulent international clone that have been significantly associated with neonatal invasive infections and a few cases of infections in nonpregnant adults [29, 35]. Interestingly, PCR analysis showed amplification of *hvgA* gene for *S. agalactiae* capsular type III (GBS1428) strain, recognized as belonging to the hypervirulent ST-17 clone. The GBS1428 strain was hyperhemolytic and also showed amplification for the *lmb*, *fbsA*, *fbsB*, *iag*, *hylb*, *PI-1*, and *PI-2b* genes. Patient history indicated that the GBS1428 strain was isolated from urine sample of a 71-year-old man with colorectal carcinoma, presenting obesity and hypertension as comorbidities.

Recent investigations emphasized the relevance of understanding multifactorial virulence factors in the proper management of urinary tract infection and the prevention of antimicrobial resistance of pathogens [36]. Presently, a significant association between the presence of genes coding for virulence factors of *S. agalactiae* strains and a high number of cases of UTI in cancer patients was verified. Data will help understand the *S. agalactiae* pathogenicity and increasing reports of urinary infections, including South America [36]. Moreover, different virulence gene profiles were observed among the *S. agalactiae* strains, including urinary tract infection and invasive blood isolates. In France, 81.5% of *S. agalactiae* strains isolated from adults during the period 2007–2010 were from the blood [37].

In Latin America, one previous work reported cases of invasive infections due to *S. agalactiae* in adults with diverse comorbidities, including some patients with cancer [2]. In Brazil, there is little information of *S. agalactiae* strains isolated from oncologic patients [3]. Therefore, this is the first study showing virulence factor genes and molecular typing profiles of *S. agalactiae* isolated exclusively from cancer patients. A previous study published in 2016, based on retrospective medical records, emphasized the vulnerability of cancer patients to *S. agalactiae* infections in Brazil [3].

Antimicrobial susceptibility profiles of *S. agalactiae* strains isolated from cancer patients were displayed in Table 2. All tested strains were susceptible to penicillin, ceftriaxone, levofloxacin, chloramphenicol, vancomycin, and linezolid, independent of capsular types. Resistance to tetracycline, azithromycin, erythromycin, and clindamycin was observed in, 85.5%, 9%, 9%, and 5.5% of *S. agalactiae* strains, respectively. Detection of inducible clindamycin resistance by the double-disk (D) diffusion test and presence of gene *mefA/E*, correlated with activation of drug efflux by pumps of *S. agalactiae* strains, were displayed in Table 3. The presence of iMLSB phenotypes was observed in *S. agalactiae* strains capsular type, II (n = 1), IV (n = 1), and V (n = 2). *S. agalactiae* GBS1431/IV strain was the only cancer isolate that expressed a MDR profile, although gene *mefA/E* was not detected. The presence of macrolide resistance *mef*A/E gene was observed only in erythromycin-resistant *S. agalactiae* GBS1502/Ia and GBS1436/V strains. Considering all *S. agalactiae* strains isolated from cancer patients, the occurrence of gene *mefA/E* was verified in capsular types Ia (42%), II (13%), III (34%), and V (23%).

Antimicrobial susceptibility analysis by using the Etest® strip identified *S. agalactiae* strains as follows: 100% susceptible to ampicillin (MIC ≤ 0.25 μg/mL), penicillin (MIC ≤ 0.12 μg/mL), clindamycin (MIC ≤ 0.25 μg/mL), linezolid (range: ≤ 1–2 μg/mL), vancomycin (MIC ≤ 0.5 μg/mL), moxifloxacin (range: ≤ 0.25–1 μg/mL); 94.5% ciprofloxacin (MIC ≤ 1 μg/mL) and 67.3% norfloxacin (MIC ≤ 4 μg/mL); 5.5% intermediate to ciprofloxacin (MIC = 2 μg/mL) and 25.5% to norfloxacin (MIC < 8 μg/mL); and 7.2% non-susceptible to norfloxacin (MIC = 16 μg/mL).

The infection has been recognized as one of the major obstacles to the successful management of patients with malignant diseases. Standard antibiotic regimens for cancer patients with neutropenia and fever are directed at most of the bacteria that can cause infections. However, a subset of resistant bacteria belonging to the Gram-positive group (*Staphylococcus aureus* and *Streptococcus* spp.) remains untreated unless specific antibiotics are added to the treatment [38]. Penicillin is conventionally used as the first-line agent for the prophylaxis and treatment of *S. agalactiae* infections [8, 11, 12]. The uniform susceptibility of *S. agalactiae* strains to beta-lactam antibiotics detected in the present study was similar to previous findings from different countries [8, 14, 26]. High levels of erythromycin resistance in *S. agalactiae* have been detected in Asia, Africa, Europe, and the USA [5, 8, 13, 15]. Presently, erythromycin resistance and inducible clindamycin resistance phenotype were verified. In China, a considerable proportion of *S. agalactiae* strains were found resistant to clindamycin (29.67%) and quinolones (25.27%) [39]. Fluoroquinolones (FQ) have been used for prophylaxis

Table 3 Profile of *S. agalactiae* strains resistant to erythromycin and clindamycin isolated from cancer patients

S. agalactiae/capsular type	Antibiotic		Multidrug resistance profile	*D* test	Phenotype	*mefA/E*
	Cli	Ery				
GBS1502/Ia	S	R	MDS	Negative	M	+
GBS1301/II	R	S	MDS	Negative	L	−
GBS1441/II	R	R	MDS	Positive	iMLS	−
GBS1431/IV	R	R	MDR	Positive	iMLS	−
GBS1308/V	S	R	MDS	Positive	iMLS	−
GBS1436/V	S	R	MDS	Positive	iMLS	+

Cli, clindamycin; *Ery*, erythromycin; *MDR*, multidrug resistance; *MDS*, multidrug sensitive; the *D* test was performed when the strains showed phenotype resistance to clindamycin or/and erythromycin. The presence of gene *mefA/E* was performed by PCR. Blank control reactions without any DNA template were carried out simultaneously in PCR assays

against infections in cancer patients, but their impact on the resistance mechanisms still require further investigation [40]. In Argentina, FQ resistance *S. agalactiae* in non-invasive infections (14.8%) was also reported by using a five-disk scheme designed for FQ resistance detection including levofloxacin, ciprofloxacin, norfloxacin, ofloxacin, pefloxacin, or moxifloxacin [41]. FQ resistance of *S. agalactiae* was also reported in studies from China (48%), France (1.5%), and Italy (2.99%) [42–44]. At present, the FQ resistance of *S. agalactiae* strains was verified in 7.2% of adult patients. Data suggest that norfloxacin resistance is increasing in the Rio de Janeiro metropolitan area, Brazil. In addition to antimicrobial resistance profiles, virulence properties, and pathogenic potential of *S. agalactiae* strains isolated from cancer patients were demonstrated. Further studies remain necessary in order to investigate FQ-resistant *S. agalactiae* invasive and non-invasive clinical isolates in addition to improve the health conditions and prevention of *S. agalactiae* infections in children and adults, especially oncologic patients.

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Authors' contributions G.F.S. and P.E.N. participated in the design and discussion of the research. G.F.S. and P.S.L.C. carried out the experimental part of the work, wrote the original draft, carried out the analysis of the data, and wrote the final manuscript. M.C.C. carried antimicrobial susceptibility. G.F.S., P.S.L.C., K.S.D., A.L.M.G., and P.E.N. contributed to literature review and manuscript discussion. All authors have read and approved the final manuscript.

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Data availability All data generated or analyzed during this study are included in this published article

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interests.

Ethical approval and consent to participate Ethical approval for the study was obtained from the Institutional Ethics Commission, Instituto Nacional do Cancer (INCA)/Rio de Janeiro Pedro Ernesto Hospital University (CONEP-CAAE: 04124313.0.0000.5259).

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