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ANTIBIOTIC SUSCEPTIBILITY PROFILE OF VIRIDANS GROUP STREPTOCOCCI WITH RESPECT TO PREVALENCE OF DENTAL CARIES

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ABSTRACT

Antibiotic susceptibility profile of viridans group streptococci (VGS) was evaluated with respect to the prevalence of dental caries against penicillin, amoxicillin, cephalothin, cefazolin, cefotaxime, ceftazidime, imipenem, chloramphenicol, clindamycin, trimethoprim, azithromycin, erythromycin, clarithromycin, ciprofloxacin, levofloxacin, doxycycline, tetracycline, gentamicin, streptomycin, tobramycin, teicoplanin, vancomycin, rifampin and linezolid. A total of 175 and 350 isolates of VGS were obtained from the oral cavity of carious and non-carious subjects, respectively. All the isolates of VGS were maintained on sodium azide blood agar medium. The standard disc diffusion method was used for the determination of antibiotic susceptibility pattern of VGS against different antibiotics. Compared to all used antibiotics, the overall incidence of resistant isolates to Erythromycin was noted higher against carious (68%, 119/175) as well as non-carious (38.6%, 135/350) VGS isolates. The incidence of resistant isolates belonging to different species obtained from carious and non-carious subjects revealed that *S. mutans*, *S. anginosus*, *S. intermedius*, and *S. acidominimus* were the most resistant isolates and exhibited varying degrees of resistance against multiple tested antibiotics. For most cases, Imipenem, Trimethoprim, Teicoplanin, Linezolid and cephalosporins were found to be the most effective antibiotics as more than 90% VGS were susceptible.

Key words: VGS, carious, dental caries, disc diffusion method, normal flora

INTRODUCTION

Like other infections, worldwide in dentistry, the emergence of antibiotic resistance related dental caries is also a serious public health issue. The main reason is the longer use of any antibiotic or increase in antibiotic consumption (Berbel *et al*., 2022; Ahmadi *et al*., 2021; Singh *et al*., 2020). Dental caries is an orofacialo dontogenic infection (infections within tooth and dental supporting structures), multi-factorial, widespread and expensive to treat. Four major factors are necessary to produce dental caries such as dental plaque (bacterial plaque), dietary carbohydrate substrate (sugar), susceptible tooth surface and time. It is very difficult task to determine one major factor associated with dental caries because they are interlinked with each other. Only when all four factors are present dental caries will occur. An important and essential role of bacterial dental plaque has been well documented in widespread dental caries (Ahmadi *et al*., 2021). Dental plaque is defined as tenacious microbial deposit which forms on hard surfaces within the oral cavity and consists of microbial cells and their products together with host compounds mainly derived from saliva. The role of microbial cells in initiating dental caries has been well established. The most common example of microbial community is viridans group streptococci (VGS) (Ahmed *et al*., 2022). VGS are among the most numerous facultative oral streptococci isolated from oral cavity. They are categorized into five groups i.e. mutans group, anginosus group, mitis group, sanguinis group and salivarius group (Facklam, 2002 and Wongcharoen *et al*., 2013). VGS have been thought to be of low virulence because they are not primary pathogens. However, VGS can act as opportunistic pathogens under favorable conditions and involved in a variety of oral infections such as dental caries, dentoalveolar and periodontal disorders. VGS are also associated; often in combination with other bacterial species; with extra oral infections such as infective endocarditis, congenital heart disease, myocardial and cerebral infarction, pneumonia, acute bronchopulmonary infections, empyema thoracis and lung abscess, sepsis, nosocomial infections, liver abscess, bacteremia, acute and chronic urethritis, fatal shock syndrome, Reiter syndrome, meningitis, brain abscess, cavernous sinus thrombosis, septic arthritis and other suppurative infections (Ahmed *et al*., 2023). The role of VGS in initiating dental caries has been well documented. Dental caries is a prevalent disease among all age groups and continues to be a major health problem in the world today (Ahmed *et al*., 2022). In order to treat this disease a variety of preventive measures have been proposed. For instance, the crucial use of antibiotic therapy has been well recognized to control caries is after any surgical interventions like pulp debridement or incision drainage. Dentists prefer to prescribe few systemic

antibiotics such as penicillin, tetracyclines, amoxicillin, metronidazole, macrolides, and clindamycin to control dental infections (Lopardo *et al*., 2022; Ahmadi *et al*., 2021; Chaudhry *et al*., 2013). Moreover, broad spectrum antibiotics are frequently being prescribed instead of use of narrow spectrum antibiotics. However, use of antibiotic is not a permanent solution or it doesn't help much in the treatment of dental caries because the blood vessels in oral cavity have been damaged by the bacterial infections which were the source of body's antibacterial defense. Therefore, the antibiotics cannot reach the inside of the tooth to cure infection. Moreover, antibiotics do not fix the tooth inflammation as toothache is mostly caused by tooth inflammation rather than any infection, so analgesics like ibuprofen and paracetamol is preferred to be used during inflammatory pain instead of using antibiotic. In most cases, antibiotic should not be given in toothache. It is mostly prescribed to treat tooth abscess by dentist. Hence no complete protection is available to cure the dental decay (Ahmed *et al*., 2022; Haque *et al*., 2019; Oberoi *et al*., 2015). In view of above literatures this study was conducted to determine the antibiotic susceptibility pattern of VGS isolated from oral cavity of carious and non-carious subjects.

MATERIALS AND METHODS

In the present study, a total of 175 and 350 isolates of viridians group streptococci (VGS) were used that obtained from oral cavity of carious and non-carious subjects respectively from different localities of Karachi, Pakistan. The subjects having history of use of antibiotics during previous one month were not included in the study. When the specimens were collected, the subjects were interviewed and the questionnaire was completed. The subjects were grouped on the basis of prevalence of dental caries as follows: Carious subjects i.e., subjects having dental caries (a visible hole or pits on the tooth surface was considered as an indicator for presence of dental caries) whereas non-carious subjects i.e., subjects having no dental caries. All the isolates of VGS were maintained on Sodium azide blood agar slants. The antibiotic susceptibility pattern of VGS was determined by Kirby Bauer standard disc diffusion method (Cheesbrough, 2000; Versalovic *et al*., 2011). Tryptic Soy Broth (Oxoid) was used for the preparation and standardization of bacterial inoculum and Tryptic Soy Agar (Oxoid) was used for the determination of antibiotic susceptibility pattern. In the present study, 24 antibiotics (Oxoid) were used which were selected from different groups with respect to chemical structure viz., β-lactam group [Subgroups: Penicillins (penicillin and amoxicillin), Cephalosporins (cephalothin, cefazolin, cefotaxime and ceftazidime) and Carbapenems (imipenem)]; Phenicols (chloramphenicol); Lincosamides (clindamycin); Pyrimidine analogs (trimethoprim); Macrolides (azithromycin, erythromycin and clarithromycin); Quinolones (ciprofloxacin and levofloxacin); Tetracyclines (doxycycline and tetracycline); Aminoglycosides (gentamicin, streptomycin and tobramycin); Glycopeptides (teicoplanin and vancomycin) and Miscellaneous group (rifampin and linezolid). Table 1 presents the name, potency and classification of antibiotics and standard criteria recommended by Clinical and Laboratory Standards Institute (CLSI) for interpretation of antibiotic susceptibility (Chaudhry *et al*., 2013; Andrews, 2005). All inoculated Tryptic soy agar plates containing discs were incubated at 35-37˚C for 18- 24 h. After incubation, the diameter of inhibitory zone was measured to the nearest millimeter and the susceptibility or resistance was interpreted on the basis of criteria mentioned in the Table 1.

RESULTS AND DISCUSSION

The antibiotic susceptibility results are presented in Tables 2, 3, 3A, 3B, 3C, and 3D. Compared to all used antibiotics, the overall incidence of resistant isolates to Erythromycin was noted higher against carious (68%, 119/175) and non-carious (38.6%, 135/350) VGS isolates. The reasons could be the difference in origin of isolation of VGS, variation among tested species and sample sized used in the study. Whereas, for both cases, Imipenem, Trimethoprim, Teicoplanin, Linezolid and a Cephalosporins group were found to be most effective antibiotics as more than 90% VGS were susceptible to these antibiotics. In the present study, it was interesting to note that most of antibiotics showed strong antimicrobial potential against VGS recovered from non-carious subjects as compared to carious subjects. There could be several factors, for instance, different source of VGS used in the study or VGS might contain antibiotic resistance genes to various degrees, even in subjects with no history of exposure to any antibiotics as well as alteration in antibiotic binding proteins in isolates that specifically influence for theses antibiotics (Haque *et al*., 2019; Henning and Sunde, 2001). The incidence of resistant isolates belonging to different species obtained from carious and non-carious subjects was also determined and revealed that *S. mutans*, *S. anginosus*, *S.*

intermedius, and *S. acidominimus* were observed to be most resistant isolates with varying degree of resistance against various tested antibiotics. Little is known about antibiotic susceptibility information in these species, and there is a distinct lack of multidrug resistance literature available especially for the oral VGS.

From the Penicillin group, Penicillin and Amoxicillin were used in this study. Regarding Beta-lactam antibiotics, this group contains beta-lactam ring (a three-carbon and one-nitrogen cyclic amine structure) in their molecular structure and has strong antimicrobial activities via inhibiting the synthesis of the cell wall of many Gram positive and Gram negative bacteria. This group of antibiotics is classified into 5 different classes including penicillin, cephalosporins, penems, carbapenems, and monobactams. Amoxicillin is broad spectrum penicillins and is being frequently used in the prophylaxis of dental infections because of its excellent absorption and slow excretion. Currently, in the case of amoxicillin resistance, Amoxicillin is being added in combination of metronidazole or amoxicillin clavulanate with strong antibacterial activities against Gram negative bacteria as compared to Gram positive bacteria (Ahmadi *et al*., 2021; Pelczar, 1993; Cawson, 1991). In the present study, the emergence of resistance to Amoxicillin was noted higher compared to Penicillin in carious as well as non-carious subjects. The emergence of resistance against Amoxicillin and Penicillin was noted as 49.1% (86/175) and 29.7% (52/175) from carious and 24% (84/350) and 18.9% (66/350) from non-carious subjects respectively (Table 2). The antibiotic susceptibility pattern of different species to Amoxicillin was fairly low as most of the isolates obtained from carious subjects were found resistant. The incidence of resistant isolates was noted as *S. mitis* 69.2% (09/13), *S. mutans* 62.1% (18/29), *S. intermedius* 55.6% (05/09), *S. salivarius* 50% (03/06), *S. anginosus* 44.2% (42/95) and *S. uberis* 13.3% (02/15). In case of *S. sanguinis* and *S. acidominimus* three and one isolates were obtained respectively and all were resistant while out of 04 isolates of *S. oralis*, three were found resistant. On the other hand, in case of isolates recovered from non-carious subjects, the highest incidence of resistant isolates for Amoxicillin was observed against *S. oralis* (28.6%, 04/14) followed by *S. anginosus* (28%, 52/186), *S. acidominimus* (25%, 01/04), *S. mitis* (21.3%, 10/47), *S. uberis* (21.1%, 04/19), *S. mutans* (19.1%, 09/47), *S. intermedius* (13.3%, 02/15) and *S. sanguinis* (11.8%, 02/17). Whereas none of the isolates of *S. salivarius* was found resistant to Amoxicillin (Table 3).

Penicillin, as compared to Amoxicillin, was found more effective because incidence of resistant isolates was lower than Amoxicillin (Table 2). Penicillin is first line narrow-spectrum antibiotic that commonly used in dentistry for the treatment of various oral and extra-oral infections due to its appropriate antimicrobial properties, cost effectiveness and low rate of side effects (Ahmadi *et al*., 2021; Cox and Wright, 2013; Pelczar, 1993). In the present study, in case of isolates from carious subjects, the resistance pattern was noted as *S. uberis* 80% (12/15), *S. sanguinis* 66.7% (02/03), *S. oralis* 50% (02/04), *S. salivarius* 50% (03/06), *S. intermedius* 44.4% (04/09), *S. mutans* 34.5% (10/29), *S. anginosus* 16.8% (16/95), *S. mitis* 15.4% (02/13) and single isolate of *S. acidominimus* obtained in this study was resistant. While, isolates recovered from non-carious subjects showed a resistance pattern comparable to that of Amoxicillin. The highest incidence of resistant isolates was noted for *S. uberis* (78.9%, 15/19) followed by *S. acidominimus* (50%, 02/04), *S. sanguinis* (41.2%, 07/17), *S. oralis* (35.7%, 05/14), *S. mutans* (29.8%, 14/47), *S. intermedius* (13.3%, 02/15), *S. mitis* (12.8%, 06/47), *S. anginosus* (7.5%, 14/186) while the single isolate of *S. salivarius* obtained from non-carious subjects was found resistant to this antibiotic (Table 3).

In the present study, four types of Cephalosporins i.e. **Cephalothin, Cefazolin, Cefotaxime and Ceftazidime** were tested. Previous literature also mentioned that this group has few side effects and better antimicrobial properties against variety of bacteria with combination of metronidazole. Cefazolin are among the most commonly used first generation Cephalosporins in dentistry (Mahon *et al*., 2014; Cox and Wright, 2013; Pelczar, 1993). For carious subjects, the incidence of isolates resistant to Ceftazidime (5.1%, 09/175) was found slightly higher than Cefazolin (3.4%, 06/175), Cephalothin (2.9%, 05/175) and Cefotaxime (2.3%, 04/175) while in case of non-carious subjects, Cefotaxime (1.7%, 06/350) showed slightly higher incidence of resistant isolates than Cefazolin (1.1%, 04/350), Cephalothin (1.1%, 04/350) and Ceftazidime (0.3%, 01/350) (Table 2). The emergence of resistance against tested antibiotics was also noted with respect to species isolated from carious and non-carious subjects (Table 3). For Ceftazidime, the incidence of resistant isolates obtained from carious subjects was noted as 25% (01/04) *S. oralis*, 22.2% (02/09) *S. intermedius*, 13.3% (02/15) *S. uberis* and 2.1% (02/95) *S. anginosus* while only one isolates of *S. uberis* (5.3%, 01/19) obtained from non-carious subjects was resistant (Table 3). For Cefazolin, in case of carious subjects, 25% (01/04) *S. oralis*, 6.9% (02/29) *S. mutans* and 3.2% (03/95) *S. anginosus* were resistant. While, in case of non-carious subjects, 10.5% (02/19) *S. uberis*, 2.1% (01/47) *S. mitis* and 0.5% (01/186) *S. anginosus* were found resistant to Cefazolin. All the remaining isolates of VGS obtained from

carious and non-carious subjects were found susceptible to this antibiotic. In case of Cephalothin, only 5.3% (05/95) isolates of *S. anginosus* recovered from carious subjects and 4.3% (02/47) of *S. mitis* and 1.2% (02/186) of *S. anginosus* isolated from non-carious subjects were found resistant. In case of Cefotaxime, few isolates of *S. mutans* (6.9%, 02/29) and *S. anginosus* (2.1%, 02/95) isolated from carious subjects were found resistant while only 12.8% (06/47) *S. mutans* isolated from non-carious subjects were found resistant to this antibiotic (Table 3).

From Carbapenems, Imipenem was included in the study. Imipenem acts as a bactericidal antimicrobial through the inhibition of cell wall synthesis of gram negative and gram positive bacteria. It is used to treat few serious infections such as endocarditis (extra-oral infections) and respiratory tract (including pneumonia), urinary tract etc., (Haque *et al*., 2019; Pelczar, 1993). The overall incidence of resistant isolates obtained from carious and non-carious subjects was noted as 2.3% (04/175) and 0.6% (02/350) respectively (Table 2). Only 3.4% (01/29) *S. mutans* and 3.2% (03/95) *S. anginosus* obtained from carious and 4.3% (02/47) isolates of *S. mutans* recovered from non-carious subjects were found resistant to Imipenem (Table 3A).

In the present study, **Chloramphenicol from Phenicols group was** included. Chloramphenicol is a broad-spectrum drug that effective against various bacterial species but not frequently prescribed due to adverse effect e.g. bone marrow toxicity. It is bacteriostatic but might be bactericidal when used against highly sensitive bacteria. Chloramphenicol inhibits bacterial growth by inhibiting protein synthesis and binding to the bacterial ribosome to block peptidyltransferase. It has bactericidal activity against few penicillin-streptomycin resistant bacteria encountered in infected root canals (Jubeh *et al*., 2020; Cox and Wright, 2013; Pelczar, 1993). The overall incidence of resistant isolates obtained from carious and non-carious subjects was noted as 44% (77/175) and 17.1% (60/350) respectively (Table 2). In case of isolates of different species, the only isolate of *S. acidominimus* obtained from carious subjects was found resistant. The incidence of resistant isolates for other species was noted as *S. mutans* 69% (20/29), *S. salivarius* 50% (03/06), *S. anginosus* 47.4% (45/95), *S. intermedius* 33.3% (03/09), *S. sanguinis* 33.3% (01/03), *S. oralis* 25% (01/04), *S. mitis* 15.4% (02/13) and *S. uberis* 6.7% (01/15). As regards isolates from non-carious subjects, 42.6% (20/47) *S. mutans*,17.2% (32/186) *S. anginosus*, 15.8% (03/19) *S. uberis* and 10.6% (05/47) *S. mitis* were resistant (Table 3A).

Clindamycin, the member of Lincosamide group, was also included in the study. Lincosamides are broad-spectrum bacteriostatic group of antibiotics that mostly act against Gram positive anaerobic bacteria by binding to the bacterial ribosome and inhibiting the protein synthesis. Past studies observed that Clindamycin has a greater antimicrobial effect against aerobic as well anaerobic bacteria than other Lincosamide for controlling various infections and the agent could be an excellent choice for allergic patients to beta lactam group (Jubeh *et al*., 2020; Mahon *et al*., 2014; Pelczar, 1993). The overall incidence of resistant isolates was found as 26.9% (47/175) and 15.1% (53/350) from carious and non-carious subjects respectively (Table 2). When emergence of resistance was noted with respect to different species isolated from carious subjects, the highest incidence of resistant isolates was noted as 83.3% (05/06) for *S. salivarius* followed by *S. intermedius* (55.6%, 05/09), *S. mitis* (53.8%, 07/13), *S. uberis* (40%, 06/15), *S. anginosus* (19%, 18/95), *S. mutans* (13.8%, 04/29) and *S. sanguinis* (10%, 02/03). None of the isolates of *S. oralis* and *S. acidominimus* obtained from carious subjects was found resistant. In case of isolates from non-carious subjects, only 42.1% (08/19) isolates of *S. uberis*, 41.2% (07/17) of *S. sanguinis*, 38.3% (18/47) of *S. mitis*, 13.3% (02/15) of *S. intermedius*, 10.6% (05/47) of *S. mutans*, 07% (13/186) of *S. anginosus* were found resistant while none of the isolates of *S. oralis*, *S. salivarius* and *S. acidominimus* was found resistant to this antibiotic (Table 3A).

From Pyrimidine analogs group of antibiotics, Trimethoprim was included in the study. Trimethoprim is a synthetic antibacterial agent that often used in combination of sulfamethoxazole; after Penicllins and Macrolides; for treatment of different dental enamel defects (Faustino-Silva *et al*., 2020; Pelczar, 1993). The overall incidence of resistant isolates was noted as 6.3% (11/175) and 0.9% (03/350) from carious and non-carious subjects respectively (Table 2). The incidence of resistant isolates belonging to different species obtained from carious subjects included *S. mutans* 17.2% (05/29), *S. mitis* 7.7% (01/13) and *S. anginosus* 5.3% (05/95). The incidence of resistant isolates obtained from non-carious subjects was also low and found as 4.3% (02/47) for *S. mutans* and 2.1% (01/47) for *S. mitis* (Table 3A).

Table 1.Interpretation chart for antibiotics.

S. No	Name and classes of antibiotics	Abbreviation	Disc Potency (µg)	Diameter of Zone of Inhibition (millimeter)		
				Susceptible	Intermediate	Resistant
	β- Lactam group					
	Penicillins					
1	Penicillin	PEN	10	≥22	12-21	≤11
2	Amoxicillin	AMX	10	≥15	12-14	≤11
	Cephalosporins					
3	Cephalothin	CF	30	≥18	15-17	≤14
4	Cefazolin	CZ	2	≥18	15-17	≤14
5	Cefotaxime	CTX	10	≥23	15-22	≤14
6	Ceftazidime	TAZ	10	≥18	15-17	≤14
	Carbapenem					
7	Imipenem	IPM	10	≥16	14-15	≤13
	Phenicols					
8	Chloramphenicol	CHL	10	≥18	13-17	≤12
	Lincosamides					
9	Clindamycin	CLI	2	≥21	15-20	≤14
	Pyrimidine analogs					
10	Trimethoprim	TMP	5	≥16	11-15	≤10
	Macrolides					
11	Azithromycin	AZM	15	≥18	14-17	≤13
12	Erythromycin	ERY	5	≥23	14-22	≤13
13	Clarithromycin	CLR	2	≥18	14-17	≤13
	Fluoroquinolone					
14	Ciprofloxacin	CIP	1	≥21	16-20	≤15
15	Levofloxacin	LEV	1	≥17	14-16	≤13
	Tetracyclines					
16	Doxycycline	DOX	30	≥16	13-15	≤12
17	Tetracycline	TET	30	≥19	15-18	≤14
	Aminoglycosides					
18	Gentamicin	GEN	10	≥15	13-14	≤12
19	Streptomycin	STR	10	≥10	7-9	≤12
20	Tobramycin	TOB	10	≥15	13-14	≤12
	Glycopeptides					
21	Teicoplanin	TPN	30	≥14	11-13	≤10
22	Vancomycin	VAN	5	≥17	15-16	≤14
	Miscellaneous					
23	Linezolid	LNZ	10	≥23	19-22	≤20
24	Rifampin	RA	2	≥20	17-19	≤16

Table 2.Comparison of antibiotic susceptibility pattern of viridans group streptococci isolated from Carious and non-carious subjects.

Antibiotics	Carious (n=175)				Non-carious (n=350)			
	Resistant		Susceptible		Resistant		Susceptible	
	No. of isolates	%	No. of isolates	%	No. of isolates	%	No. of isolates	%
β- Lactam group								
Penicillins								
Penicillin	52	29.7	123	70.3	66	18.9	284	81.1
Amoxicillin	86	49.1	89	50.9	84	24	266	76.0
Cephalosporins								
Cephalothin	05	2.9	170	97.1	04	1.1	346	98.9
Cefazolin	06	3.4	169	96.6	04	1.1	346	98.9
Cefotaxime	04	2.3	171	97.7	06	1.7	344	98.3
Ceftazidime	09	5.1	166	94.9	01	0.3	349	99.7
Carbapenem								
Imipenem	04	2.3	171	97.7	02	0.6	348	99.4
Phenicols								
Chloramphenicol	77	44	98	56.0	60	17.1	290	82.9
Lincosamides								
Clindamycin	47	26.9	128	73.1	53	15.1	297	84.9
Pyrimidine analogs								
Trimethoprim	11	6.3	164	93.7	03	0.9	347	99.1
Macrolides								
Azithromycin	43	24.6	132	75.4	44	12.6	306	87.4
Erythromycin	119	68.0	56	32.0	135	38.6	215	61.4
Clarithromycin	50	28.6	125	71.4	61	17.4	289	82.6
Quinolone								
Ciprofloxacin	74	42.3	101	57.7	56	16	294	84.0
Levofloxacin	71	40.6	104	59.4	106	30.3	244	69.7
Tetracyclines								
Doxycyclines	86	49.1	89	50.9	84	24.0	266	76.0
Tetracycline	77	44	98	56.0	89	25.4	261	74.6
Aminoglycosides								
Gentamicin	82	46.9	93	53.1	123	35.1	227	64.9
Streptomycin	96	54.9	79	45.1	109	31.1	241	68.9
Tobramycin	76	43.4	99	56.6	95	27.1	255	72.9
Glycopeptides								
Teicoplanin	06	3.4	169	96.6	02	0.6	348	99.4
Vancomycin	55	31.4	120	68.6	59	16.9	291	83.1
Miscellaneous								
Linezolid	15	8.6	160	91.4	05	1.4	345	98.6
Rifampin	71	40.6	104	59.4	61	17.4	289	82.6

In case of Macrolide group of antibiotics; three antibiotics i.e. Azithromycin, Erythromycin and Clarithromycin were included. The overall incidence of resistant isolates to Erythromycin from carious (68%, 119/175) and non-carious (38.6%, 135/350) subjects was found higher compared to Clarithromycin (carious: 28.6%, 50/175; non-carious: 17.4%, 61/350) and Azithromycin (carious: 24.6%, 43/175; non-carious: 12.6%, 44/350) (Table 2). Macrolides, a broad-spectrum group, includes Erythromycin, Azithromycin and Clarithromycin are bacteriostatic agents contain a macrocyclic lactone ring that inhibit protein synthesis and act against bacterial ribosome as a translation modulators. This group also has strong antimicrobial potential against Gram positive and Gram negative bacteria (Berbel *et al*., 2022; Singh *et al*., 2020). Among Macrolides, Erythromycin commonly prescribes for inactivation of dental caries. It has potential to decrease the formation of dental plaque with strong antibacterial activity against various species belonging to VGS such as *Streptococcus mutans* (Berbel *et al*., 2022; Singh *et al*., 2020; Mahon *et*

al., 2014; Pelczar, 1993). Erythromycin is used as an alternative treatment for penicillin allergic patients. In the past, most oral VGS were susceptible to this agent; however, the resistance of oral VGS to this agent is increasing day by day (Kim and Lee, 2020). Comparison of emergence of resistance among species obtained from carious and non-carious subjects indicated that, in case of carious subjects, the highest incidence of resistant isolates against Erythromycin was for *S. sanguinis* (100%, 03/03) followed by *S. mutans* (86.2%, 25/29), *S. salivarius* (83.3%, 05/06), *S. oralis* (75%, 03/04), *S. anginosus* (71.6%, 68/95), *S. uberis* (46.7%, 07/15), *S. mitis* (46.2%, 06/13) and *S. intermedius* (11.1%, 01/09). The single isolate of *S. acidominimus* was also resistant. While, in case of non-carious subjects, none of the isolates of *S. intermedius* and *S. sanguinis* was found resistant to Erythromycin whereas the highest incidence of resistant isolates belonging to other species was noted as *S. mutans* 76.4% (36/47), *S. acidominimus* 75% (03/04), *S. oralis* 57.1% (08/14), *S. uberis* 42.1% (08/19), *S. anginosus* 39.2% (73/186) and *S. mitis* 12.8% (06/47). The single isolate of *S. salivarius* was also resistant (Table 3B).

Table 3.Antibiogram pattern of different species of viridans group streptococci.

Organisms	Total No. of Isolates	Penicillin				Cephalosporin							
		PEN		AMX		CF		CZ		CTX		TAZ	
		R	S	R	S	R	S	R	S	R	S	R	S
S. anginosus	Carious (95)	16.8 (16)	83.2 (79)	44.2 (42)	55.8 (53)	5.3 (05)	94.7 (90)	3.2 (03)	96.8 (92)	2.1 (02)	97.9 (93)	2.1 (02)	95.8 (91)
	Non-carious (186)	7.5 (14)	92.5 (172)	28 (52)	72 (134)	1.2 (02)	99 (184)	0.5 (01)	99.5 (185)	0	100 (186)	0	100 (186)
S. mutans	Carious (29)	34.5 (10)	65.5 (19)	62.1 (18)	37.9 (11)	0	100 (29)	6.9 (02)	93.1 (27)	6.9 (02)	93.1 (27)	0	100 (29)
	Non-carious (47)	29.8 (14)	70.2 (33)	19.1 (09)	80.9 (38)	0	100 (47)	0	100 (47)	12.8 (06)	84.2 (41)	0	100 (47)
S. mitis	Carious (13)	15.4 (02)	84.6 (11)	69.2 (09)	30.8 (04)	0	100 (13)	0	100 (13)	0	100 (13)	0	100 (13)
	Non-carious (47)	12.8 (06)	84.2 (41)	21.3 (10)	78.7 (37)	4.3 (02)	95.7 (45)	2.1 (01)	97.9 (46)	0	100 (47)	0	100 (47)
S. uberis	Carious (15)	80.0 (12)	20.0 (03)	13.3 (02)	86.7 (13)	0	100 (15)	0	100 (15)	0	100 (15)	13.3 (02)	86.7 (13)
	Non-carious (19)	78.9 (15)	21.1 (04)	21.1 (04)	79.0 (15)	0	100 (19)	10.5 (02)	89.5 (17)	0	100 (19)	5.3 (01)	94.7 (18)
S. intermedius	Carious (09)	44.4 (04)	55.6 (05)	55.6 (05)	44.4 (04)	0	100 (09)	0	100 (09)	0	100 (09)	22.2 (02)	77.8 (07)
	Non-carious (15)	13.3 (02)	86.7 (13)	13.3 (02)	86.7 (13)	0	100 (15)	0	100 (15)	0	100 (15)	0	100 (15)
S. sanguinis	Carious (03)	66.7 (02)	33.3 (01)	100 (03)	0	0	100 (03)	0	100 (03)	0	100 (03)	0	100 (03)
	Non-carious (17)	41.2 (07)	58.8 (10)	11.8 (02)	88.2 (15)	0	100 (17)	0	100 (17)	0	100 (17)	0	100 (17)
S. oralis	Carious (04)	50.0 (02)	50.0 (02)	75.0 (03)	25.0 (01)	0	100 (04)	25.0 (01)	75.0 (03)	0	100 (04)	25.0 (01)	75.0 (03)
	Non-carious (14)	35.7 (05)	64.3 (09)	28.6 (04)	71.4 (10)	0	100 (14)	0	100 (14)	0	100 (14)	0	100 (14)
S. salivarius	Carious (06)	50.0 (03)	50.0 (03)	50.0 (03)	50.0 (03)	0	100 (06)	0	100 (06)	0	100 (06)	0	100 (06)
	Non-carious (01)	100 (01)	0	0	100 (01)	0	100 (01)	0	100 (01)	0	100 (01)	0	100 (01)
S. acidominimus	Carious (01)	100 (01)	0	100 (01)	0	0	100 (01)	0	100 (01)	0	100 (01)	0	100 (01)
	Non-carious (04)	50.0 (02)	50.0 (02)	25.0 (01)	75.0 (03)	0	100 (04)	0	100 (04)	0	100 (04)	0	100 (04)
Total	Carious (175)	29.7 (52)	70.3 (123)	49.1 (86)	50.9 (89)	2.9 (05)	97.1 (170)	3.4 (06)	96.6 (169)	2.3 (04)	97.7 (171)	5.1 (09)	94.9 (166)
	Non-carious (350)	18.9 (66)	81.1 (284)	24 (84)	76 (266)	1.1 (04)	98.9 (346)	1.1 (04)	98.9 (346)	1.7 (06)	98.3 (344)	0.3 (01)	99.7 (349)

Figures in parenthesis are number of isolates

TABLE 3A

Organisms	Total No. of Isolates	Carbapenem		Phenicols		Lincosamides		Pyrimidine analogs	
		IPM		CHL		CLI		TMP	
		R	S	R	S	R	S	R	S
S. anginosus	Carious (95)	3.2 (03)	96.8 (92)	47.4 (45)	52.6 (50)	19 (18)	81.1 (77)	5.3 (05)	94.7 (90)
	Non-carious (186)	0	100 (186)	17.2 (32)	82.8 (154)	7 (13)	93 (173)	0	100 (186)
S. mutans	Carious (29)	3.4 (01)	96.6 (28)	69.0 (20)	31.0 (09)	13.8 (04)	86.2 (25)	17.2 (05)	82.8 (24)
	Non-carious (47)	4.3 (02)	95.7 (45)	42.6 (20)	57.4 (27)	10.6 (05)	89.4 (42)	4.3 (02)	95.7 (45)
S. mitis	Carious (13)	0	100 (13)	15.4 (02)	84.6 (11)	53.8 (07)	46.2 (06)	7.7 (01)	92.3 (12)
	Non-carious (47)	0	100 (47)	10.6 (05)	89.4 (42)	38.3 (18)	61.7 (29)	2.1 (01)	97.9 (46)
S. uberis	Carious (15)	0	100 (15)	6.7 (01)	93.3 (14)	40.0 (06)	60.0 (09)	0	100 (15)
	Non-carious (19)	0	100 (19)	15.8 (03)	84.2 (16)	42.1 (08)	57.9 (11)	0	100 (19)
S. intermedius	Carious (09)	0	100 (09)	33.3 (03)	66.7 (06)	55.6 (05)	44.4 (04)	0	100 (09)
	Non-carious (15)	0	100 (15)	0	100 (15)	13.3 (02)	86.7 (13)	0	100 (15)
S. sanguinis	Carious (03)	0	100 (03)	33.3 (01)	66.7 (02)	10.0 (02)	33.3 (01)	0	100 (03)
	Non-carious (17)	0	100 (17)	0	100 (17)	41.2 (07)	58.8 (10)	0	100 (17)
S. oralis	Carious (04)	0	100 (04)	25.0 (01)	75.0 (03)	0	100 (04)	0	100 (04)
	Non-carious (14)	0	100 (14)	0	100 (14)	0	100 (14)	0	100 (14)
S. salivarius	Carious (06)	0	100 (06)	50.0 (03)	50.0 (03)	83.3 (05)	16.7 (01)	0	100 (06)
	Non-carious (01)	0	100 (01)	0	100 (01)	0	100 (01)	0	100 (01)
S. acidominimus	Carious (01)	0	100 (01)	100 (01)	0	0	100 (01)	0	100 (01)
	Non-carious (04)	0	100 (04)	0	100 (04)	0	100 (04)	0	100 (04)
Total	Carious (175)	2.3 (04)	97.7 (171)	44 (77)	56 (98)	26.9 (47)	73.1 (128)	6.3 (11)	93.7 (164)
	Non-carious (350)	0.6 (02)	99.4 (348)	17.1 (60)	82.9 (290)	15.1 (53)	84.9 (297)	0.9 (03)	99.1 (347)

Figures in parenthesis are number of isolates

TABLE 3B

Organisms	Total No. of Isolates	Macrolides						Quinolone			
		AZM		ERY		CLR		CIP		LEV	
		R	S	R	S	R	S	R	S	R	S
S. anginosus	Carious (95)	16.8 (16)	83.2 (79)	71.6 (68)	28.4 (27)	42.1 (40)	57.9 (55)	48.4 (46)	51.6 (49)	33.7 (32)	66.3 (63)
	Non-carious (186)	10.8 (20)	89.2 (166)	39.2 (73)	60.8 (113)	28 (52)	72 (134)	18.3 (34)	81.7 (152)	26.3 (49)	73.7 (137)
S. mutans	Carious (29)	41.4 (12)	58.6 (17)	86.2 (25)	13.8 (04)	17.2 (05)	82.8 (24)	17.2 (05)	82.8 (24)	69.0 (20)	31.0 (09)
	Non-carious (47)	17.0 (08)	83.0 (39)	76.4 (36)	23.4 (11)	10.6 (05)	89.4 (42)	8.5 (04)	91.5 (43)	57.4 (27)	42.6 (20)
S. mitis	Carious (13)	30.8 (04)	69.2 (09)	46.2 (06)	53.8 (07)	23.1 (03)	76.9 (10)	69.2 (09)	30.8 (04)	53.8 (07)	46.2 (06)
	Non-carious (47)	12.8 (06)	87.2 (41)	12.8 (06)	87.2 (41)	6.4 (03)	93.6 (44)	23.4 (11)	76.6 (36)	12.8 (06)	87.2 (41)
S. uberis	Carious (15)	26.7 (04)	73.3 (11)	46.7 (07)	53.3 (08)	13.3 (02)	86.7 (13)	13.3 (02)	86.7 (13)	13.3 (02)	86.7 (13)
	Non-carious (19)	31.6 (06)	68.4 (13)	42.1 (08)	57.9 (11)	5.3 (01)	94.7 (18)	15.8 (03)	84.2 (16)	15.8 (03)	84.2 (16)
S. intermedius	Carious (09)	11.1 (01)	88.9 (08)	11.1 (01)	88.9 (08)	0	100 (09)	66.7 (06)	33.3 (03)	66.7 (06)	33.3 (03)
	Non-carious (15)	0	100 (15)	0	100 (15)	0	100 (15)	13.3 (02)	86.7 (13)	20.0 (03)	80.0 (12)
S. sanguinis	Carious (03)	33.3 (01)	66.7 (02)	100 (03)	0	0	100 (03)	66.7 (02)	33.3 (01)	33.3 (01)	66.7 (02)
	Non-carious (17)	11.8 (02)	88.2 (15)	0	100 (17)	0	100 (17)	0	100 (17)	29.4 (05)	70.6 (12)
S. oralis	Carious (04)	25.0 (01)	75.0 (03)	75.0 (03)	25.0 (01)	0	100 (04)	0	100 (04)	0	100 (04)
	Non-carious (14)	7.1 (01)	92.9 (13)	57.1 (08)	42.9 (06)	0	100 (14)	7.1 (01)	92.9 (13)	0	100 (14)
S. salivarius	Carious (06)	50.0 (03)	50.0 (03)	83.3 (05)	16.7 (01)	0	100 (06)	50.0 (03)	50.0 (03)	33.3 (02)	66.7 (04)
	Non-carious (01)	100 (01)	0	100 (01)	0	0	100 (01)	100 (01)	0	0	100 (01)
S. acidominimus	Carious (01)	100 (01)	0	100 (01)	0	0	100 (01)	100 (01)	0	100 (01)	0
	Non-carious (04)	0	100 (04)	75.0 (03)	25.0 (01)	0	100 (04)	0	100 (04)	0	100 (04)
Total	Carious (175)	24.6 (43)	75.4 (132)	68 (119)	32 (56)	28.6 (50)	71.4 (125)	42.3 (74)	57.7 (101)	40.6 (71)	59.4 (104)
	Non-carious (350)	12.6 (44)	87.4 (306)	38.6 (135)	61.4 (215)	17.4 (61)	82.6 (289)	16 (56)	84 (294)	30.3 (106)	69.7 (244)

Figures in parenthesis are number of isolates

TABLE 3C

Organisms	Total No. of Isolates	Tetracycline				Aminoglycosides					
		DOX		TET		GEN		STR		TOB	
		R	S	R	S	R	S	R	S	R	S
S. anginosus	Carious (95)	34.7 (33)	65.3 (62)	44.2 (42)	55.8 (53)	34.7 (33)	65.3 (62)	56.8 (54)	43.2 (41)	60 (57)	40 (38)
	Non-carious (186)	21.5 (40)	78.5 (146)	26.3 (49)	73.7 (137)	24.7 (46)	75.3 (140)	37.6 (70)	62.4 (116)	40.3 (75)	59.7 (111)
S. mutans	Carious (29)	89.7 (26)	10.3 (03)	24.1 (07)	75.9 (22)	75.9 (22)	24.1 (07)	55.2 (16)	44.8 (13)	17.2 (05)	82.8 (24)
	Non-carious (47)	59.6 (28)	40.4 (19)	17.0 (08)	83.0 (39)	78.7 (37)	21.3 (10)	29.8 (14)	70.2 (33)	8.5 (04)	91.5 (43)
S. mitis	Carious (13)	53.8 (07)	46.2 (06)	46.2 (06)	53.8 (07)	46.2 (06)	53.8 (07)	46.2 (06)	53.8 (07)	23.1 (03)	76.9 (10)
	Non-carious (47)	31.9 (15)	68.1 (32)	25.5 (12)	74.5 (35)	25.5 (12)	74.5 (35)	19.1 (09)	80.9 (38)	19.1 (09)	80.9 (38)
S. uberis	Carious (15)	46.7 (07)	53.3 (08)	40.0 (06)	60.0 (09)	26.7 (04)	73.3 (11)	26.7 (04)	73.3 (11)	13.3 (02)	86.7 (13)
	Non-carious (19)	42.1 (08)	57.9 (11)	31.6 (06)	68.4 (13)	26.3 (05)	73.7 (14)	31.6 (06)	68.4 (13)	15.8 (03)	84.2 (16)
S. intermedius	Carious (09)	33.3 (03)	66.7 (06)	77.8 (07)	22.2 (02)	66.7 (06)	33.3 (03)	88.9 (08)	11.1 (01)	66.7 (06)	33.3 (03)
	Non-carious (15)	13.3 (02)	86.7 (13)	26.7 (04)	73.3 (11)	86.7 (13)	13.3 (02)	20.0 (03)	80.0 (12)	6.7 (01)	93.3 (14)
S. sanguinis	Carious (03)	66.7 (02)	33.3 (01)	66.7 (02)	33.3 (01)	100 (03)	0	66.7 (02)	33.3 (01)	33.3 (01)	66.7 (02)
	Non-carious (17)	41.2 (07)	58.8 (10)	29.4 (05)	70.6 (12)	11.8 (02)	88.2 (15)	29.4 (05)	70.6 (12)	11.8 (02)	88.2 (15)
S. oralis	Carious (04)	75.0 (03)	25.0 (01)	50.0 (02)	50.0 (02)	50.0 (02)	50.0 (02)	75.0 (03)	25.0 (01)	0	100 (04)
	Non-carious (14)	28.6 (04)	71.4 (10)	14.3 (02)	85.7 (12)	35.7 (05)	64.3 (09)	7.1 (01)	92.9 (13)	0	100 (14)
S. salivarius	Carious (06)	83.3 (05)	16.7 (01)	66.7 (04)	33.3 (02)	100 (06)	0	33.3 (02)	66.7 (04)	16.7 (01)	83.3 (05)
	Non-carious (01)	100 (01)	0	100 (01)	0	100 (01)	0	0	100 (01)	0	100 (01)
S. acidominimus	Carious (01)	0	100 (01)	100 (01)	0	0	100 (01)	100 (01)	0	100 (01)	0
	Non-carious (04)	25.0 (01)	75.0 (03)	50.0 (02)	50.0 (02)	50.0 (02)	50.0 (02)	25.0 (01)	75.0 (03)	25.0 (01)	75.0 (03)
Total	Carious (175)	49.1 (86)	50.9 (89)	44 (77)	56 (98)	46.9 (82)	53.1 (93)	54.9 (96)	45.1 (79)	43.4 (76)	56.6 (99)
	Non-carious (350)	24 (84)	76 (266)	25.4 (89)	74.6 (261)	35.1 (123)	64.9 (227)	31.1 (109)	68.9 (241)	27.1 (95)	72.9 (255)

Figures in parenthesis are number of isolates

TABLE 3D

Organisms	Total No. of Isolates	Glycopeptides				Miscellaneous			
		TPN		VAN		LNZ		RA	
		R	S	R	S	R	S	R	S
S. anginosus	Carious (95)	6.3 (06)	93.7 (89)	35.8 (34)	64.2 (61)	2.1 (02)	97.9 (93)	46.3 (44)	53.7 (51)
	Non-carious (186)	1.1 (02)	98.9 (184)	14.5 (27)	85.5 (159)	0	100 (186)	19.4 (36)	80.6 (150)
S. mutans	Carious (29)	0	100 (29)	17.2 (05)	82.8 (24)	13.8 (04)	86.2 (25)	10.3 (03)	89.7 (26)
	Non-carious (47)	0	100 (47)	17.0 (08)	83.0 (39)	10.6 (05)	89.4 (42)	17.0 (08)	83.0 (39)
S. mitis	Carious (13)	0	100 (13)	23.1 (03)	76.9 (10)	23.1 (03)	76.9 (10)	23.1 (03)	76.9 (10)
	Non-carious (47)	0	100 (47)	8.5 (04)	91.3 (43)	0	100 (47)	0	100 (47)
S. uberis	Carious (15)	0	100 (15)	13.3 (02)	86.7 (13)	0	100 (15)	40.0 (06)	60.0 (09)
	Non-carious (19)	0	100 (19)	15.8 (03)	84.2 (16)	0	100 (19)	52.6 (10)	47.4 (09)
S. intermedius	Carious (09)	0	100 (09)	55.6 (05)	44.4 (04)	44.4 (04)	55.6 (05)	66.7 (06)	33.3 (03)
	Non-carious (15)	0	100 (15)	73.3 (11)	26.7 (04)	0	100 (15)	13.3 (02)	86.7 (13)
S. sanguinis	Carious (03)	0	100 (03)	100 (03)	0	66.7 (02)	33.3 (01)	33.3 (01)	66.7 (02)
	Non-carious (17)	0	100 (17)	29.4 (05)	70.6 (12)	0	100 (17)	29.4 (05)	70.6 (12)
S. oralis	Carious (04)	0	22.2 (04)	25.0 (01)	75.0 (03)	0	100 (04)	50.0 (02)	50.0 (02)
	Non-carious (14)	0	100 (14)	0	100 (14)	0	100 (14)	0	100 (14)
S. salivarius	Carious (06)	0	100 (06)	33.3 (02)	66.7 (04)	0	100 (06)	83.3 (05)	16.7 (01)
	Non-carious (01)	0	100 (01)	0	100 (01)	0	100 (01)	0	100 (01)
S. acidominimus	Carious (01)	0	100 (01)	0	100 (01)	0	100 (01)	100 (01)	0
	Non-carious (04)	0	100 (04)	25.0 (01)	75.0 (03)	0	100 (04)	0	100 (04)
Total	Carious (175)	3.4 (06)	96.6 (169)	31.4 (55)	68.6 (120)	8.6 (15)	91.4 (160)	40.6 (71)	59.4 (104)
	Non-carious (350)	0.6 (02)	99.4 (348)	16.9 (59)	83.1 (291)	1.4 (05)	98.6 (345)	17.4 (61)	82.6 (289)

Figures in parenthesis are number of isolates

As regards Clarithromycin, another member of Macrolide group, the agent is believed to be worked as a new generation of erythromycin and often used for dental abscesses and for patients who are sensitive to penicillin (Pelczar, 1993). The highest incidence of resistant isolates obtained from carious subjects was noted as 42.1% (40/95) for *S. anginosus* followed by *S. mitis* 23.1% (03/13), *S. mutans* 17.2% (05/29) and *S. uberis* 13.3% (02/15) while, none of the isolates of *S. intermedius*, *S. sanguinis*, *S. oralis*, *S. salivarius* and *S. acidominimus* was found resistant. Similarly, none of the isolates of *S. intermedius*, *S. sanguinis*, *S. oralis*, *S. salivarius* and *S. acidominimus* obtained from non-carious subjects was found resistant while, the highest incidence of resistant isolates obtained from non-carious subjects was noted as 28% (52/186) for *S. anginosus* followed by *S. mutans* 10.6% (05/47), *S. mitis* 6.4% (03/47) and *S. uberis* 5.3% (01/19) (Table 3B).

As far as Azithromycin concern, it considers being the most effective than other macrolides but commonly does not prescribed for odontogenic infections as first line treatment (Pelczar, 1993). For this agent, the highest incidence of resistant isolates obtained from carious subjects was found as 50% (03/06) for *S. salivarius*followed by *S. mutans* (41.4%, 12/29), *S. sanguinis* (33.3%, 01/03), *S. mitis* (30.8%, 04/13), *S. uberis* (26.7%, 04/15), *S. oralis* (25%, 01/04), *S. anginosus* (16.8%, 16/95) and *S. intermedius* (11.1%, 01/09). The single isolate of *S. intermedius* was also resistant. On the other hand, none of the isolates of *S. intermedius* and *S. acidominimus* obtained from non-carious subjects showed resistance to Azithromycin while the highest incidence of resistant isolates was found as 31.6% (06/19) for *S. uberis* followed by *S. mutans* (17%, 08/47), *S. mitis* (12.8%, 06/47), *S. sanguinis* (11.8%, 02/17), *S. anginosus* (10.8%, 20/186) and *S. oralis* (7.1%, 01/14). The single isolate of *S. salivarius* was found resistant to this antibiotic (Table 3B).

In case of **fluoroquinolone group, Ciprofloxacin and Levofloxacin were included** in the study. Fluoroquinolone is a broad-spectrum bactericidal antibiotic group that effectively acts against most of bacterial pathogens by preventing the synthesis of DNA (Pelczar, 1993). The overall incidence of resistant isolates obtained from carious subjects was noted as 42.3% (74/175) for Ciprofloxacin (second generation of quinolone) and 40.6% (71/175) for Levofloxacin while the incidence of resistant isolates recovered from non-carious subjects was noted as 30.3% (106/350) for Levofloxacin and 16% (56/350) for Ciprofloxacin (Table 2). Comparative study of emergence of resistance among different species isolated from carious and non-carious subjects (Table 3B) revealed that none of the isolates of *S. oralis* obtained from carious subjects was found resistant to Ciprofloxacin and the single isolate of *S. acidominimus* was found resistant. Besides, the incidence of resistant isolates belonging to other species was noted as 69.2% (09/13) for *S. mitis* followed by *S. intermedius* (66.7%, 06/09), *S. sanguinis* (66.7%, 02/03), *S. salivarius* (50%, 03/06), *S. anginosus* (48.4%, 46/95), *S. mutans* (17.2%, 05/29) and *S. uberis* (13.3%, 02/15). On the other hand, in case of non-carious subjects, none of the isolates of *S. sanguinis* and *S. acidominimus* was found resistant to Ciprofloxacin while the highest number of resistant isolate was noted as 23.4% (11/47) for *S. mitis* followed by *S. anginosus* (18.3%, 34/186), *S. uberis* (15.8%, 03/19), *S. intermedius* (13.3%, 02/15), *S. mutans* (8.5%, 04/47) and *S. oralis* (7.1%, 01/14) and the single isolate of *S. salivarius* was found resistant (Table 3B).

In case of Levofloxacin, this agent belongs to a broad spectrum antibiotic group offluoroquinolone used either parenterally or orally in implant dentistry for severe infections, especially in the maxillary sinus. Moreover, it could be utilized as prophylaxis in penicillin allergic patients for mandibular third molar extraction (Cawson, 1991; Pelczar, 1993). For Levofloxacin, none of the isolates of *S. oralis* obtained from carious subjects was found resistant while the highest incidence of resistant isolates to this antibiotic was noted as 69% (20/29) for *S. mutans* followed by *S. intermedius* (66.7%, 06/09), *S. mitis* (53.8%, 07/13), *S. anginosus* (33.7%, 32/95), *S. sanguinis*(33.3%, 01/03), *S. salivarius* (33.3%, 02/06) and *S. uberis* (13.3%, 02/15). A single isolate of *S. intermedius* was obtained from carious subjects which was also resistant. Comparatively, in case of non-carious subjects, none of the isolates of *S. oralis*, *S. salivarius* and *S. acidominimus*was found resistant to this antibiotic while the highest incidence of resistant isolates was noted as 57.4% (27/47) for *S. mutans* followed by *S. sanguinis* (29.4%, 05/17), *S. anginosus* (26.3, 49/186), *S. intermedius* (20%, 03/15), *S. uberis* (15.8%, 03/19) and *S. mitis* (12.8%, 06/47) (Table 3B).

Another tested group of antibiotics was Tetracycline. For this study, Doxycycline and Tetracycline were used. Tetracycline is a bacteriostatic antibiotic group that mostly works against Gram-positive and Gram-negative bacteria by inhibiting the protein synthesis through binding to the ribosomal subunit. In dentistry, the agent is mostly prescribed for periodontal infections as Tetracycline gradually released from tooth surface (Lopardo *et al*., 2022; Mahon *et al*., 2014; Pelczar, 1993; Cawson, 1991). The overall incidence of resistant isolates obtained from carious subjects was found higher for Doxycycline (49.1%, 86/175) compared to Tetracycline (44%, 77/175) while both antibiotics showed quite similar incidence of resistant isolates obtained from non-carious subjects. It was noted as 25.4% (89/350) for Tetracycline and 24% (84/350) for Doxycycline (Table 2). Doxycycline is used to treat periodontal disease. It also helps to improve tooth attachment and reduce gum pockets. At the low potency of this agent, it does not treat bacterial infections, but it might help to prevent breakdown of gum tissue (Pelczar, 1993). Study of emergence of antibiotic resistance among species isolated from carious and non-carious subjects showed that the only isolate of *S. acidominimus* from carious subjects was found resistant to Doxycycline while the

highest incidence of resistant isolates was noted among *S. mutans* (89.7%, 26/29) followed by *S. salivarius* (83.3%, 05/06), *S. oralis* (75%, 03/04), *S. sanguinis* (66.7%, 02/03), *S. mitis* (53.8%, 07/13), *S. uberis* (46.7%, 07/15), *S. anginosus* (34.7%, 33/95) and *S. intermedius* (33.3%, 03/09). On the other hand, the highest incidence of resistant isolates was observed as 59.6% (28/47) for *S. mutans* followed by *S. uberis* (42.1%, 08/19), *S. sanguinis* (41.2%, 07/17), *S. mitis* (31.9%, 15/47), *S. oralis* (28.6%, 04/14), *S. acidominimus* (25%, 01/04), *S. anginosus* (21.5%, 40/186) and *S. intermedius* (13.3%, 02/15). The single isolate of *S. salivarius* was also resistant to Doxycycline (Table 3C).

In case of Tetracycline, the highest incidence of resistant isolates obtained from carious subjects was noted as 77.8% (07/09) for *S. intermedius* followed by *S. sanguinis* (66.7%, 02/03), *S. salivarius* (66.7%, 04/06), *S. oralis* (50%, 02/04), *S. mitis* (46.2%, 06/13), *S. anginosus* (44.2%, 42/95), *S. uberis* (40%, 06/15) and *S. mutans* (24.1%, 07/29). The single isolate of *S. acidominimus* was also resistant. While, for isolates obtained from non-carious subjects, the highest incidence of resistant isolates was noted as 50% (02/04) for *S. acidominimus* followed by *S. uberis* (31.6%, 06/19), *S. sanguinis* (29.4%, 05/17), *S. intermedius* (26.7%, 04/15), *S. anginosus* (26.3%, 49/186), *S. mitis* (25.5%, 12/47), *S. mutans* (17%, 08/47) and *S. oralis* (14.3%, 02/14), while the single isolate of *S. salivarius* was also found resistant (Table 3C).

In the present study, **Gentamicin, Streptomycin and Tobramycin of Aminoglycosides group were used** for determination of antibiotic susceptibility. The aminoglycoside group of antibiotics contains a large structurally related polycationic compounds containing two or more amino sugars connected by glycoside linkage to a hexose core. In this group, amikacin, gentamicin, kanamycin, neomycin, netilmicin, paromomycin, rhodostreptomycin, streptomycin, tobramycin and apramycin are included (Mahon *et al*., 2014; Cox and Wright, 2013; Pelczar, 1993). They act by inhibiting protein synthesis and also disrupt the normal permeability of cell wall of bacteria. Generally, aminoglycoside are not effective against anaerobes, enterococci and streptococci. To extend their spectrum of activity, sometimes this group is used in combination with the beta lalctam drugs because beta lactam drugs interfere with cell wall synthesis which allows the aminoglycoside to enter the cell more easily (Nester *et al*., 2004; Pelczar, 1993). The overall incidence of resistant isolates obtained from carious subjects was found higher for Streptomycin (54.9%, 96/175) compared to Gentamicin (46.9%, 82/175) and Tobramycin (43.4%, 76/175) while the overall incidence of resistant isolates obtained from non-carious subjects was higher for Gentamicin (35.1%, 123/350) compared to Streptomycin (31.1%, 109/350) and Tobramycin (27.1%, 95/350) (Table 2). The incidence of resistant isolates belonging to different species obtained from carious and non-carious subjects are presented in Table 3C. For Streptomycin, the highest incidence of resistant isolates obtained from carious subjects was noted as 88.9% (08/09) for *S. intermedius* followed by *S. oralis* (75%, 03/04), *S. sanguinis* (66.7%, 02/03), *S. anginosus* (56.8%, 54/95), *S. mutans* (55.2%, 16/29), *S. mitis* (46.2%, 06/13), *S. salivarius* (33.3%, 02/06) and *S. uberis* (26.7%, 04/15), while the single isolate of *S. acidominimus* was also found resistant. On the other hand, the highest incidence of resistant isolates obtained from non-carious subjects was noted for *S. anginosus* (37.6%, 70/186) followed by *S. uberis* (31.6%, 06/19), *S. mutans* (29.8%, 14/47), *S. sanguinis* (29.4%, 05/17), *S. acidominimus* (25%, 01/04), *S. intermedius* (20%, 03/15), *S. mitis* (19.1%, 09/47) and *S. oralis* (7.1%, 01/14). Whereas the only isolate of *S.salivarius* was susceptible to Streptomycin.

In case of Gentamicin, the single isolate of *S. acidominimus* obtained from carious subjects was found susceptible while the highest incidence of resistant isolates was noted for *S. salivarius* (100%, 06/06) and *S. sanguinis* (100%, 03/03) followed by *S. mutans* (75.9%, 22/29), *S. intermedius* (66.7%, 06/09), *S. oralis* (50%, 02/04), *S. mitis* (46.2%, 06/13), *S. anginosus* (34.7%, 33/95) and *S. uberis* (26.7%, 04/15). The highest incidence of resistant isolates obtained from non-carious subjects was noted for *S. intermedius* (86.7%, 13/15) followed by *S. mutans* (78.7%, 37.47), *S. acidominimus* (50%, 02/04), *S. oralis* (35.7%, 05/14), *S. uberis* (26.3%, 05/19), *S. mitis* (25.5%, 12/47), *S. anginosus* (24.7%, 46/186) and *S. sanguinis* (11.8%, 02/17). The only isolate of *S. salivarius* was also resistant (Table 3C).

For Tobramycin, none of the isolates of *S. oralis* obtained from carious subjects was found resistant while the highest incidence of resistant isolates was noted against *S. intermedius* (66.7%, 06/09) followed by *S. anginosus* (60%, 57/95), *S. sanguinis* (33.3%, 01/03), *S. mitis* (23.1%, 03/13), *S. mutans* (17.2%, 05/29), *S. salivarius* (16.7%, 01/06) and *S. uberis* (13.3%, 02/15). The only isolate of *S. acidominimus* was also resistant. None of the isolates of *S. oralis* and single isolate of *S. salivarius* obtained from non-carious subjects were found resistant to Tobramycin while the highest incidence of resistant isolates was observed for *S. anginosus* (40.3%, 75/186) followed by *S. acidominimus* (25%, 01/04), *S. mitis* (19.1%, 09/47), *S. uberis* (15.8%, 03/19), *S. sanguinis* (11.8%, 02/17), *S. mutans* (8.5%, 04/47) and *S. intermedius* (6.7%, 01/15) (Table 3C).

Next group of antibiotics selected for the study was Glycopeptide. Teicoplanin and Vancomycin from this group were included in the study. The overall incidence of resistant isolates obtained from carious and non-carious subjects was noted higher for Vancomycin [carious 31.4% (55/175); non-carious 16.9% (59/350)] compared to Teicoplanin [carious 3.4% (06/175); non-carious 0.6% (02/350)] (Table 2). The teicoplanin, a new glycopeptide antibiotic could decrease the occurrence and severity of bacteraemia following dental extraction process (Maskell *et al*., 1986). As regards emergence of resistance among species against these antibiotics, only 6.3% (06/95) and 1.1% (02/186) isolates of *S. anginosus* obtained from carious and non-carious subjects respectively were found resistant to Teicoplanin (Table 3D).

In case of vancomycin, for isolates obtained from carious subjects, the highest incidence of resistant isolates was noted for *S. sanguinis* (100%, 03/03) followed by *S. intermedius* (55.6%, 05/09), *S. anginosus* (35.8%, 34/95), *S. salivarius* (33.3%, 02/06), *S. oralis* (25%, 01/04), *S. mitis* (23.1%, 03/13), *S. mutans* (17.2%, 05/29) and *S. uberis* (13.3%, 02/15) whereas the only isolate of *S. acidominimus* was not found resistant. The topical use of vancomycin could be helpful for treatment of dental caries by eliminating the most of species belonging to oral VGS which has been implicated in the cariogenic process. For VGS obtained from non-carious subjects, the highest incidence of resistant isolates against Vancomycin was noted for *S. intermedius* (73.3%, 11/15) followed by *S. sanguinis* (29.4%, 05/17), *S. acidominimus* (25%, 01/04), *S. mutans* (17%, 08/47), *S. uberis* (15.8%, 03/19), *S. anginosus* (14.5%, 27/186) and *S. mitis* (8.5%, 04/47) while none of the isolates of *S. oralis* and a single isolate of *S. salivarius* was found resistant (Table 3D).

Rifampin and Linezolid used in present study have been categorized as miscellaneous group of antibiotics. The overall incidence of resistant isolates obtained from carious and non-carious subjects was noted higher for Rifampin compared to Linezolid. It was noted as 40.6% (71/175) and 17.4% (61/350) for Rifampin and 8.6% (15/175) and 1.4% (05/350) for Linezolid from carious and non-carious subjects respectively (Table 2). Linezolid antibiotic belongs to the family of oxazolidinones. Its strong antibacterial potential against multi-drug-resistant Gram positive bacteria has been well documented due to its effectiveness by inhibiting synthesis of protein (Poveda-Roda *et al*., 2007). Among species, a total of 66.7% isolates of *S. sanguinis* obtained from carious subjects were found resistant to Linezolid followed by *S. intermedius* (44.4%, 04/09), *S. mitis* (23.1%, 03/13), *S. mutans* (13.8%, 04/29) and *S. anginosus* (2.1%, 02/95). On the other hand, few isolates of *S. mutans* (10.6%, 05/47) obtained from non-carious subjects were found resistant to Linezolid (Table 3D).

Rifampin is a synthetic bactericidal derivative of the antibiotic Rifamycin B. Most of strains belonging to VGS are observed to be sensitive towards this agent. Rifampin acts by inhibition of RNA synthesis in bacteria (Jubeh *et al*., 2020; Mahon *et al*., 2014; Pelczar, 1993; Tuohy and Washington, 1997). The highest incidence of resistant isolates obtained from carious subjects against Rifampin was noted for *S. salivarius* (83.3%, 05/06) followed by *S. intermedius* (66.7%, 06/09), *S. oralis* (50%, 02/04), *S. anginosus* (46.3%, 44/95), *S. uberis* (40%, 06/15), *S. sanguinis* (33.3%, 01/03), *S. mitis* (23.1%, 03/13) and *S. mutans* (10.3%, 03/29) and the single isolate of *S. acidominimus* was also found resistant. On the other hand, none of the isolates of *S. mitis, S. oralis, S. sanguinis, S. salivarius* and *S. acidominimus* obtained from non-carious subjects were found resistant to Rifampin while the highest incidence of resistant isolates was noted for *S. uberis* (52.6%, 10/19) followed by *S. sanguinis* (29.4%, 05/17), *S. anginosus* (19.4%, 36/186), *S. mutans* (17%, 08/47) and *S. intermedius* (13.3%, 02/15) (Table 3D).

CONCLUSION

Different bacteria naturally inhabit in the oral cavity as a normal flora, for instance VGS. These VGS frequently act as an opportunistic pathogen or could be served as a resource reservoir for pathogens that subsequently cause serious infections. So, in the present study, the basic goal of antibiotic susceptibility pattern of VGS was to find possible antibiotic resistance as well as to assure susceptibility to drugs of choice for particular infections either oral or extra-oral infections.

To identify emerging patterns of resistance, it is necessary to periodically assess the antibiotic susceptibility pattern of VGS against the most commonly used antibiotics. This would enable medical professionals to choose the most effective medication to treat infections (oral and extra-oral infections) linked to VGS, as well as to limit side effects brought on by infections with antibiotic-resistant strains.

Results of present study though are not in agreement to previous studies which could be due to differences with regard to the sample size, sample types, morphological variations, study parameters, methods uses, potency used for antibiotics that need to be determined. But the outcomes of this study might therefore are valuable as they provide a different angle on the subjects.

Finally, it is concluded that the overuse or inappropriate use of antibiotics could be a significant reason for development of resistance to antimicrobial drugs which could damage the body's immune system and antibiotics to become less effective by longer course of any antibiotic. In this respect, dental caries could be best prevented by proper oral hygiene and other measures such as daily tooth cleaning habit by proper brushing with fluoride toothpaste after drinking or eating, flossing, mouth rinsing, avoid frequent sipping and snacking, healthy diet for teeth, use of tap water (water fluoridation), dental sealants and visit dentist regularly or in case of any need.

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