Original Research

Association between *Streptococcus bovis* and colorectal cancer among Libyan patients

Salah Bashir, Attiya Alatery*

Department of Microbiology and Immunology, Faculty of Pharmacy, University of Tripoli, Tripoli, Libya

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***Corresponding Author**
attiya2182000@yahoo.co.uk

Abstract

Streptococcus bovis/gallolyticus was considered as lower grade pathogen involved in endocarditis. Recent accumulating evidence has suggested that *Streptococcus bovis/gallolyticus* plays an important role in the initiation and development of colorectal cancer. This study was aimed to address the association between *Streptococcus bovis/gallolyticus* and colorectal cancer among Libyan patients, to determine the dominant biotype of *Streptococcus bovis/gallolyticus* associated with colorectal cancer patients and to evaluate the antibiotic susceptibly patterns of isolated strains. The study involved 20 colorectal cancer patients, 20 patients with large adenomas polyp and 20 people with healthy colonic mucosa as a control group. All the candidates were subjected to colonoscopy and histopathological examinations and conformation. The suspected and normal cases were then diagnosed according to the protocol used by the medicine specialist and grouped in accord with the study aim. All biopsies were handled and treated to isolate the suspected positive colonies of *Streptococcus bovis/gallolyticus*. Of the 20 colorectal cancer patients, seven patients (35%) were found to be *Streptococcus bovis/gallolyticus* carriers, (95% CI 1.22 - 1.72, $p < 0.05$). Nine patients (45%) were diagnosed colorectal cancer positive at age above 60 years old, eight patients (40%) at age 40 - 60 years old and three patients (15%) at age bellow 40 years old. Also, nine out of 20 patients (45%) with large adenomas polyp were found to be *Streptococcus bovis/gallolyticus* carriers, (95% CI 2.16 - 2.71, $p < 0.05$). Of the 20 healthy people with colonic mucosa, *Streptococcus bovis/gallolyticus* never been isolated. *Streptococcus. bovis* biotype II/I and *Streptococcus. equinis* were both susceptible to the above mentioned antibiotic classes, although *Streptococcus bovis* biotype I was highly resistance to most clinically used antibiotics. However, there was strong relationship between *Streptococcus bovis/gallolyticus* and colorectal cancer or large polyp formation. However, it is not well understood whether the bacterium has a pathogenic role in the initiation and progression of neoplasia or just an epiphenomenon of colorectal neoplasms.

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Introduction

Streptococcus bovis/gallolyticus (*S. bovis/gallolyticus)*, is normally detected in the gastrointestinal tract of about 10% of the human population [1]. Interestingly, the fecal carriage of *S. bovis/gallolyticus* was shown to be increased about 5-fold in patients with colorectal cancer (CRC) [2]. About 80% of the patients who presented *S. bovis/gallolyticus* bacteremia had CRC, and the incidence of association of colonic neoplasia with *S. bovis/gallolyticus* endocarditis was shown to be 62%. Actually, the association of *S. bovis/gallolyticus* bacteremia with CRC has been found variable among different geographical and ethnic groups [3]. Studies on *S. bovis/gallolyticus* have shown that associations between *S. bovis* bacteraemia and carcinoma of the colon were biotype-specific. However, the extent, nature and basis of this association are still not completely understood. In fact, adenomas, which have risk of malignant transformation about 25%, were found to be associated with *S. bovis/gallolyticus* bacteria more often than other types of bacteria. *S. bovis/gallolyticus* has long been linked to the development of CRC, although, it has no yet been determined whether a relation between S. *bovis/gallolyticus* and CRC is etiologically or incidentally. There are a lot of clues together provide quite

evidence for the etiological role of *S. bovis/gallolyticus* in colon cancer development. *S. bovis/gallolyticus* significantly more frequent in colonic polyps and colonic carcinoma than any other stype of *Enterococcus* group. The another clue is the striking association between bacteremia caused by *S. bovis/gallolyticus* and colonic neoplasia and bacterial endocarditis (94%), rather than bacteremia caused by closely related organisms such as *S. bovis* variant and *S. salivarius* suggests the possibility of specific bacterium-host interactions lead to cancer development [4]. Moreover, the appearance of new colonic lesions after the incidence of *S. bovis/gallolyticus* bacteremia endocarditis, provides more evidence that *S. bovis/gallolyticus* is not merely a consequence of the tumor lesion [5]. A previous study has dominated that increased stool carriage of *S. bovis/gallolyticus* is principally found in patients with malignant/premalignant lesions of the colon while *S. bovis/gallolyticus* bacteria were rarely isolated from normal subjects [6]. Another key clue supporting the etiological role of *S. bovis/gallolyticus* patients diagnosed with colon cancer have only 3 - 6% chance to develop *S. bovis/gallolyticus* endocarditis. This is far lower than the percentage of the detection of CRC in patients with *S. bovis/gallolyticus* bacteremia/endocarditis, which has more than 70% [7]. Many studies have proposed the etiological role of *S. bovis/gallolyticus* by different mechanisms as procarcinogenic, proinflammatory properties, selective adhesion to tumour tissue, selective colonizing in tumour cell [8].

Since the CRC is a heterogeneous disease caused by many proposed etiological factors such as *S. bovis/gallolyticus* bacteria, this bacterium might play a role in CRC development and progression by different mechanism of carcinogenicity. Therefore, the aim of this study was undertaken to find out the association between *S. bovis/gallolyticus* and CRC among Libyan patients, determine the most predominant bio-type and antibiotic susceptibly pattern of *isolates*.

Materials and methods

Patient's characteristics: Tissue biopsies were collected from April to July, 2017. A total of 60 patients (20 normal tissue, 20 polyp tissue and 20 confirmed CRC) who go through colonoscopy procedure for any reasons were enrolled in this study. 36 patients (60%) were males and 24 patients (40%) were females, their ages ranged between 16 and 90 years with a mean age of 57.5 years. Exclusion criteria included an inadequate preparation for colonoscopy, age younger than 16 years. None of the patients enrolled in this study have received any antibacterial agents in the month prior. Colonoscopy procedures involve the use of a four-foot long, flexible tube, called a colonoscopy, which is inserted into the rectum while the person is under sedation. The colonoscopy (Olympus Optical Co.) is equipped with light, camera and specialized device used snip tissue samples, after conducting colonoscopy the patients had been asked a series of questions including demographic data such as age, gender and residency. And other questions about patient's medical history and lifestyle. The consensus of the patients or that of their trustee was obtained before taking the biopsy.

Bacterial culture: A sample was sniped off by specialized device proximal to the colonoscopy, 3 cm in length was placed in sterile container contain 2 ml of BHI broth (BD Difco USA) and transferred to the microbiology laboratory following the colonoscopy procedures. Samples were incubated at 37 ºC for 18 hours in presence of ertapenem disks (BD Difco USA) to hinder the growth of Gram-negative rods. At the end of incubation, 5 µL of BHI broth were spread on the surface of Bile Esculine Azide agar (BD Difco USA) and re-incubated anaerobically at 37 ºC for 18 hours.

Identification of microorganisms: The isolated colonies then initially been investigated to make presumptive identification of *S. bovis*. Colonies of *S. bovis* characterized by small white, mucoid, creamy, orange-centered colonies were further confirmed by Gram stain and catalase test. S. *bovis* bacteria grew on broth of basal medium at 45 ºC, but not grew at 10 ºC and 50 ºC. 2.0% NaCl was added to permit the growth while at 6.5% NaCl did not and showed no haemolysis on blood agar. Identified *S. bovis* were selected for further investigations using automated system using automated BD phoenix microbiology system (PAMS, MSBD biosciences, sparks Md, USA).

Statistical analysis: Data were collected and statistically analysed by using statistical package of the social science software (version 22.0, SPSS). The results of data were given in the form of rates and expressed as percentage. Chi-square and Kruskal-Wallis tests were used to measure the association between the variables. Odds ratios (OR) with the 95% confidence intervals were reported and statistical significance was considered at p value.

Ethical considerations: The study was carried out in compliance with the Helsinki Declaration on the ethical principles of medical research involving human subjects following approval by the institutional review committee of University of Tripoli and a subsequent permission from

each hospital. Informed consent was waived by the Review Committee of the University due to the retrospective nature of the study, as all the data were collected from routine medical records. Confidentiality was guaranteed by omitting names or any personal identifiers. In addition, data were kept secured via out the research process to limit accessibility to a third party.

Results

Demographic data of patients: A total of 60 patients were classified into three groups to satisfy the statistically approved data, 20 patients as control, 20 patients diagnosed as polypic and 20 patients confirmed as CRC positive. 36 patients (60%) were males and 24 patients (40%) were females, their ages ranged between 16 and 90 years with mean age of 57.6 ± 17.3 years (95% CI 53.08 - 62.04, p > 0.05). The confirmed CRC population was further categorized into three groups based on the age: < 40 years, 40 - 60 years and > 60 years to address at which age the polyp might develop into CRC in suspected patients. Nine patients (45%) were diagnosed CRC positive at age above 60 years old, eight patients (40%) at age 40 - 60 years old and three patients (15%) at age bellow 40 years old. In this study, the tumour, lymph nodes and metastasis (TNM) classification system was used to stage the patients, where the majority of the cases (n = 9, 45%) was categorized as stage IV patients, followed by stage III-C (n = 6, 30%), the III-B (n = 3, 15%) and finally III-A (n = 2, 10%). The CRC positive cases were further classified based on the site of the carcinoma whether right sided or left-sided CRC. The right sided CRC has been associated with worse survival and bad prognosis than left-sided CR [9]. This study shows a comparable result between the left and right side CRC, the left-side CRC was slightly higher (n = 11, 55%), than the right sided counterparts (n = 9, 45%) (95% CI 1.03 - 1.84, p > 0.05). Furthermore, this study showed that colon carcinomas were the most common form (n = 17, 46.5%) (95% CI 0.33 - 0.76, p < 0.05) compared to the rectal carcinoma which represents (n = 3, 35%) (95% CI 0.33 - 0.76, p < 0.05). The histopathological pattern of studied biopsies has shown that most of the patients were moderately grade dysplasia (n = 13, 55%) (95% CI 0.31 - 0.88, p > 0.05), followed by well differentiated carcinomas (n = 6, 25%) (95% CI 0.31 - 0.88, p > 0.05) and lastly poorly differentiated cancers (n = 1, 20%) (95% CI 0.31 - 0.88, p > 0.05). All demographic data have been summarized in **Table 1**.

Table 1: Demographic data of Libyan patients with collateral cancer.

Parameters		Total n = 60 (100%)	Male n = 36 (60%)	Female n = 24 (40%)	Test t/χ^2	95% CI	P value
Mean age ± SD		57.56 ± 17.3	63.55 ± 16.3	48.58 ± 14.5	17.370[b]	53.08-62.04	> 0.05
Patients Group	Normal	20	13	07	1.250[a]	1.97-1.21	> 0.05
	Polypic	20	13	07			
	CRC	20	10	10			
Age Group	<40	10	04	06	62.800[a]	53.08-62.04	< 0.05
	40-60	19	06	14			
	>60	31	26	05			
City of Origin	Tripoli	58	34	24	4.138[a]	0.97-1.12	> 0.05
	Sabaha	01	01	-			
	Rojban	01	01	-			
Clinical Stages	III-A	02	02	00	4.491[a]	0.64-1.40	> 0.05
	III-B	03	02	01			
	III-C	06	02	04			
	IV	09	04	05			
Site of Cancer	Right side	09	05	04	1.460[a]	0.27-0.62	> 0.05
	Left side	11	06	05			
Location of cancer	Colon	17	15	02	1.356[a]	0.33-0.76	< 0.05
	Rectal	03	03	00			
Histo-pathological	Low grade dysplasia	01	0	01	3.405[a]	0.31-0.88	> 0.05
	Moderate grade dysplasia	13	10	03			
	High grade dysplasia.	06	03	03			
Antibiotics use		05	02	03	0.999[a]	1.01-1.14	> 0.05

[a]Chi-square test and [b]independent *t*-test

Microbial ethology: This study was critically aimed to identify the associations of *S. bovis* with CRC among Libyan patients who had colonoscopy examination. Notably, the obtained results were confirmed such significant associations by 7/20 (35%) (95% CI 1.22 - 1.72, $p < 0.05$). Also, this study establishes the overriding of biotype II/I in CRC Libyan patients by 5/7 (71.4%) compared to 2/7 (28.5%) for the *S. bovis* biotype I. In this study, *S. equinis* which considered the most relevant bacterial species to *S. bovis* and phenomenal human's isolates was detected in adenomas polyp and CRC biopsies in values 5/20 (25%) and 6/20 (30%), respectively, where the p value indicates a strong association with CRC and colon polyps. On the other hand, *S. bovis* represented the main predominant isolates from large adenomas polyp biopsies, 9/20 (45%). Contrary to what we have found in CRC group, the *S. bovis* biotype I prevalent by 5/9 (55.5%) than biotype II/I 4/9 (44.4%). Interestingly, *S. bovis* was absent from specimens collected from normal mucosal group but rather, other species of *Streptococcus* beyond SBSEC such as *S. ubaris*, *S. agalactis* and *S. procinus* were isolated from this group (**Table 2**). Regarding the distributions of *S. bovis* isolates according to the locations of carcinomas, this study has shown that five patients (71.4%) of *S. bovis* I have been distributed in rectal cancer biopsies as compared to two patients (28.5%) distributed in colon cancer biopsies. Moreover, *S. bovis* biotype II/I considered the more prevalent biotype in colon by five patients (55.5%) but it was slightly decreased in rectal (n = 4, 44.4%) and according to the p = 0.0001, this study considers such distribution is significant (**Table 3**).

Table 2: Prevalence of *Streptococci* among Libyan patient's groups

Patients group[a]	*S. bovis* I		*S. bovis* II/I		*S. equinis*		*S. ubaris*		*S. agalactis*		*S. procinus*	
	n	%	n	%	n	%	n	%	n	%	n	%
Normal	0	00	0	00	0	00	3	15	2	10	1	05
Polypic	5	71.42	4	44.4	6	30	0	00	0	0	0	00
CRC	2	28.57	5	55.5	5	25	0	00	0	0	0	00

[a]Total number of samples was 60 samples, in which 20 sample for each patient's group.

Table 3: Distribution of bacteria according to the location of polyp and CRC

Location	*S. bovis* I		*S. bovis* II/I		*S. equinis*		*S. ubaris*		*S. agalactis*		*S. procinus*	
	n	%	n	%	n	%	n	%	n	%	n	%
Colon	2	28.5	5	55.5	5	45.4	0	0	0	0	0	0
Rectal	5	71.4	4	44.5	6	54.5	0	0	0	0	0	0

Figure 1 demonstrates the co-occurrence of S. *bovis* with other bacterial species that may modify and/or augment its carcinogenic properties of such suspected organisms. In polypic group, nine samples over 20 samples were proved to be mixed. Of these nine samples, one sample contains *S. bovis* biotype *I* with *S. equinis* and three samples contain *S. bovis* biotype II/I with *S. equinis*. Whereas, two of nine samples contain *S. bovis* biotype I with *E. faeclis* but three of nine samples contain *S. bovis* biotype II/I with *E. faeclis.* Notably, in CRC group, the mixed samples represent 11 samples where no of tested biopsies proved to be mixed of *S. bovis* biotype I with *S. equinis*. On the other hand, three out of 11 samples contain *S.bovis* biotype II/I with *S. equinis* and one sample contains *S. bovis* biotype I with *E. faeclis*. Moreover, seven samples contain *S. bovis* biotype II/I with *E. faeclis*. As all confirmed CRC patients attended the clinic at stage beyond the early confirmed stages the results showed an association between the different CRC confirmed stages and the type of *S. bovis/S. Equinus* Complex (SBSEC). Nevertheless, this study proves that the prevailing of *S. bovis* I and II/I was the highest in stage IIIA (n = 1, 50%) and (n = 3, 60%), respectively, compared to the other advanced CRC stages IIIB, IIIC and IV. Moreover, the prevailing of *S. equinis* in stage IIIA represents 40% which considered equal to the same bacteria in stage IV, which might be a clue that S. *equinis* plays role in CRC initiation and progressions. Contrary to *S. bovis which* might be only initiate the CRC as it has been declined significantly during the advanced CRC stages, **Table 4**.

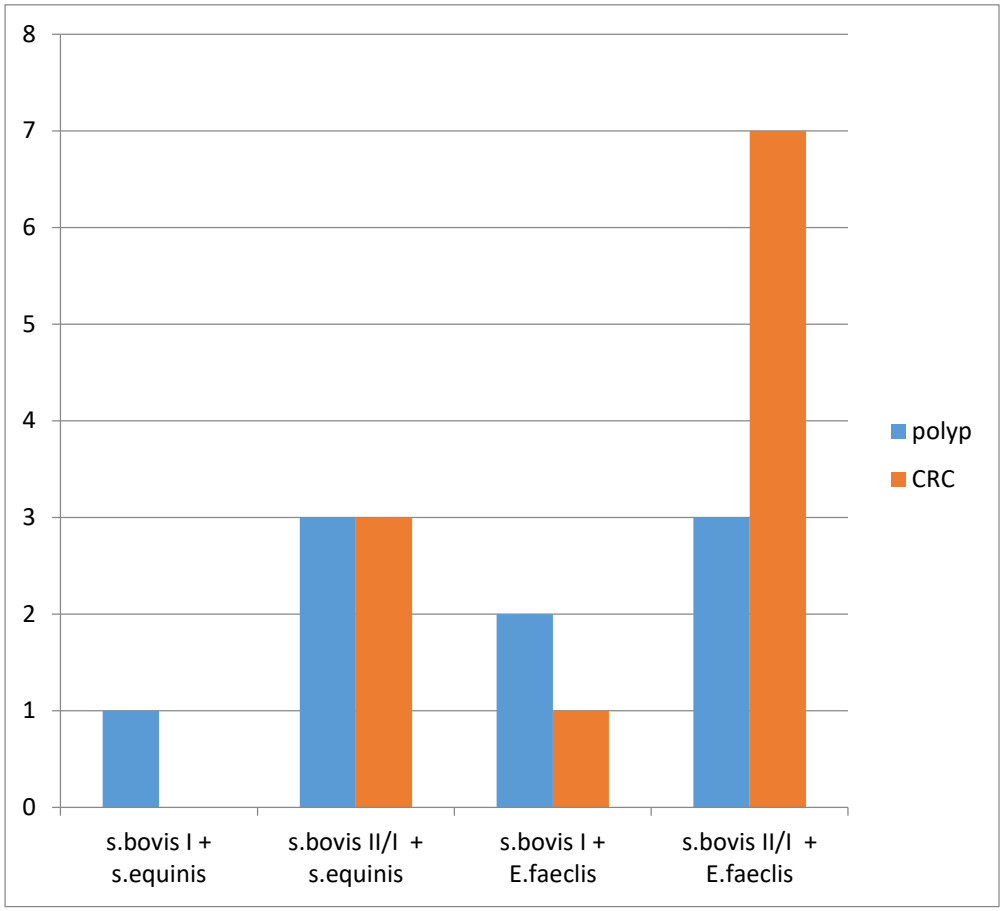

Figure 1: Co-occurrence of S. *bovis* bio-type I and II/I with *S. equinis* and *E. faeclis* across CRC and polyp patient's groups.

Table 4: Prevalence of *S. bovis and S. equinis* across CRC stages.

Stage	*S. bovis* I n (%)	*S. bovis* II/I n (%)	*S. equinis* n (%)
IIIA	1 (50%)	3 (60%)	2 (40%)
IIIB	0 (00%)	1 (20%)	1 (20%)
IIIC	1 (50%)	0 (00%)	0 (00%)
IV	0 (00%)	1 (20%)	2 (40%)

Antimicrobial susceptibility patterns of SBSEC: According to the overall profile of antimicrobial susceptibility testing findings obtained for both CRC, polyp and normal mucosal group, *S. bovis* biotype I isolate have shown unexpected resistance pattern to different classes of antibiotics. In contrast *to S. bovis* biotype II/I and *S. equinis*, *S. bovis* biotype I has shown remarkable resistance to some penicillins such as, oxacilline and penicilin G and intermediately resistance to amoxicillin but susceptible to augmentin®. Notably, *S. bovis* biotype I have resistance to different type of antibiotic belong to second generation and third generation cephalosporin, fluoroquinolones, aminoglycosides, macrolides, and carbapenemis. In contrary, S. *bovis* biotype II/I and *S. equinis* were both susceptible to the above mentioned antibiotic classes. The results obtained from this study have shown *S. bovis* biotype I is highly resistance to other clinically used antibiotics such as vancomycin, teicoplanin, tetracycline co-trimoxazol, telithtomycin, prisinamycin mupirocin, nitrofurantion and rifapmin while susceptible to chloramphenicol and linezolid (**Table 5**).

Table 5: Antibiotic susceptibility of different antibiotics against *SBSEC* isolated from different patient's groups

Antibiotics classes	Antibiotics	*Streptococcus bovis*		*Streptococcus equinis*
		biotype I	biotype II/I	
Penicillin	Amoxicillin	I	S	S
	Penicilin G	R	S	S
	Oxacilline	R	S	S
	Augmantine	S	S	S
Cephalosporin	Cefuroxime	R	S	S
	Cefotaxime	R	S	S
	Cefepime	R	S	S
	Cefotraxime	R	S	S
Fluoroquinolones	Levofloxacin	R	S	S
	Moxifloxacin	R	S	S
	Ciprofloxacin	R	S	S
Aminoglycoside	Gentamycin-syn	R	S	S
	Gentamycin	R	S	S
Macrolidis	Clindamycin	R	S	S
	Erythromycin	R	S	S
Carbapenemis	Meropenem	R	S	S
	Imipenem	R	S	S
miscellaneous antibiotics	co-trimoxazole	R	S	S
	Teicoplanin	R	S	S
	Vancomycin	R	S	S
	Telithtomycin	R	S	S
	Prisinamycin	R	S	S
	Chloramphenicol	S	S	S
	Linezolid	S	S	S
	Tetracycline	R	S	S
	Mupirocin	R	S	S
	Nitrofurantoin	R	S	S
	Rifapmin	R	S	S

R: resistance, S: susceptible, and I: intermediate.

Discussion

Over the years, members of the SBSEC were recognized and perhaps treated as lower grade pathogenic bacteria [10]. However, it is not clear if SBSEC members maybe the cause or a consequence of CRC [2]. Nowadays, the pathogenicity of certain SBSEC members is even more evident and well documented while many case reports wide spectrum of diseases that may cause and many studies revealing molecular mechanisms of virulence factors for the SBSEC [11]. Although *S. bovies* have been shown to have the strongest association with colorectal cancer [12, 13]. In concord with the current study, many other studies have identified *S. bovis*, as being enriched in CRC patients and highly associated with CRC [14]. Regarding *S. bovis biotypes*, this study establishes the prevailing of biotype II/I in CRC Libyan patients, which is contrary to a study conducted in Taiwan that have shown overriding of biotype II/2. However, in western countries *S. bovis* biotype I was the most predominate [15]. The variation in *S. bovis* biotype was diverse according to the geographic region. This study also

revealed that *S. bovis* was the predominant isolates of SBSEC from large adenomas polyp biopsies. This is comparable to study done in Malaysia where it found of *S. bovis* isolates was isolated from patients with colonic polyps [16]. A published study done in Sudan in 2011 denied the presence of *S. bovis* in large adenomas polyp [17]. *S. equinis* was considered the most relevant bacterial species to *S. bovis* and phenomenal human's isolates that cause infective endocarditis and peritonitis [18]. In this study, *S. equinis* was detected in adenomas polyptic and CRC biopsies. This study proves that prevailing of *S. bovis* I and II/I was the highest in stage IIIA, compared to the other advanced CRC stages IIIB, IIIC and IV. These results are supported by study conducted in Spain in 2017, as they concluded that the prevalence of *S. bovis* is significantly decreased as CRC proceeded [19]. The other published studies supported our findings as the humoral immune response against the ribosomal protein L7/L12 from *S. bovis* was significantly increased in early stages of CRC [20]. This immune response will control and eradicate the *S. bovis* as results this will led to a decrease in *S. bovis* at the late stage of CRC. Moreover, the prevailing of *S. equinis* in stage IIIA considered equal to the same bacteria in stage IV, this might be a clue that S. *equinis* plays a role in CRC initiation and progressions. Contrary to *S. bovis which* might be only initiate the CRC as it has significantly been declined during the advanced CRC stages. Collectively, the obtained results raise the question of whether it is the malignant environment of the colon that promotes growth of *S. bovis* or if *S. bovis* contributes in some way to the malignant environment. Changes in local conditions and disruption of capillary channels at the site of neoplasias allow *S. bovis* to proliferate and gain entry into the blood stream. The adherence of *S. bovis* to intestinal epithelial cells seems to be the initial process in colonization and subsequent infection of the host and the relationship between bacteraemia/endocarditis and carcinoma of the colon suggests the existence of *S. bovis* adhesions which allow colonization of colonic and vascular tissues [21]. Production of inflammatory cytokines, such as TNF-a, IL-1ß and IL-6 and the chemokine IL-8, contribute to the normal host defence mechanisms, leading to the formation of nitric oxide and free radicals, such as superoxide, peroxynitrites and hydroxyl radicals, as well as alkylperoxy radicals. Owing to their potent mutagenicity, all these molecular species can contribute to neoplastic processes by modifying cellular DNA. In addition, production of angiogenic factors, such as IL-8 triggered by *S. bovis* antigens, in the colonic mucosa may favour the progression of colon carcinogenesis [22]. The antimicrobial susceptibility profile for the SBSEC isolates has shown unanticipated resistance pattern to resistance to some penicillin's classes, contrary to study done in Brazil, on clinical isolates of *S. bovis* isolated from patients suffering from spontaneous bacterial peritonitis have shown regular sensitivity to penicillin where intravenous penicillin is the antimicrobial agent of first choice [23]. Another study published in France was conducted by the disk diffusion technique on *S. bovis* recovered from blood has shown no remarkable resistance to any of the tested penicillins [24]. The study also claims the penicillin resistance in *S. bovis* has not yet been reported [24]. Although no enough information is available for the antimicrobial susceptibility profile of *S. bovis*, it was claimed that the reduced susceptibility to penicillin was associated with mobile genetic elements that were detected [18]. The biotype *of S. bovis* play a significant role in antimicrobial susceptibility which might due to the difference in their structures. The results obtained from this study have shown *S. bovis* biotype I was highly resistance to clinically used antibiotics such as vancomycin, teicoplanin, tetracycline co-trimoxazol, telithtomycin, prisinamycin mupirocin, nitrofurantion and rifapmin, while susceptible to chloramphenicol and linezolid. In contrary to S. *bovis* biotype II/I and *S. equinis* as they were susceptible to the above mentioned antibiotics. Other studies reveal acquired resistances were detected for tetracyclines, telithromycin and none of the tested strains displayed resistance to chloramphenicol or vancomycin, rifampin and linezolid. The results of the susceptibility investigation of *S. bovis* and the data from the literature was a little confused and limited as *S. bovis* taxonomy and nomenclature has progressively changed according to the description of new species originally grouped [25]. *S. bovis* group acts as reservoir for resistance genes that might pass it to photogenic bacterial species. In a study conducted by Rodrı´guez-Avial [26] in Spain in 2004 found that *Streptococcus bovis* isolates showed the highest rates of resistance to erythromycin and clindamycin, 45.6% and 27.7%, respectively. Also they found that telithromycin-resistant strains belonged to the *S. bovis* group harbouring both *erm* (B) and/or *mef* (A) gene, telithromycin resistance in streptococci depend on the *erm* (B) gene expression strains belonged to the S. bovis group harbouring both erm (B) and/or mef (A) gene, telithromycin resistance in streptococci depend on the erm (B) gene expression [25]. Nowadays, growing evidence suggests that *S. bovis/gallolyticus play* important roles in the progression and development of colon cancer.

Conclusion

This study concludes that *S. bovis/gallolyticus* play a key role among Libyan CRC patients, moreover such bacteria found prominently in the pre-cancer stage of CRC (i.e. polyps) which might indicate the role of *S. bovis/gallolyticus in* the initiation and transform the normal mucosal to cancer by different mechanises. It is also concluded that the main *S. bovis/gallolyticus bio*-type isolated distributed in CRC was *biotype* II/I. Contrary, the large adenomas polyp predominated by the *S. bovis biotype* I. Although, this study reports that the major of *S. bovis I* have been distributed in rectal cancer and *S. bovis biotype* II/I considered the more prevalent biotype in colon, in CRC patients the *S. gallolyticus* co-occurred slightly with *S. equinis*, but by highly in polypic group of *S. gallolyticus* coincident with *S. equinis.*

Ethical issues

Including plagiarism, Informed Consent, data fabrication or falsification and double publication or submission have completely been observed by authors.

Author's contribution

Both authors contributed equally, proofread and approved the final version of this manuscript.

Conflict of interest

The authors have declared that there is no potential competing interest.

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