

Association of *Streptococcus bovis* with colorectal carcinoma

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Summary:

Background: - This study was carried out to investigate the ability of *Streptococcus bovis* to colonise colorectal cancer.

Patients and Methods: - A total of 106 outpatients were subjected for colonoscopy. Carcinoma biopsies from patients with colorectal cancer tissue from patient with polyps and normal mucosa stool and blood from all patient and controls were cultured and identified for *S.bovis*.

Results: - The histopathological findings confirmed that 38 patients had colorectal carcinoma, 27 patients with benign polyps and 41 with normal colonic mucosa. The faecal carriage rate of *S.bovis* was 15(39.5%) in patient with colorectal cancer, 5(18.5%) in patients with polyp and 7(17.1%) in control.

Conclusion: - Faecal colonization by *Streptococcus bovis* in colorectal cancer patient was higher than in control healthy people and patients with polyp.

Keywords: - *Streptococcus bovis*. Colorectal Carcinoma (CRC).

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Introduction:

Colorectal cancer (CRC) is the fourth commonest form of cancer occurring worldwide, and the number of new cases of CRC has been increasing rapidly since 1975.(1) The involvement of the intestinal microflora in the pathogenesis of colon cancer has been hypothesized (2). Several bacteria have been reported in association with colonic cancer, the strongest and best documented relationship focuses on *Streptococcus bovis* (1975) (3). Many single case reports have demonstrated an association between *S.bovis* and carcinoma of the colon. The first report was published by Klein *et al* (3), they found that prevalence of *S.bovis* in fecal cultures from patients with carcinoma of the colon was significantly increased as compared to that in control (3). *S.bovis* is Gram-positive cocci classified as group D streptococci on the basis of their reaction with group D specific antiserum; grow in 6.5% salt broth or the pyrrolidonyl arylamidase (PYR) enzyme. *S.bovis* divided into two biotypes 1 and 11. The biotype 1 strain is much more frequently isolated from patient with endocarditis or gastrointestinal diseases or both (4) (5). The majorities of *S.bovis* biotype 1 strain (the classical) produce extracellular glucan from sucrose, ferment mannitol and hydrolyze starch, whereas *S.bovis* biotype 11 strains (the variant) are generally negative for these traits (5). It has been shown that high percentage of patients who presented with *S.bovis* bacteremia had also colorectal tumor (2). On the other hand, it was reported that fecal carriage of *S.bovis* was increased in patient with colon carcinoma (3). The association of *S.bovis* with CRC might be a powerful tool to identify people with early. Stage of CRC. Therefore the present study aim to determine if *S.bovis* selectively colonizes colorectal cancer and polyps

Patients and Methods:

A total of 106 outpatients were subjected for colonoscopy, between December 2008 and September 2009 at Gastrointestinal unit.

Stool and blood samples, were submitted from all subject before colonoscopy. Selected tissue biopsies from tumor, polyps and mucosa obtained from patients during colonoscopy were cultured for *S.bovis*. as well as stool, blood and normal mucosa were cultured from control group. Tissue biopsies and stools were separately plated into bile aesculin azide agar as performed according to Potter *et al* (6), and incubated aerobically at 37 degree centigrade for 24 hours. Aesculin hydrolyzing colonies from each sample were plated onto 5% sheep blood agar plate and incubated at 37 degree centigrade at least 24 hours. All colonies of the cultures were Gram stained first to confirm the presence of Gram-positive cocci, in short clains. Then tested for catalase and pyrrolidonyl peptidase (PYR) activity. Some unique features distinguishing group D streptococci, mainly *S.bovis* from enterococci species included inability to grow in 6.5% NaCl and hydrolyzing starch(7). Also the API 20 strep system kit was used to identify *S.bovis* to biotype level. Blood cultures were incubated and regularly subcultured for two weeks before being categorized as negative.

Results:

The histopathological findings confirmed that 38 patients had colorectal carcinoma, 27 patients with benign polyps and 41 normal healthy people (normal colonic tissue without mucosal, tumor or polyps), these confirmed as a control group. The median age for patients with colorectal carcinoma was 69 years, range (50-83years), for patients with polyps was 64 years, range (29-77 years) and for control group 59 years, range (17-81 years). The male to female ratio was 1.0:8 in the patients with colorectal cancer, 1.2:0.9 in patients with polyp and 0.8:1.1 in the control group.

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Table (1) shows that *S.bovis* was isolated from stool of 15(39.5%) patients with colorectal cancer, 5 (18.5%) from patient with benign polyps, and 7(17.1%) of the control group. Also the organism was isolated from tissue biopsy tumor of 13 (34.2%) patients with colorectal cancer and 5 (18.5 %) patients with benign polyps. All *S.bovis* positive cultures were bioype 11 except one isolated from control group. All blood cultures were negative except two samples were positive from patient with colorectal cancer.

Table 1: carrier rate of S.bovis among 106 subject showed (38) patients with colorectal cancer, (27) patients with benign polyps and (41) normal control group.

Clinical samples from:	Patients with CRC(38)	Patients with polyp (27)	Control group (41)
	No. (%)	No (%)	No (%)
Tumour	13 (34.2)	-	-
Polyps	3 (7.9)	5 (18.5)	-
Normal mucosa	8 (21.1)	3 (11.1)	2 (4.9)
Stool	15 (39.5)	5 (18.5)	7 (17.1)
Blood culture	2 (5.3)	0	0

Discussion:

S.bovis is a normal inhabitant of the human gastrointestinal tract, as demonstrated by the fact that it can be found in the faecal specimens of about 5-10% of healthy population (4). Our results suggested that *S.bovis* isolated from stool of 9 (17.1 %) of healthy control group. An increased percentage of *S.bovis* has been reported in cases with inflammatory bowel disease or colonic cancer (3). This study indicated that faecal carriage of *S.bovis* is higher in patients with colorectal cancer (39.5 %) than in patients with benign polyp (18.5%) and control group (17.1%). These result are generally in agreement with other workers, they reported that the faecal carriage of *S.bovis* rate were 17-55 % significantly greater than control group (8) (9). Previous study indicated that faecal carriage of *S.bovis* was significantly higher in patient with colorectal cancer (56%) than in the control (11%) (3). However, others found no significant difference in the preoperative faecal carriage rate of *S.bovis* between the patients with colorectal cancer and control populations (11% versus 13%) (6). the differences in the result may be due to the use of different methods of detection of the *S.bovis* organism. Sometimes *S.bovis* could be confused with some viridians streptococci. It has been speculated that undefined physical or biochemical factors in the gastrointestinal tract of patients with colonic carcinoma may encourage *S.bovis* fecal carriage, or alternatively that *S.bovis* may be locally carcinogenic (3). There are conflicting data on the importance of *S.bovis* common antigen, which may be a specific marker of *S.bovis* bacteremia, and may facilitate tumour attachment before translocation to the blood stream (10). The

faecal isolates of *S.bovis* without bacteremia represent the intestinal overgrowth of the species but no transmucosal invasion. Focal mucosal weakness, either from pre-cancerous metaplasia or other benign process provides an entry for the pathogen to cross the physical barrier and access to blood stream and systemic circulation (11). The hypothesis that ulceration of the neoplastic lesion would directly open a pathway for the bacteria to enter the blood stream does not explain the case of association between *S.bovis* and non ulcerated colonic polyp's adenoma. It seems more likely that mucosal disruption may occur due to vascular changes related to several gastrointestinal diseases (4). Performing screening colonoscopy after *S.bovis* infection allows the detection of colonic neoplasia in early or pre-cancerous stage in most cases (12) (13). Moreover, it has been suggested that a negative diagnostic assessment at the time of infection is not enough, because a colonic polyp or cancer may develop several years after *S.bovis* infection (13). Although the knowledge about the true pathophysiological gastrointestinal neoplasia needs further studies. It has been demonstrated that endoscopic screening is able to detect occult benign, pre-malignant and cancerous disease of the colon in most patients with *S.bovis* infection (14). The need for an appropriate endoscopic screening for polyps and malignancies even in asymptomatic patients when an *S.bovis* is recognized (15)

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