PJN
ISSN 1680-5194

PAKISTAN JOURNAL OF NUTRITION

ANSInet
308 Lasani Town, Sargodha Road, Faisalabad - Pakistan
Mob: +92 300 3008585, Fax: +92 41 8815544
E-mail: editorpjn@gmail.com

Pakistan Journal of Nutrition 9 (3): 269-278, 2010
ISSN 1680-5194

Nutritional Status and the Risk for Colorectal Adenomas: A Case-Control Study in Hospital Kuala Lumpur, Malaysia

Amutha Ramadas[1] and Mirnalini Kandiah[2]
[1]School of Medicine and Health Sciences,
Monash University, Sunway Campus, Selangor, Malaysia
[2]Department of Nutrition and Dietetics, Faculty of Medicine and Health Sciences,
Universiti Putra Malaysia, Selangor, Malaysia

Abstract: The most important and possible risk factor of colorectal adenomas is the individual's nutritional status. The role of nutritional status in the aetiology of colorectal adenomas remains an area of active investigation, as the exact relationship between nutritional status and colorectal adenomas remains unclear. The objective of this case-control was to determine the nutritional status of subjects with colorectal adenomas as compared with healthy subjects at Hospital Kuala Lumpur over a period of one year. A total of 118 subjects were recruited (n case = 59 and n control = 59). A pre-tested questionnaire was used to collect socio-demographic information and dietary intake. Lipid profile was determined using standard Roche diagnostic kits. The data were analyzed using SPSS version 12.0. The intake of beta-carotene, alpha-carotene, lycopene, vitamin A and crude fiber found to be significantly different between the groups ($p<0.05$), while beta-carotene, alpha-carotene, lycopene, vitamin C, vitamin D, vitamin E and crude fiber significantly reduced the risk. Although the percentages intake of nutrient achieved according to RNI were below the recommended value, percentages of RNI achieved for vitamin C, D, E and folate were found to be significantly different between male subjects ($p<0.05$). Our results support the notion that certain nutritional factors are of importance for the development of these pre-cancerous lesions. Identification of risk factors through this case-control study should be able to supplement the available data in order to develop an intervention package that focuses on multiple risk factors to reduce the chances for developing colorectal adenomas or colorectal cancer.

Key words: Nutritional status, dietary intake, anthropometric measurements, colorectal adenoma

INTRODUCTION

Colorectal Cancer (CRC) was estimated to be the third and fourth most commonly occurring cancer worldwide among men and women respectively in the year 2002 (IARC, 2002). Colorectal cancer was estimated to contribute to 9.5% and 9.3% of total cancer cases among males and females respectively in the same year. Among Malaysians, colon cancer ranked third among cancers reported, accounting for 7.8% and 6.0% of all cancer cases in males and females respectively in 2003 (NCR, 2004). The age-standardized rate for colon cancer in males and females were 13.9 and 11.2 respectively. Cancer of the rectum, on the other hand, ranked fifth among cancers reported in Malaysian males (6.8%) and females (4.1%) respectively.

Colorectal cancer develops over a period of several years and nearly all arise from benign, neoplastic adenomatous polyps (Bond, 2000; Kahn *et al*., 1998). The progress of adenoma to cancer may take five to ten years (Young *et al*., 2002). These polyps are benign growths that protrude from the inner walls of the colon and rectum and are relatively common in people over the age of 50. It is estimated that the average 60 year-old without special risk factors for polyps had a 25% chance of having a polyp (ASGE, 2006). Data on the incidence of Colorectal Adenoma (CRA) in the Malaysian population is yet to be reported. The closest available study done in Singapore showed that the prevalence of CRA amongst males was 20.4% for Chinese, 4.6% for Malays and 7.9% for Indians (Lee, 1987).

The most important and possible risk factor of CRC and CRA is the individual's diet. The role of diet in the aetiology of CRA remains an area of active investigation, as the exact relationship between diet and CRA remains unclear.

Diet and lifestyle factors have been implicated in the development of the sporadic adenomatous polyps (Larsen *et al*., 2006; Wark *et al*., 2006) while mutation in genes and DNA may also cause conditions known as Familial Adenomatous Polyposis Syndrome (FAP) or Hereditary Non-Polyposis Colorectal Cancer (HNPCC) syndrome, which lead to development of multiple polyps (Burt, 2000).

Results from several observational studies have suggested that three main dietary factors may or may not protective against cancer of the large bowel, i.e. low fat

Corresponding Author: Amutha Ramadas, School of Medicine and Health Sciences, Monash University, Sunway Campus, Selangor, Malaysia

intake, high fiber intake and high fruits and vegetables intake (Schatzkin *et al*., 2000). An inverse relationship was also reported between level of total physical activity and the risk for adenomatous polyps of the colon and rectum (Sandler *et al*., 1995). Tobacco smoking and alcohol consumption may increase the risk of colonic polyps (Kahn *et al*., 1998; Todoroki *et al*., 1995; Otani *et al*., 2003).

MATERIALS AND METHODS

Selection of subjects: Cognitively sound men and women who were at least 30 years of age and had completed a colonoscopy between January 2005 and December 2005 were invited to participate in the study with informed consent. Hospital Kuala Lumpur (HKL) served as the clinical centre and the source of participants for this study. Ethical approval was obtained prior commencement of the research.

The inclusion criteria for selection of cases were patients newly diagnosed with one or more histologically confirmed CRA removed through polypectomy; had no other types of polyps (hyperplastic polyps, FAP and HNPCC); free from other chronic diseases and who are not involved in other studies. It is vital for individuals with other polyps and chronic diseases to be excluded from the study, as the risk factors for such conditions have already been established and thus may interfere with the results of the study. The exclusion criteria included: history of colorectal and/or any other cancers or, bowel resection, polyposis syndrome, or inflammatory bowel disease; unsatisfactory colon preparation or incomplete colonoscopy; taking cholesterol-lowering drugs and have chronic medical conditions or dietary restrictions that would substantially limit their ability to complete the study.

Three hundred and forty three patients who fulfilled these criteria were selected by the surgeon in the Surgical Department of HKL. Of these patients, 157 responded to the invitation letter that was sent and attended a briefing session. Seventy five percent or 118 of those who attended the briefing session agreed to take part in this study and gave informed consent. Fifty nine subjects who had histologically confirmed adenomatous polyps removed were recruited as cases and an equal number of subjects who were found to be negative for colorectal adenomatous polyps upon colonoscopy and fulfilled the other inclusion criteria were recruited as control subjects.

Data collection: All data were collected during a face to face interview with the subjects at HKL. A pre-tested, structured questionnaire was used to record the socio-economic information (age, ethnicity, marital status, educational status, occupation and income).

Three days 24 h diet recalls (1 weekend and 2 weekdays) were obtained from the subjects. Details of foods and drinks taken each day were recorded. It is important to have repeated 24 h diet recalls, as the food intake by subjects differs every day. This is mainly because the respondents are free-living subjects and not subjected to any dietary restriction. It is important that consecutive days were not selected and one weekend was included to make sure the variety of food consumed is recorded (Gibson, 2005).

A food album on commonly consumed food in household measures was used to facilitate subjects to improve accuracy of the recalls and household measurements of the food and drink consumed by the subjects. The first and the second recalls were done during the face-to-face interview, and the subjects were followed up through phone calls for the third dietary recall. The data were then entered into Nutritionist Pro 2.4 to be analyzed.

Nutritionist Pro (First Data Bank, USA) single version 2.4 dietary software was used to analyze nutrient intakes based on the 24 h diet recalls. The foods and beverages consumed by the respondents for 3 days were entered in the program. Wherever necessary recipes were obtained and each ingredient was entered into the software. The software was then used to calculate the average energy and nutrient intakes of the subjects. The data obtained were entered into SPSS to be analyzed.

Anthropometric measurements: Anthropometric measurements were taken directly after the interview session. Height was measured to the nearest to 0.1 cm using a body meter (GIMA) and weight was measured to the nearest to 0.1 kg using an electronic weighing scale (TANITA). Body Mass Index (BMI) was calculated and was classified according to recommendation by WHO (1995). Waist circumferences were measured using a non-elastic measuring tape and measured to the nearest 0.1 cm and categorized according to the respective classification of WHO (1995).

The Omron body fat monitor HBF-302 (Omron Healthcare Co., Ltd., UK) was used to obtain subjects' body fat percentage and total body fat mass with accuracy up to 0.1% and 0.1 kg respectively. The measurement of body fat using the Omron body fat monitor is based on the bioelectric impedance principle which is a non-invasive method based on the principle that the resistance to an applied minor electric current is inversely related to the amount of fat-free mass within the body (Lukaski *et al*., 1985). The cut-off points for percentage of body fat were those recommended by Omron HBF-302. The OMRON's body fat monitor has been validated in previous studies (Martín-Moreno *et al*., 2001; Lintsi *et al*., 2004).

Determination of biomarkers: Venous blood was collected by a trained and qualified nurse from the Faculty of Medicine and Health Science, Hospital Kuala Lumpur. Fifteen millilitres of fasting blood samples was drawn into empty tubes. Tubes were protected from light

with aluminium foil and were centrifuged within three hours after collection at 3000 rpm at 4°C for 10 min. The plasma was then separated and transferred into polypropylene micro centrifuge tube and was kept at -80°C up to three months until further analysis.

Plasma lipids and lipoproteins were quantified using enzymatic methods by using Roche-Diagnostics standards and kits (Warnick *et al*., 1982; Carr *et al*., 1993) with an auto analyzer Hitachi 747. This method uses the combined action of polymers, polyanions, and detergent to solubilise cholesterol from HDL but not from very LDL and chylomicrons.

Data analysis: All statistical analyses were performed using SPSS version 15.0. Descriptive statistics such as frequencies, percentages, means and standard deviations were used to describe the data. Independent *t*-test was used to determine differences between case and control groups for continuous variables. The data on nutrient intake was then categorized into tertiles to facilitate the risk calculation. The crude and adjusted odds ratios and their corresponding 95% confidence intervals were determined using binary logistic regression using the enter method. The odds ratio was adjusted for variables such as age, ethnicity, income, alcohol consumption, smoking status and energy intake based on previous studies (Bowers *et al*., 2006; Otani *et al*., 2006). p-value of <0.05 was considered as significant.

RESULTS AND DISCUSSION

Socio-demographic characteristics: The majority of the study participants were Chinese and married (Table 1) though there were no significant differences between the study groups. The majority of the male subjects were in the 60-69 years old age bracket, while female subjects were in the 50-59 years age group. Rajendra *et al*. (2005) have reported higher incidence of CRA in Malaysians as the age increases. Peters *et al*. (2004), for example, reported that the mean age of participants with histologically verified adenoma was 63.5 years, which was significantly different from the mean age of healthy controls (62.7 years). Another study (Erhardt *et al*., 2003) reported that the mean age of patients with CRA (59 years) was significantly higher than the healthy controls (54 years) and the data is very much closer to the mean age reported here. Rajendra *et al*. (2005) also reported that race does not have any association with CRA.

A similar distribution of subjects in both groups was seen for educational status categories. The majority of the participants in either group were either unemployed or retired. The next biggest occupational group was the blue collar job category, which is mainly made up of drivers, tailors, labourers and general workers. The majority of the respondents were found in the low-income group with monthly personal income of <RM500. No previous study has correlated these variables with the risk for CRA.

Nutrient intakes: Of all the important macro and micronutrients studied, beta-carotene, alpha-carotene, lutien, retinol and crude fibre were found to significantly differ in their intakes between the study groups (Table 2). Vitamin C intake was found to differ significantly only among the male subjects. The percentages of RNI achieved by the males (Fig. 1) and the females (Fig. 2) revealed that the intake of most macro and micronutrients were way below the recommended values. Among the male subjects, only protein was consumed way above its recommendation. The male controls achieved more of the RNI for calcium, while the cases had less. However, the percentages achieved by the males for vitamin C, vitamin E and folate were significantly different at $p<0.05$. Among the female subjects, the percentages of RNI achieved for protein and calcium were higher than the recommended value, while the female controls achieved more of the RNI for vitamin A, while the cases had lower than what is recommended. The percentages of RNI achieved for other nutrients were below the recommended value and none were significantly different.

Highest tertile of intake of carotenoids such as b-carotene, a-carotene and lycopene were found to be protective of CRA in all subjects, regardless of gender (Table 3). There were reductions in the risk by 73-80% when highest tertile of intakes compared to the lowest. In a previous study, an increase intake of carotene was suggested to lower the risk for CRA by 40% when the highest tertile of intake compared with the lowest (Lubin *et al*., 1997). However, Senesse *et al*. (2005) found that although beta-carotene seems to be protective in non-smokers, the adverse effect of the nutrient in smokers should be taken as a caution. Some studies suggested gender difference in response to CRA risk. The risk of CRA in the highest quartile was approximately half of that of men in the lowest quartile for alpha-carotene (OR = 0.38, 95% CI = 0.18-0.84), beta-carotene (OR = 0.51, 95% CI = 0.24-1.07) and total carotenoids (OR = 0.48, 95% CI = 0.22-1.03) (Jiang *et al*., 2005). Conversely, Malila *et al*. (1999) found no significant association between carotenoids and the risk for CRA.

Vitamin C intake also found to be protective with reduction of risk by 72% in all subjects. However, the reduction in risk was found to be exclusive to men (Table 3). In previous study by Enger *et al*. (1996), dietary intake of vitamin C showed a weaker inverse association (OR, 0.8; 95% CI, 0.5-1.5). Tseng *et al*. (1994) however, suggested the reduction in the risk is only confined to women, in contrary to the findings on this study. Supplemented vitamin C has shown mixed results in its relationship with CRA (Greenberg *et al*., 1994; Senesse *et al*., 2005).

Table 1: Socio-demographic characteristics of the participants

	Males		Females		All	
Variables	Case (n = 42)	Control (n = 33)	Case (n = 17)	Control (n = 26)	Case (n = 59)	Control (n = 59)
Age (years)						
<40	1 (2.4)	1 (3.0)	0 (0.0)	3 (11.5)	1 (1.7)	4 (6.8)
40-49	6 (14.3)	7 (21.2)	2 (11.8)	8 (30.8)	8 (13.6)	15 (25.4)
50-59	10 (23.8)	11 (33.3)	7 (41.2)	9 (34.6)	17 (28.8)	20 (33.9)
60-69	18 (42.9)	11 (33.3)	7 (41.2)	4 (15.6)	25 (42.4)	15(25.4)
>70	7 (16.7)	3 (9.1)	1 (5.9)	2 (7.7)	8 (13.6)	5 (8.5)
Mean±SD	59.8±9.8	57.4±11.0	57.9±8.3	52.2±10.9	59.3±9.3*	55.0±11.2*
Ethnicity						
Malays	15 (35.7)	9 (27.3)	3 (17.6)	9 (34.6)	18 (30.5)	18 (30.5)
Chinese	17 (40.5)	13 (39.4)	10 (58.8)	8 (30.8)	27 (45.8)	21 (35.6)
Indians	10 (23.8)	10 (30.3)	3 (17.6)	9 (34.6)	13 (22.0)	19 (32.2)
Others	0 (0.0)	1 (3.0)	1 (5.9)	0 (0.0)	1(1.7)	1 (1.7)
Marital status						
Single	2 (4.8)	4 (12.1)	3 (17.6)	1 (3.8)	5 (8.5)	5 (8.5)
Married	39 (92.9)	28 (84.9)	11 (64.7)	24 (92.4)	50 (84.7)	51 (86.4)
Widowed/Divorced	1 (2.4)	1 (3.0)	3 (17.7)	1 (3.8)	4 (6.8)	2 (5.1)
Education status						
Primary	12 (28.6)	10 (30.3)	7 (41.2)	8 (30.8)	19 (32.2)	18 (30.5)
Secondary	16 (38.1)	13 (48.5)	8 (47.0)	10 (38.5)	24 (40.7)	26 (44.0)
Pre-U/Tertiary	14 (33.4)	10 (30.3)	2 (11.8)	8 (30.8)	16 (27.1)	18 (25.5)
Occupation						
Unemployed/retired	26 (63.7)	18 (54.6)	13 (76.4)	17 (65.4)	39 (66.1)	35 (59.3)
Blue collar	7 (16.7)	7 (21.2)	2 (11.8)	6 (23.1)	9 (15.3)	13 (22.0)
Businessmen	3 (7.1)	1 (3.0)	1 (5.9)	0 (0.0)	3 (5.1)	1 (1.7)
Government	1 (2.4)	2 (6.1)	0 (0.0)	1 (3.8)	2 (3.4)	4 (6.8)
Professionals	3 (7.1)	4 (12.1)	0 (0.0)	1 (3.8)	3 (5.1)	5 (8.5)
Others	1 (3.0)	1 (3.0)	1 (5.9)	0 (0.0)	3 (5.1)	1 (1.7)
Personal income (RM)						
<500	16 (38.1)	15 (45.5)	12 (70.6)	16 (61.5)	28 (47.5)	31 (52.5)
500-999	5 (11.9)	2 (6.1)	4 (23.9)	3 (11.5)	9 (15.3)	5 (8.5)
1000-1999	13 (31.0)	9 (27.3)	0 (0.0)	4 (15.4)	13 (22.0)	13 (22.0)
2000-2999	2 (4.8)	3 (9.1)	0 (0.0)	3 (11.5)	2 (3.4)	6 (10.2)
>3000	6 (14.3)	4 (12.1)	1 (5.9)	0 (0.0)	7(11.9)	4 (6.8)
Mean±SD	1721.6±360.9	2936.1±1045.1	770.1±366.9	4786.9±570.1	1113.0±938.0	1214.2±399.2

*p<0.05

Vitamin D, but not calcium was found to lower the risk for CRA by 69% (Table 3). However, vitamin D and calcium are generally studied together and few studies have shown the protective effect of both micronutrients in subjects with CRA. Oh *et al.* (2005) suggested that higher total calcium and vitamin D intakes were associated with reduced risk, though the intakes of vitamin D may be attenuated by high retinol intake. Hartman *et al.* (2005) also reported that dietary calcium and total vitamin D may be inversely associated with adenoma recurrence. Grau *et al.* (2003) further elaborated that calcium supplementation actually work together vitamin D states to reduce the risk.

The highest tertile of vitamin E was found to reduce the risk by 67% compared to the lowest tertile after adjusting for confounders (Table 3). Similar findings were reported by McKeown *et al.* (1998) where group supplemented vitamin E together with vitamin C resulted in significant reduction in risk. The antioxidant properties of vitamin E may be a reason for the reduction in the risk. However, there was no evidence that vitamin E reduced the incidence of adenomas (RR = 1.08, 95% CI = 0.91-1.29) (Greenberg *et al.*, 1994). The limited available evidence suggests vitamin E has conflicting association with CRA. Dietary intake vitamin E had shown either to have protective effect or no significant relationship with risk for CRA.

Crude fibre was found to be protective of colorectal adenoma in all subjects, when compared to the lowest tertile (Table 3). As the Malaysian Food Composition Table does not provide values for dietary fibre, crude fibre intake has been used as a measure of fibre intake in the subjects. Evidence for an association between dietary fibre and colorectal neoplasia has been equivocal and some data suggest that there may be sex differences in response to fibre. Pooled analysis of data from two large randomized controlled trials; the Wheat Bran Fibre Trial and the Polyp Prevention Trial indicated that the reduction in risk is more evident in men compared to women. (Jacobs *et al.*, 2006). A prospective

Table 2: Nutrients intake of the participants

Variables (Mean±SD)	Males		Females		All	
	Case (n = 42)	Control (n = 33)	Case (n = 17)	Control (n = 26)	Case (n = 59)	Control (n = 59)
Energy (kcal)	1461±431.1	1562.2±458.8	1447.3±381.3	1501.3±385.6	1457.06±414.12	1535.39±425.62
Macronutrient						
Carbohydrate (g)	196.7±64.5	268.7±55.0	198.2±57.2	198.5±62.9	197.13±62.02	204.20±58.3
Protein (g)	62.9±17.1	65.7±18.7	58.5±14.2	58.5±14.2	61.67±16.34	66.98±19.95
Fat (g)	48.2±18.4	53.2±24.1	47.9±15.0	48.8±17.5	48.08±17.40	51.29±21.38
Vitamins						
beta-carotene (µg)	873.3±591.5*	1555.4±1416.5*	802.2±645.6**	1631.1±1033.5**	852.78±602.76**	1588.80±1248.98**
alpha-carotene (µg)	171.5±109.9*	354.5±276.3*	136.6±106.1*	435.7±346.3*	161.07±108.81**	390.38±307.17**
Lutien (µg)	901.8±321.1	1813.8±679.4	197.3±145.6	689.9±518.3	764.13±285.43	1423.60±608.39
Lycopene (µg)	402.0±236.9*	2638.2±1315.4*	1323.9±626.1	3272.4±2121.2	793.34±349.04**	2936.74±670.49**
Vitamin A (µg)	4731.0±2127.3**	6944.6±3902.9**	5008.3±2007.5	6304.4±2730.5	4810.9±2080.1	662.5±3423.5
Retinol (µg)	1055.9±505.6*	1457.9±736.4*	1049.3±451.6	1107.5±567.6	1053.98±486.82*	1303.45±684.72*
Vitamin C (mg)	44.0±29.1*	66.1±44.8*	63.6±109.4	84.2±95.1	49.65±63.09	74.10±71.35
Vitamin D (mg)	1.4±1.0	1.2±1.0	0.7±0.6	0.9±0.6	1.3±0.9	1.1±0.8
Vitamin E (mg)	3.2±1.2*	5.1±4.7*	3.8±2.1	5.0±3.8	3.39±1.53*	5.08±4.14*
Folate (mg)	80.6±34.6**	126.2±77.2**	83.4±44.0	112.0±69.8	81.4±37.7	119.9±73.7
Minerals						
Calcium (mg)	538.0±287.7	567.5±257.2	425.8±171.5	521.0±265.1	505.65±263.15	547.03±256.19
Iron (mg)	12.0±5.1	15.6±13.8	13.7±6.2	14.4±8.2	12.47±5.43	15.04±11.57
Crude fiber (g)	3.8±2.3**	6.6±4.3**	4.2±2.7*	7.6±6.5*	3.93±2.42**	7.07±5.34**

*p<0.05; **p<0.01

Table 3: Crude and adjusted odds ratio of nutrient intakes of participants

Variables	Males		Females		All	
	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)
Macronutrient						
Carbohydrate						
T1	1.00	1.00	1.00	1.00	1.00	1.00
T2	1.20 (0.36-3.92)	1.42 (0.39-5.18)	2.86 (0.61-3.84)	2.44 (0.66-3.89)	1.53 (0.22-2.32)	1.45 (0.16-2.23)
T3	1.36 (0.11-2.16)	0.36 (0.10-1.32)	1.11 (0.21-5.80)	1.90 (0.27-13.54)	1.58 (0.65-3.88)	1.52 (0.56-4.16)
Protein						
T1	1.00	1.00	1.00	1.00	1.00	1.00
T2	2.43 (0.74-8.0)	2.98 (0.76-11.70)	1.19 (0.02-2.10)	1.25 (0.02-3.53)	1.55 (0.21-1.42)	1.42 (0.14-2.22)
T3	1.85 (0.27-4.6)	1.98 (0.27-3.54)	1.47 (0.10-2.30)	1.60 (0.09-4.41)	1.80 (0.75-4.34)	1.66 (0.61-4.53)
Fat						
T1	1.00	1.00	1.00	1.00	1.00	1.00
T2	1.80 (0.54-5.89)	1.65 (0.47-5.82)	1.23 (0.27-5.67)	2.30 (0.39-4.74)	1.63 (0.24-3.60)	1.51 (0.18-3.44)
T3	1.60 (0.19-2.89)	1.59 (0.17-3.04)	1.62 (0.12-3.22)	1.32 (0.17-5.00)	1.64 (0.68-3.94)	1.54 (0.60-3.98)
Vitamins						
Beta-carotene						
T1	1.00	1.00	1.00	1.00	1.00	1.00
T2	0.83 (0.25-2.76)	0.17 (0.29-3.66)	0.43 (0.27-2.52)	0.64 (0.24-2.24)	0.96 (0.38-2.43)	1.11 (0.41-3.02)
T3	0.25 (0.08-0.80)*	0.23 (0.06-0.86)*	0.08 (0.01-0.54)*	0.07 (0.01-0.58)*	0.18 (0.07-0.48)*	0.21(0.07-0.59)*
Alpha-carotene						
T1	1.00	1.00	1.00	1.00	1.00	1.00
T2	0.11 (0.06-3.47)	0.33 (0.06-4.97)	0.60 (0.33-7.85)	0.31 (0.19-8.92)	0.26 (0.05-3.15)	0.32 (0.04-3.69)
T3	0.21 (0.06-0.74)	0.22 (0.06-0.80)*	0.20 (0.04-1.07)	0.09 (0.01-0.81)*	0.20 (0.07-0.53)*	0.20 (0.07-0.55)*
Lutien						
T1	1.00	1.00	1.00	1.00	1.00	1.00
T2	0.60 (0.19-1.94)	0.66 (0.18-2.41)	0.17 (0.02-1.91)	0.05 (0.00-0.99)*	0.62 (0.23-1.66)	0.46 (0.15-1.37)
T3	0.25 (0.07-0.95)*	0.28 (0.07-1.10)	0.51 (0.13-2.02)	0.35 (0.07-1.88)	0.72 (0.31-1.65)	0.73 (0.29-1.81)
Lycopene						
T1	1.00	1.00	1.00	1.00	1.00	1.00
T2	0.79 (0.05-13.50)	0.93 (0.03-30.68)	1.02 (0.23-4.53)	0.44 (0.07-2.84)	0.88 (0.29-0.95)*	0.73 (0.37-0.99)*
T3	0.37 (0.12-1.14)	0.35 (0.10-1.25)	0.14 (0.02-0.82)	0.08 (0.01-0.77)	0.24 (0.10-0.60)*	0.27 (0.10-0.75)*
Vitamin A						
T1	1.00	1.00	1.00	1.00	1.00	1.00
T2	0.31 (0.10-1.00)	0.28 (0.08-1.06)	0.40 (0.07-2.37)	0.75 (0.09-6.05)	0.15 (0.06-0.38)*	0.13 (0.04-0.38)*
T3	1.11 (0.63-5.13)	1.99 (0.69-5.07)	1.75 (0.40-3.88)	1.62 (0.29-3.49)	0.64 (0.24-1.68)	0.54 (0.17-1.73)
Retinol						
T1	1.00	1.00	1.00	1.00	1.00	1.00
T2	1.00 (0.31-3.28)	0.89 (0.24-3.31)	0.22 (0.05-1.09)	0.15 (0.02-1.01)	1.59 (0.64-3.93)	1.45 (0.54-3.88)
T3	0.82 (0.07-2.73)	0.77 (0.04-3.66)	0.80 (0.15-4.25)	0.73 (0.04-2.76)	0.38 (0.15-0.96)*	0.36 (0.13-1.04)

Table 3: Crude and adjusted odds ratio of nutrient intakes of participants (Continued)

	Males		Females		All	
Variables	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)	Crude OR (95% CI)	Adjusted OR (95% CI)
Vitamin C						
T1	1.00	1.00	1.00	1.00	1.00	1.00
T2	0.75 (0.24-2.39)	0.55 (0.15-2.01)	1.02 (0.46-8.78)	0.95 (0.68-3.76)	0.96 (0.38-2.41)	0.90 (0.33-2.44)
T3	0.28 (0.09-0.92)*	0.19 (0.05-0.73)*	0.24 (0.04-1.53)	0.35 (0.05-2.68)	0.32 (0.13-0.78)*	0.28 (0.11-0.77)*
Vitamin D						
T1	1.00	1.00	1.00	1.00	1.00	1.00
T2	0.15 (0.04-0.59)*	0.11 (0.02-0.60)*	0.47 (0.28-1.63)	0.96 (0.13-7.17)	0.21 (0.08-0.54)*	0.17 (0.06-0.51)*
T3	0.43 (0.13-1.42)	0.34 (0.09-1.35)	0.40 (0.89-2.78)	0.33 (0.71-4.11)	0.45 (0.18-1.13)	0.31 (0.11-0.89)*
Vitamin E						
T1	1.00	1.00	1.00	1.00	1.00	1.00
T2	0.29 (0.39-4.24)	0.46 (0.40-5.30)	0.36 (0.08-1.64)	0.51 (0.10-2.58)	0.63 (0.35-4.07)	0.41 (0.07-5.33)
T3	0.20 (0.06-0.69)	0.23 (0.07-0.84)	0.15 (0.03-0.85)	0.23 (0.03-1.76)	0.23 (0.09-0.61)*	0.33 (0.12-0.92)*
Folate						
T1	1.00	1.00	1.00	1.00	1.00	1.00
T2	0.38 (0.10-1.46)	0.19 (0.04-0.99)	0.88 (0.20-3.76)	2.37 (0.30-18.74)	0.40 (0.14-1.17)	0.32 (0.10-1.08)
T3	0.21 (0.06-0.70)	0.14 (0.03-0.60)	0.27 (0.05-1.42)	0.32 (0.05-2.00)	0.67 (0.30-1.53)	0.63 (0.26-1.53)
Minerals						
Calcium						
T1	1.00	1.00	1.00	1.00	1.00	1.00
T2	3.43 (1.03-11.45)	3.14 (0.83-11.91)	2.00 (0.46-8.78)	1.86 (0.38-9.08)	1.43 (0.58-3.48)	1.16 (0.44-3.10)
T3	0.77 (0.25-2.93)	0.67 (0.18-2.43)	0.22 (0.04-1.39)	0.33 (0.04-2.65)	0.59 (0.24-1.46)	0.49 (0.17-1.42)
Iron						
T1	1.00	1.00	1.00	1.00	1.00	1.00
T2	0.42 (0.17-2.98)	1.00 (0.75-3.18)	0.60 (0.12-3.90)*	0.72 (0.09-6.82)*	0.88 (0.24-3.41)	0.86 (0.31-4.82)
T3	0.41 (0.13-1.29)	0.65 (0.17-2.48)	0.37 (0.27-6.87)	0.73 (0.40-4.68)	0.96 (0.38-5.66)	1.00 (0.68-3.91)
Other						
Crude fibre						
T1	1.00	1.00	1.00	1.00	1.00	1.00
T2	1.14 (0.34-3.86)	1.11 (0.28-4.45)	0.29 (0.04-1.98)	0.06 (0.03-1.12)	0.21 (0.08-0.55)*	0.19 (0.06-0.57)*
T3	0.19 (0.06-0.65)*	0.15 (0.04-0.62)*	0.17 (0.03-1.09)	0.07 (0.01-0.95)*	0.14 (0.05-0.40)*	0.20 (0.04-0.36)*

*p<0.05

study of 88,757 women (Fuchs *et al*., 1999) for example, also did not find any significant protective effect of dietary fibre on CRA in women.

Anthropometric measurements: The mean BMI was slightly higher among the case subjects as compared to the controls, regardless of the gender (Table 4). The majority of the participants fell in the overweight and obese category. A study using a larger number of samples found that men in the upper quartiles of BMI have higher risk of recurrent adenomas, but there was no effect on women (Davidow *et al*., 1996). Yet, Sass *et al*. (2004) found no relationship between weight and BMI and recurrence of adenomas. Despite this, Chung *et al*. (2006) found that higher BMI was strongly associated with increased risk of advanced adenoma (OR = 10.8, 95% CI = 4.6-25.3). Incidence of colorectal polyps was also found to be related to obesity (Tashiro *et al*., 2004). The cross-sectional study found that 51% of obese patients have polyps as compared to 29% in non-obese. While the mean waist circumference suggested the case subjects to have higher mean than the controls, only a minority of them had abdominal obesity (≥102 cm for men and ≥88 cm for women). Almendingen *et al*. (2001) proposed that high body fatness is a promoter of adenoma growth. This is based on their findings where increasing percentage of body fat (p = 0.02) and BMI (p = 0.006) highly associated with adenomas growth.

Although the mean percentages of body fat were almost equal between groups, a majority of the male respondents had high percentage of body fat though this pattern was not seen in the female groups. The percentage of body fat also found to be insignificantly different between study group, although there were other studies that found otherwise (Giovannucci *et al*., 1996; Morimoto *et al*., 2002). A study found that Japanese patients with CRA showed significantly more visceral fat area in comparison with the controls [OR = 2.19; 95% CI = 1.47-3.28). These results suggest an association of visceral fat accumulation (Otake *et al*., 2005).

Lipid profile: The mean total cholesterol and LDL-C were found to be in undesirable range in men, while mean triglyceride, total cholesterol and LDL-C were in the undesirable range in women (Table 5). There were significant differences in the plasma HDL-C in females, with cases having lower mean HDL-C compared to the controls. Conversely, mean plasma LDL-C was higher among female cases than controls.

A study by Bayerdorffer *et al*. (1993) supported these findings, where the authors concluded that patients with CRA have lower HDL cholesterol levels and higher LDL

Table 4: Anthropometrical measurements of the participants

Variables	Males		Females		All	
	Case (n = 42)	Control (n = 33)	Case (n = 17)	Control (n = 26)	Case (n = 59)	Control (n = 59)
Body Mass Index (kg/m^2)						
Underweight	1 (2.5)	3 (9.1)	1 (6.3)	0 (0.0)	2 (3.4)	3 (5.1)
Normal	19 (46.3)	15 (42.5)	9 (56.3)	12 (46.2)	28 (47.5)	27 (45.8)
Overweight	20 (48.8)	13 (39.4)	5 (31.3)	7 (26.9)	25 (42.4)	20 (33.9)
Obese	2 (4.9)	2 (6.1)	1 (6.3)	7 (26.9)	3 (5.1)	9 (15.3)
Mean±SD	25.1±3.1	24.4±3.8	25.6±4.9	23.9±3.7	24.8±4.5	24.9±4.3
Waist circumference (cm)						
Normal	38 (90.5)	30 (90.9)	8 (47.2)	19 (73.1)	46 (78.0)	49 (83.1)
High risk	4 (9.5)	3 (9.1)	9 (52.9)	7 (26.9)	13 (22.0)	10 (16.9)
Mean±SD	90.3±9.4	88.3±9.3	84.3±9.3	82.5±12.9	88.6±9.7	85.6±11.8
Percentage of body fat (%)						
Low/normal	6 (14.3)	3 (9.1)	5 (29.4)	9 (34.6)	11 (18.6)	12 (20.3)
Moderate	4 (9.5)	6 (18.2)	6 (35.3)	8 (30.8)	10 (16.9)	14 (23.7)
High	32 (76.2)	24 (72.7)	6 (35.3)	9 (34.6)	38 (64.4)	32 (54.2)
Mean±SD	27.1±5.4	27.4±6.5	33.5±5.2	33.0±5.6	28.9±6.1	30.1±6.7

Table 5: Lipid profile of the participants

Variables	Males		Females		All	
	Case (n = 42)	Control (n = 33)	Case (n = 17)	Control (n = 26)	Case (n = 59)	Control (n = 59)
Lipid profile						
Triglycerides (mmol/L)						
Desirable (<1.73)	12 (28.6)	13 (39.4)	6 (35.3)	11 (42.3)	18 (30.5)	24 (40.7)
Borderline (1.73-2.29)	20 (47.6)	11 (33.3)	3 (17.6)	8 (30.8)	23 (39.0)	19 (32.2)
Increased risk (>2.29)	10 (23.8)	9 (27.3)	8 (47.1)	7 (26.9)	18 (30.5)	16 (27.1)
Mean±D	2.0±1.1	2.3±1.1	2.6±2.1	2.2±1.1	2.2±1.5	2.3±1.1
Total cholesterol (mmol/L)						
Desirable (<5.2)	10 (23.8)	0 (0.0)	4 (23.5)	0 (0.0)	15 (25.4)	0 (0.0)
Borderline (5.2-6.19)	2 (4.8)	0 (0.0)	0 (0.0)	1 (3.8)	2 (3.4)	1 (1.7)
Increased risk (>6.2)	30 (71.4)	33 (100.0)	13 (76.5)	25 (96.2)	43 (72.9)	58 (98.3)
Mean±SD	8.4±1.7	6.8±2.9	8.9±2.1	7.5±2.9	8.6±1.8$^{\varphi}$	7.2±2.9$^{\varphi}$
HDL (mmol/L)						
Desirable (>1.6)	32 (76.2)	31 (93.9)	13 (76.5)	24 (92.3)	45 (76.3)	55 (93.2)
Borderline (1.03-1.59)	3 (7.1)	1 (3.0)	1 (5.9)	2 (7.7)	4 (6.8)	3 (5.1)
Increased risk (<1.59)	7 (16.7)	1 (3.0)	3 (17.6)	0 (0.0)	10 (16.9)	1 (1.7)
Mean±SD	3.1±1.1	2.0±0.9	2.2±0.9$^{\varphi}$	3.7±1.6$^{\varphi}$	2.1±0.9$^{\varphi}$	3.3±1.3$^{\varphi}$
LDL (mmol/L)						
Desirable (<3.4)	14 (33.3)	0 (0.0)	5 (29.4)	0 (0.0)	19 (32.2)	0 (0.0)
Borderline (3.4-4.09)	6 (14.3)	0 (0.0)	1 (5.9)	2 (7.7)	7 (11.9)	2 (3.4)
Increased risk (>4.1)	22 (52.4)	33 (100.0)	11 (64.7)	24 (92.3)	33 (55.9)	57 (58.7)
Mean±SD	7.1±2.1	4.6±1.9	7.5±3.1$^{\varphi}$	4.2±1.9$^{\varphi}$	7.2±2.4$^{\varphi}$	4.1±1.9$^{\varphi}$

$^{\varphi}p<0.01$

levels; these lipoproteins may have prognostic significance for the development of CRA. Another study by Park *et al.* in the year 2000 found significant association between total cholesterol and risk for CRA, but no conclusive findings in relationship with HDL-C and LDL-C. In this case-control study, significant relationship was found between total cholesterol and LDL with risk for CRA, but there HDL was not found to influence the risk. Otani *et al.* (2006) suggested that a higher serum triglyceride level may be related to a larger number of adenomas. Adenoma development involving an elevated serum triglyceride level may be modified by smoking as higher prevalence of CRA was found in smokers.

Conclusion and recommendations: Our results support the notion that nutritional status and factors associated with it are of importance for the development of these pre-cancerous lesions. Identification of risk factors through this case-control study should be able to supplement the available data in order to develop an intervention package that focuses on multiple risk factors to reduce the chances for developing CRA or CRC.

The sample size for this study is rather small and the fact that it focuses on subjects in the Klang Valley may limit the extrapolation of these findings to the entire Malaysian population. Thus, a larger study and possibly a prospective cohort study which incorporates study subjects from various places in Malaysia may be a better option to identify if these risk factors are applicable to Malaysians in other parts of the country.

The possibility that the associations may be confounded or modified by other genetic or dietary factors could not be excluded. The cases and controls have not been matched by age, which may affect the results in our study. However, the controls were recruited from the same population as the adenoma cases. Further, our controls have been screened and found polyp free by colonoscopy and the risk of any of them having colon cancer at the time of inclusion is not very likely.

Risk factors which have potential to be modified such as smoking habit, drinking habit, lower intake of fruits and vegetables should be intervened. An intervention study focusing on behavioural change may be able to improve one's risk for colorectal adenomas, thus subsequently reducing his/her risk for developing colorectal cancer in the future.

ACKNOWLEDGEMENTS

The authors are grateful to the Ministry of Science, Technology and Innovation (MOSTI) which funded the project under the Intensification of Research Priorities Areas (IRPA) programme (IRPA 06-02-04-0682-EA001).

REFERENCES

Almendingen, K., B. Hofstad and M.H. Vatn, 2001. Does high body fatness increase the risk of presence and growth of colorectal adenomas followed up in situ for 3 years? Am. J. Gastro., 96: 2238-2246.

American Society for Gastrointestinal Endoscopy, 2006. Understanding Polyps and Their Treatment [Online]. Available: http://www.asge.org/nspages/practice/ management/brochures/polyps_ brochure.cfm. Accessed on 10 July 2006.

Bayerdorffer, E., G.A. Mannes, W.O. Richter, T. Ochsenkühn, G. Seeholzer, W. Köpcke, B. Wiebecke and G. Paumgartner, 1993. Decreased high-density lipoprotein cholesterol and increased low-density cholesterol levels in patients with colorectal adenomas. Ann. Int. Med., 118: 481-487.

Bond, J.H., 2000. Polyp guideline: diagnosis, treatment and surveillance for patients with colorectal polyps. Am. J. Gastro., 95: 3053-3063.

Bowers, K., D. Albanes, P. Limburg, P. Pietinen, P.R. Taylor, J. Virtamo and R. Stolzenberg-Solomon, 2006. A prospective study of anthropometric and clinical measurements associated with insulin resistance syndrome and colorectal cancer in male smokers. Am. J. Epi., 164: 652-665.

Burt, R.W., 2000. Colon cancer screening. Gastro., 119: 837-853.

Carr, T., C.J. Anderssen and L.L. Rudel, 1993. Enzymatic determination of triglycerides, free cholesterol and total cholesterol in tissue lipid extracts. Clin. Biochem., 26: 39-42.

Chung, Y.W., D.S. Han, Y.K. Park, B.K. Son, C.H. Paik, H.L. Lee, Y.C. Jeon and J.H. Sohn, 2006. Association of obesity, serum glucose and lipids with the risk of advanced colorectal adenoma and cancer: A case-control study in Korea. Dig. Liver. Dis., 38: 668-672.

Davidow, A.L., A.L. Nangut, J.S. Jacobson, H. Ahsan, G.C. Garbowski, K.A. Forde, M.R. Treat and J.D. Waye, 1996. Recurrent adenomatous polyps and body mass index. Cancer Epi. Biomark. Prev., 5: 313-315.

Enger, S.M., M.P. Longnecker, M.J. Chen, J.M. Harper, E.R. Lee, H.D. Frankl and R.W. Haile, 1996. Dietary intake of specific carotenoids and vitamin A, C and E and prevalence of colorectal adenomas. Cancer Epi. Biomark. Prev., 5: 147-153.

Erhardt, J.G., C. Meisner, J.C. Bode and C. Bode, 2003. Lycopene, beta-carotene and colorectal adenomas. Am. J. Clin. Nutr., 78: 1219-1224.

Fuchs, C.S., E.L. Giovannucci, G.A. Colditz, D.J. Hunter, M.J. Stampfer, B. Rosner, F.E. Speizer and W.C. Willet, 1999. Dietary fiber and the risk of colorectal cancer and adenoma in women. N. Engl. J. Med., 340: 169-176.

Gibson, R.S., 2005. Reproducibility in dietary assessment. Principles of Nutritional Assessment. Oxford University Press, USA.

Giovannucci, E., G.A. Colditz, M.J. Stampfer and W.C. Willet, 1996. Physical activity, obesity and risk for colorectal adenoma in women. Cancer Causes Control, 7: 253-263.

Grau, M.V., J.A. Baron, R.S. Sandler, R.W. Haile, M.L. Beach, T.R. Church and D. Heber, 2003. Vitamin D, calcium supplementation and colorectal adenomas: Results of a randomized-trial. JNCI., 95: 1765-1771.

Greenberg, E.R., J.A. Baron, T.D. Tosteson, D.H. Freeman, G.J. Beck, J.H. Bond, T.A. Colacchio, J.A. Coller, H.D. Frankl, R.W. Haile, J.S. Mandel, D.W. Nierenberg, R. Rothstein, D.C. Snover, M.M. Stevens, R.W. Summers, R.U. Van Stolk and The Polyp Prevention Study Group, 1994. A clinical trial of antioxidant vitamins to prevent colorectal adenoma. N. Engl. J. Med., 331: 141-147.

Hartman, T., P.S. Albert, K. Snyder, M.L. Slattery, B. Caan, E. Paskett, F. Iber, J.W. Kikendall, J. Marshall, M. Shike, J. Weissfeld, B. Brewer, A. Schatzkin, E. Lanza and The Polyp Prevention Study Group, 2005. The association of calcium and vitamin D with risk of colorectal adenomas. J. Nutr., 132: 252-259.

International Association of Cancer Registries, 2002. Globocan 2002: Cancer Incidence, Mortality and Prevalence Worldwide, Version 1.0 [Online]. Available: http://www-dep.iarc.fr. Accessed on 9 February 2005.

Jacobs, E.T., E. Lanza, D.S. Alberts, C.H. Hsu, R. Jiang, A. Schatzkin, P.A. Thompson and M.E. Martinez, 2006. Fiber, sex and colorectal adenomas: Results of a pooled analysis. Am. J. Clin. Nutr., 83: 343-349.

Jiang, J., S. Suzuki, J. Xiang, K. Kuriki, A. Hosono, K. Arakawa, J. Wang, T. Nagaya, M. Kojima and N. Katsuda, 2005. Plasma carotenoid, alpha-tocopherol and retinol concentrations and risk of colorectal adenomas: A case-control study in Japan. Cancer Lett., 226: 133-141.

Kahn, H.S., L.M. Tatham, M.J. Thun and C.W. Heath, 1998. Risk factors for self-reported colon polyps. J. Gen. Internal Med., 13: 303-310.

Larsen, I.K., T. Grotmol, K. Almendingen and G. Hoff, 2006. Lifestyle as a predictor for colonic neoplasia in asymptomatic individuals. BMC Gastro., 6: 5.

Lee, Y.S., 1987. Adenomas, metaplastic polyps and other lesions of the large bowel: An autopsy survey. Ann. Acad. Med., 16: 412-420.

Lintsi, M., H. Kaarma and I. Kull, 2004. Comparison of hand-to-hand bioimpedance and anthropometry equations versus dual-energy X-ray absorptiometry for the assessment of body fat percentage in 17-18-year-old conscripts. Clin. Physiol. Funct. Imaging, 24: 85-90.

Lubin, F., P. Rozen, B. Arieli, M. Farbstein, Y. Knaani, L. Bat and H. Farbstein, 1997. Nutritional and lifestyle habits and water-fiber interaction in colorectal adenomas etiology. Cancer Epi. Biomark. Prev., 6: 79-85.

Lukaski, H.C., P.E. Johnson, W.W. Bolonchuk and G.I. Lykken, 1985. Assessment of fat-free mass using bioelectrical impedance measurements of the human body. Am. J. Clin. Nutr., 41: 810-817.

Malila, N., J. Virtamo, M. Virtanen, D. Albanes, J.A. Tangrea and J.K. Huttunen, 1999. The effect of alpha-tocopherol and beta-carotene supplementation on colorectal adenomas in middle-aged male smokers. Cancer Epi. Biomark. Prev., 8: 489-493.

Martín-Moreno, V., G.B. Gómez, G.M. Antoranz, H.S. Fernández, C.A. Gómez and O.M. De Oya, 2001. Validation of the OMRON BF 300 monitor for measuring body fat by bioelectric impedance. Aten. Primaria., 28: 174-81.

McKeown-Eyssen, G., C. Holloway, V. Jazmaji, E. Bright-See, P. Dion and W.R. Bruce, 1998. A randomized trial of vitamins C and E in the prevention of recurrence of colorectal polyps. Cancer Res., 48: 4701-4705.

Morimoto, L.M., P.A. Newcomb, R.M. Ulrich, R.M. Bostick, C.J. Lais and J.D. Potter, 2002. Risk factors for hyperplastic and adenomatous polyps: evidence for malignant potential? Cancer Epi. Biomark. Prev., 11: 1012-1018.

National Cancer Registry, 2004. Cancer Incidence in Malaysia 2003. Lim G.C.C. and Halimah Y.H. (Eds). National Cancer Registry: Kuala Lumpur.

Oh, K., W.C. Willet, C.S. Fuchs and E. Giovannucci, 2005. Dietary marine n-3 fatty acids in relation to risk of distal colorectal adenomas in women. Cancer Epi. Biomark. Prev., 14: 835-841.

Otake, S., H. Takeda, Y. Suzuki, F. Tadahisa, W. Shinichiro, I. Katsuyoshi, S. Takafumi, T. Hitoshi, N. Tadashi, M. Yuji and K. Sumio, 2005. Association of visceral fat accumulation and plasma adiponectin with colorectal adenoma: Evidence for participation of insulin resistance. Clin. Cancer Res., 11: 3642-3646.

Otani, T., M. Iwasaki, S. Ikeda, T. Kozu, S. Hiroshi, M. Michihiro, W. Keiji and T. Shoichiro, 2006. Serum triglycerides and colorectal adenoma in a case-control study among cancer screening examinees. Cancer Causes Control, 17: 1245-1255.

Otani, T., M. Iwasaki, S. Yamameto, T. Sobue, T. Hanaoka, M. Inoue and S. Tsugane, 2003. Alcohol consumption, smoking and subsequent risk of colorectal cancer in middle-aged and elderly Japanese men and women: Japan Public Health Center-based Prospective Study. Cancer Epi. Biomark. Prev., 12: 1492-1500.

Park, S.K., J.S. Joo, D.H. Kim, Y.E. Kim, D. Kang and K.Y. Yoo, 2000. Association of serum lipids and glucose with the risk of colorectal adenomatous polyp in men: A case-control study in Korea. J. Korean Med. Sci., 15: 690-695.

Peters, U., N. Chatterjee, K.A. McGlynn, R.E. Schoen, T.R. Church, R.S. Bresalier, M.M. Gaudet, A. Flood, A. Schatzkin and R.B. Hayes, 2004. Calcium intake and colorectal adenoma in a US colorectal cancer early detection program. Am. J. Clin. Nutr., 80: 1358-1365.

Rajendra, S., J.J. Ho and J. Arokiasamy, 2005. Risk of colorectal adenomas in the multiethnic Asian patient population: Race does not matter. J. Gastro. Hep., 20: 51-55.

Sandler, R.S., M.L. Pritchard and S.I. Bangdiwala, 1995. Physical activity and the risk of colorectal adenomas. Epi., 6: 602-606.

Sass, D.A., R.E. Schoen, J.L. Weissfeld, L. Weissfeld, L.F. Thaete, L.H. Kuller, M. McAdams, E. Lanza and A. Schatzkin, 2004. Relationship of visceral adipose tissue to recurrence of adenomatous polyps. Am. J. Gastro., 99: 687-93.

Schatzkin, A., E. Lanza, D. Corle, P. Lance, F. Iber, B. Caan, M. Shike, J. Weissfeld, R. Burt, R. Cooper, J.W. Kikendall, J. Cahill, L. Freedman, J. Marshall, R.E Schoen and M. Slattery, 2000. Lack of effect of a low-fat, high-fiber diet on the recurrence of colorectal adenomas. N. Eng. J. Med., 342: 1149-55.

Senesse, P., M. Touvier, E. Kesse, J. Faivre and M.C. Boutron-Ruault, 2005. Tobacco use and associations of beta-carotene and vitamin intakes with colorectal adenoma risk. J. Nutr., 135: 2468-2472.

Tashiro, M., T. Akiyama, I. Yoshikawa, K. Kume and M. Otsuki, 2004. Obesity as a risk factor for colorectal polyps in Japanese patients. Gut., 53: 156.

Todoroki, I., S. Kori, K. Shinchi, S. Honjo, Y. Sakurai, K. Wakabayashi, K. Imanishi, H. Nishikawa, S. Ogawa and M. Katsurada, 1995. Relationship of cigarette smoking, alcohol and dietary habits with sigmoid colon adenomas. Ann. Epi., 5: 478-483.

Tseng, M., S. Murray, L. Kupper and R.S. Sandier, 1994. Micronutrients and the risk of colorectal adenomas. Am. J. Epi., 144: 1005-1014.

Wark, P.A., W. Van Der Kuil, J. Ploemacher, G.N.P. Van Muijen, C.J.J. Mulder, M.P. Weijenberg, F.J. Kok and E. Kampman, 2006. Diet, lifestyle and risk of K-ras mutation-positive and -negative. Int. J. Cancer, 119: 398-405.

Warnick, G.R., J. Benderson and J.J. Albers, 1982. Dextran-sulphate-Mg^{2+} percipatation procedure for quantitation of high-density-lipoprotein cholesterol. Clin. Chem., 28: 1379-1388.

World Health Organization, 1995. Physical Status: The use and interpretation of anthropometry. WHO Technical Series Report no. 854. WHO, Geneva.

Young, G.P., P. Rozen and B. Levin, 2002. How does colorectal cancer develops? In: Rozen, P., B. Levin, G.P. Young and S.J. Spann (Eds), Colorectal Cancer in Clinical Practice: Prevention, Early Detection and Management. Martin Dunitz Ltd: United Kingdom.