UNIVERSITI PUTRA MALAYSIA

DIETARY AND LIFESTYLE FACTORS ASSOCIATED WITH RISK OFCOLORECTAL ADENOMA IN PATIENTS AT HOSPITAL KUALA LUMPUR

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Chairman : Associate Professor Mirnalini Kandiah, PhD

Faculty : Medicine and Health Sciences

Cancer is now the third leading cause of death in Malaysia and one in four Malaysians is at risk of developing cancer. In Peninsular Malaysia, there was a slight decline in percentage of colon (-0.2%) and rectal (-0.2%) cancer incidence in males in the year 2003 compared to the previous year as reported by National Cancer Registry (2004). Yet, there was an increase in percentages of these cancer incidences in women (+0.4% in colon cancer and +0.7% in rectal cancer). Colorectal cancers are thought to develop over a period of several years, and most of them develop from benign, neoplastic adenomatous polyps (Bond, 2000). Colorectal adenomas have been shown, but not always, significantly related to various dietary and lifestyle factors. These factors have yet to be reported in relation to colorectal polyps in the Malaysian population. This case-control study was carried out to determine the relationship between dietary and lifestyle characteristics, and risk for colorectal adenomas among Malaysians. After screening for inclusion and exclusion criteria, 118 men and women with good cognition and who were at least 30 years at the time of interview and have undergone colonoscopy in Hospital

Kuala Lumpur were enrolled in the this study upon obtaining ethical clearance. Fifty nine patients diagnosed with colorectal adenomas were recruited as case subjects, while a similar number of patients diagnosed negative for any polyps were recruited as controls. A structured and pre-tested interviewer administrated questionnaire was used for data collection. The fasting blood samples were collected by trained and qualified nurse, and analyzed using relevant analysis in the laboratory. The collected data were then analyzed with SPSS version 12.0. Multivariate analysis concluded that the higher servings of fruits (adjusted OR = 0.150, 95% CI = 0.052 – 0.434) and vegetables (adjusted OR = 0.344, 95% CI = 0.149 - 0.794), crude fibre intake (adjusted OR = 0.659, 95% CI = 0.481 – 0.905) and plasma levels of total cholesterol (adjusted OR = 5.370, 95% CI = 1.861 – 15.495), LDL (adjusted OR = 1.093, 95% CI = 1.022 – 2.386) and vitamin E (adjusted OR = 0.481, 95% CI = 0.306 – 0.758) found to significantly contribute to the risk for colorectal adenomas, upon adjusting for potential covariates. A larger study and possibly a prospective study which recruits study subjects from various places in Malaysia will be an excellent effort to confirm these findings. Interventions with focuses on behavioural change may be able to reduce one's risk for colorectal adenomas which in the long-term reduce his/her risk for developing colorectal cancer in the future.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Master Sains

FAKTOR-FAKTOR DIET DAN GAYAHIDUP YANG BERKAITAN DENGAN RISIKO ADENOMA KOLOREKTAL DI KALANGAN PESAKIT DI HOSPITAL KUALA LUMPUR

Oleh

AMUTHA RAMADAS

Disember 2006

Pengerusi : Profesor Madya Mirnalini Kandiah, PhD

Fakulti : Perubatan dan Sains Kesihatan

Kanser menduduki tempat ketiga dalam senarai punca kematian di Malaysia dan seorang daripada empat rakyat Malaysia berisiko mendapat kanser. Menurut laporan National Cancer Registry (2004) terdapat sedikit penurunan dalam peratusan kejadian kanser kolon (-0.2%) dan rektal (-0.2%) di kalangan lelaki Semenanjung Malaysia pada tahun 2003 berbanding tahun sebelumnya. Walaubagaimanapun, terdapat peningkatan dalam peratusan kejadian kanser ini di kalangan wanita (kanser kolon +0.4% dan kanser rektal +0.7%). Kanser kolorektal dikatakan berkembang dalam tempoh masa beberapa tahun dan kebanyakannya berpunca daripada polip adenoma neoplastik dan yang pada mulanya tidak berbahaya (Bond, 2000). Kanser kolorektal menunjukkan perkaitan yang signifikan dengan faktor diet dan gaya hidup. Namun, hubungan antara faktor – faktor ini dan polip adenoma di kalangan penduduk Malaysia masih belum dibuktikan. Kajian kes–kawalan ini bertujuan mengenalpasti hubungan antara ciri-ciri diet dan gaya hidup, dan risiko adenoma kolorektal di kalangan penduduk Malaysia. Selepas penyaringan kriteria inklusi dan eksklusi, seramai 118 orang lelaki dan wanita yang waras akal dan berumur 30 tahun

ke atas ketika ditemuramah dan telah menjalani kolonoskopi di Hospital Kuala Lumpur dipilih menyertai kajian ini. Lima puluh sembilan pesakit yang didiagnosis dengan adenoma kolorektal dipilih menyertai kumpulan kes manakala lima puluh sembilan pesakit lain yang tidak didiagnosis dengan sebarang jenis polip dipilih menyertai kumpulan kawalan. Satu borang soal-selidik yang telah diuji dan digunakan oleh seorang penemuramah dalam pengumpulan data. Sampel darah pesakit yang berpuasa diambil oleh jururawat terlatih, dan dianalisa menggunakan kaedah yang relevan di makmal sains. Data yang dikumpulkan dianalisa dengan menggunakan SPSS versi 12.0. Analisis multivariat telah menunjukkan bahawa peningkatan dalam bilangan hidangan buah – buahan (*adjusted* OR = 0.150, 95% CI = 0.052 – 0.434) dan sayuran (*adjusted* OR = 0.344, 95% CI = 0.149 - 0.794), pengambilan serat kasar (*adjusted* OR = 0.659, 95% CI = 0.481 – 0.905) serta paras kolesterol dalam plasma (*adjusted* OR = 5.370, 95% CI = 1.861 – 15.495), LDL (*adjusted* OR = 1.093, 95% CI = 1.022 – 2.386) dan vitamin E (*adjusted* OR = 0.481, 95% CI = 0.306 – 0.758) menyumbang kepada risiko adenoma kolorektal secara signifikan, selepas mengawal kovariat yang lain. Satu kajian yang lebih menyeluruh dan merangkumi subjek dari pelbagai tempat di Malaysia adalah cara yang lebih baik untuk mengesahkan hasil kajian ini. Faktor risiko yang mempunyai potensi untuk diubahsuai seperti pengambilan buah-buahan dan sayur-sayuran yang rendah dan biomarker plasma yang tidak disenangi harus diberi perhatian. Kajian intervensi yang memfokuskan perubahan dalam tingkah laku mungkin dapat mengurangkan risiko seseorang terhadap adenoma kolorektal dan seterusnya mengurangkan risiko mereka untuk mendapat kanser kolorektal.

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BMI	Body Mass Index
CI	Confidence Intervals
OR	Odds Ratio
RR	Relative Risk
WHR	Waist-Hip Ratio
CRA	Colorectal adenomas
CRC	Colorectal cancer
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
WHO	World Health Organization
NCI	National Cancer Institute
ACS	American Cancer Society
ASGE	American Society for Gastrointestinal Endoscopy

CHAPTER 1

INTRODUCTION

1.1 Background

Cancer is a general term defining any malignant neoplasm characterized by an uncontrolled growth of anaplastic cells that tend to invade surrounding tissues and to metastases to distant body sites (Anderson *et al.,* 2002). It encompasses a group of neoplastic disease where normal body cells are transformed into malignant ones. Over 200 types and subtypes of cancer have been identified. These cancers have different etiological features, manifest with different symptoms and require different treatments (Cancer Research UK, 2002).

Worldwide, more than ten million people are diagnosed with cancer and 6 million deaths occur every year (World Health Organization, 2003). In Western countries such as the US, the lifetime risk of developing cancer is almost equal for both men and women. The lifetime risk of developing cancer is one in two in men and one in three in women (American Cancer Society, 2004). The Malaysian National Cancer Registry (2003) reported that for Malaysians, at least 1 in 4 have lifetime risk for developing cancer.

Cancer type varies with age; in young adults (15-49 years old), the common cancers are cancers of the nasopharynx, leukaemia, lymphoma, lung, colon and rectum in men, and cancers of the breast, cervix, ovary, uterus, thyroid gland and leukaemia in women. In

older subjects (50 years old and above), cancers of the lung, colon, rectum, nasopharynx, prostate and stomach are predominant among men, while cancers of the breast, cervix, colon, uterus, lung and rectum occurred commonly in women (NCR, 2003).

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. Colorectal cancer was estimated to contribute to 9.5% and 9.3% of total cancer cases among males and females respectively in 2002 (International Association of Cancer Registries, 2002). Among Malaysians, colon cancer ranked third among cancers reported in males and females, accounting for 7.8% and 6.0% of all cancer cases in males and females respectively in 2003 (NCR, 2003). 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.

It is a well-known fact that almost all CRCs arise from benign, neoplastic adenomatous polyps (Bond, 2000). 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 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 (American Society for Gastrointestinal Endoscopy, 2006a). Besides sporadic adenomatous polyps that develop as a result of diet and lifestyle factors, 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).

The role of diet in the aetiology of CRC remains an area of active investigation. Of all the food groups studied, plant-based diets are constantly associated with decreased risk of colorectal neoplasia. Intakes of fruits and grain appear to be inversely related to risk of CRC and polyps although less consistent evidence has been observed for vegetables (Pecipans & Sandler, 1994). Similarly, a recent study by Michels *et al.,* 2006 found that frequent consumption of fruits was inversely related to the risk of being diagnosed with polyps, while little association was found for vegetable consumption. The authors also found legumes to be protective of colorectal adenomas (CRA). These potentially protective associations may have resulted from the high levels of dietary fibber, antioxidants and other phytochemicals in plant foods.

Micronutrients found in plant-based food have been linked to the protective effect of these foods against the development of CRA. Of all the micronutrients found in fruits and vegetables, folate, calcium and several antioxidant vitamins have been the main focus of interest (Tseng *et al.,* 1994). Antioxidant vitamins such as vitamin A, carotenoids, vitamin E and vitamin C are strong free-radical quenchers and have the ability to reduce oxidative damage to DNA (Noguchi & Niki, 1999). However, epidemiological evidence on the dietary intakes of these vitamins and minerals have been inconsistent in many recent studies and therefore warrant further investigation (Grau *et. al.*, 2003; Senesse *et al.,* 2005).

CRAs have been regularly, but not always significantly, found to be related to various lifestyle behaviours such as physical activity, tobacco smoking, alcohol consumption, as well as overweight and obesity. Therefore this study was conducted to examine the relative contribution of dietary and lifestyle factors to the occurrence of polyps in Malaysian subjects. Identification of these factors may help in the initiation of dietary and lifestyle education for behavioural change in people with polyps which in turn may arrest the development of CRC.

1.2 The problem statement

Most colorectal cancers arise from pre-existing adenomatous polyps or adenomas. Although true incidence of colorectal adenomas are difficult to be calculated, Midgley and Kerr (1999) estimated its' prevalence to be about 35% in Europe and USA, and between 10 – 15% in Asia and Africa. No Malaysian figure is available to this date. However verbal information obtained from the experts in the field of colorectal cancer revealed that the figure may be between 10% and 20%. About five percent to ten percent of adenomatous polyps are estimated to become malignant, a process that takes five to ten years (ASGE, 2006a).

The other common type of polyp is hyperplastic polyps which are non-precancerous or benign. Although all polyps will be removed during colonoscopy, people with history of having these adenomas have as much as 50% chance of developing polyps again usually within three years of diagnosis. This makes colorectal adenomas a vital risk factor for colorectal cancer.

Active investigations have been identifying the risk factors for CRA, which have been complied and presented in Figure 1.1. Although the exact association is still unclear, dietary factors such as various food items/food groups such as dietary fat (Mathew *et al.*, 2004), fruits and vegetables especially carotenoids vegetables, cruciferous vegetables, high vitamin C fruits (Witte *et al.*, 1995) and red meat (Breuer-Katschinski *et al.,* 2001a); nutrients such as antioxidant vitamins (Enger *et al.*,1996 and Lubin *et al.,* 1997), vitamin D (Platz *et. al.,* 2000 and Peters *et. al.,* 2004), calcium (Grau *et. al.*, 2003) and folate (Benito *et. al.,* 1993); high temperature cooking techniques especially cooking of red meat in high temperature (Sinha *et al.,* 1999), and unfavourable lipid profile (Park *et al.,* 2000) have been associated with the risk.

Besides dietary factors, lifestyle habits such as tobacco smoking (Larsen *et al.,* 2006 and Almendingen *et al.,* 2000), alcohol consumption (Todoroki *et al.,* 1995 and Bardou *et al.*, 2002) and physical inactivity (Hauret *et al.,* 2004 and Enger *et al.*, 1997) also have been shown to increase the risk for CRA, although there are studies which have shown insignificant relationships (Boutron–Rault *et al.,* 2001). Physical factors such as anthropometrical measurements (Giovannuci *et al.,* 1995 and Morimoto *et al.,* 2002), body composition (Almendingen *et al.* 2001), and blood pressure are factors that have least evidences linking them to the risk for CRA. No documented evidence available on Malaysian population, although Rajendra *et al.* (2005) have tried to explore general risk factors associated with CRA. They found significant increase in the risk for CRA with age and family history of CRC. This study on the other hand, actively investigates the relationship between several dietary and lifestyle risk factors for CRA.

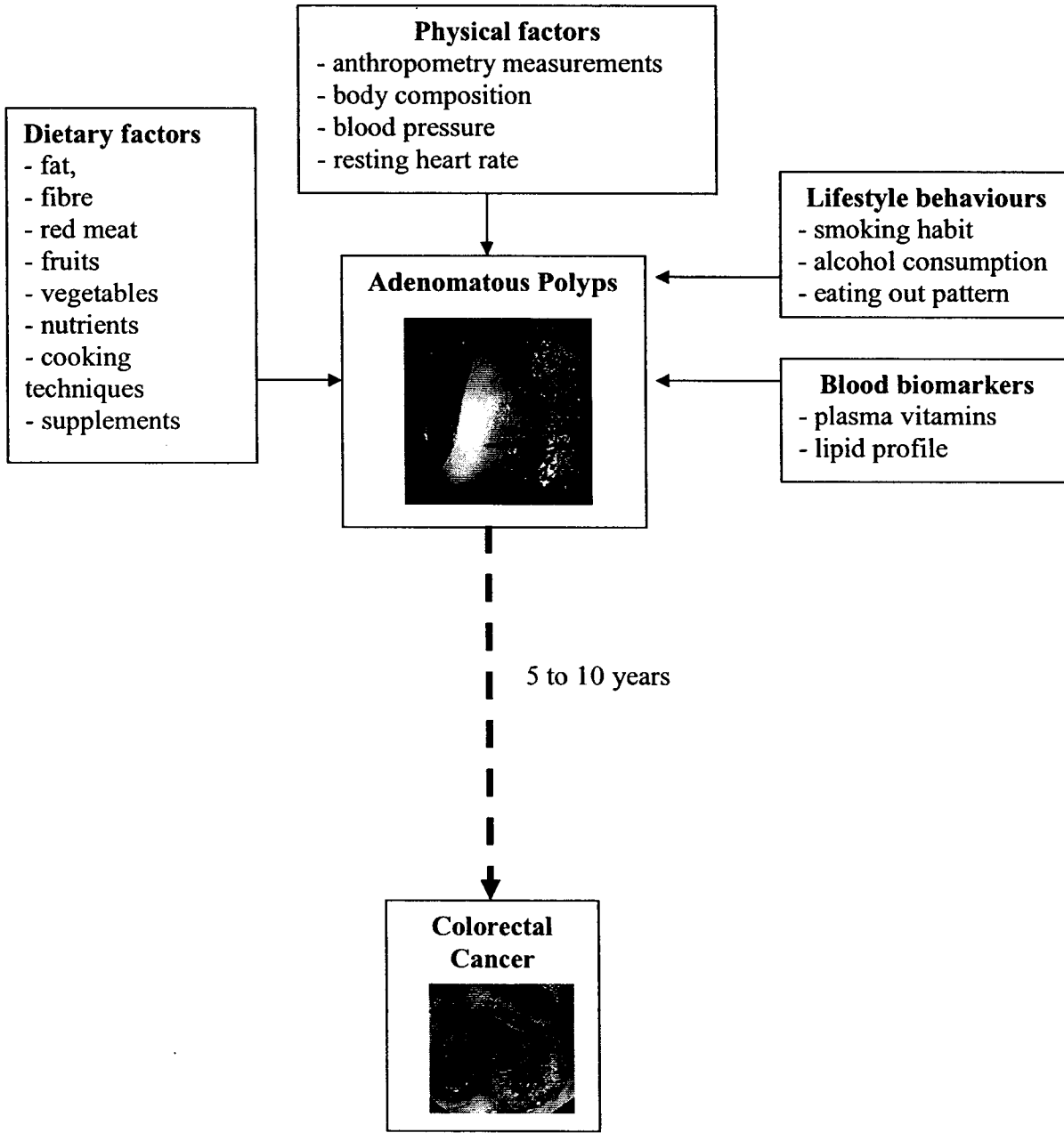

Figure 1.1: The conceptual framework - behavioural factors which will be investigated for its association with colorectal adenomas.