

## RESEARCH COMMUNICATION

# Roles of Diet, Lifetime Physical Activity and Oxidative DNA Damage in the Occurrence of Prostate Cancer among Men in Klang Valley, Malaysia

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### Abstract

**Background:** There is a paucity of information on risk factors of prostate cancer, especially those related to dietary and lifestyle among Asian populations. **Objective:** This study aimed to determine the relationship between dietary intake (macronutrients, fruits, vegetables and lycopene), lifetime physical activity and oxidative DNA damage with prostate cancer. **Design:** A case control study was carried out among 105 subjects (case n=35, control n=70), matched for age and ethnicity. Data on sociodemographic, medical, dietary intake, consumption of lycopene rich food and lifetime physical activity were obtained through an interview based questionnaire. Anthropometric measurements including weight, height and waist hip circumferences were also carried out on subjects. A total of 3mL fasting venous blood was drawn to assess lymphocyte oxidative DNA damage using the alkaline comet assay. **Results:** Cases had a significantly higher intake of fat (27.7±5.5%) as compared to controls (25.1±5.9%) (p < 0.05). Mean intakes of fruits and vegetables (3.11 ± 1.01 servings/d)(p<0.05), fruits (1.23 ± 0.59 servings/d) (p<0.05) and vegetables (1.97±0.94 servings/d) were higher in controls than cases (2.53 ± 1.01, 0.91 ± 0.69, 1.62 ± 0.82 servings/d). A total of 71% of cases did not met the recommendation of a minimum of three servings of fruits and vegetables daily, as compared to 34% of controls (p<0.05) (Adjusted OR 6.52 (95% CI 2.3-17.8)) (p<0.05). Estimated lycopene intake among cases (2,339 + 1,312 mcg/d) were lower than controls (3881 ± 3120mcg/d) (p < 0.01). Estimated lycopene intake of less than 2,498 mcg/day (50th percentile) increased risk of prostate cancer by double [Adjusted OR 2.5 (95% CI 0.99-6.31)]. Intake of tomatoes, watermelon, guava, pomelo, papaya, mango, oranges, dragon fruit, carrot, tomato sauce and barbeque sauce were higher in controls compared to cases. Intake of tomato sauce of more than 2.24g/d (25th percentile), papaya more than 22.7g/d (50th percentile) and oranges more than 19.1g/h (50th percentile) reduced prostate cancer risk by 7.4 (Adjusted OR 7.4 (95% CI 1.17-46.77)), 2.7 (Adjusted OR 2.75 (95% CI 1.03-7.39)) and 2.6 times (Adjusted OR = 2.6 (95% CI=1.01-6.67)), respectively (p<0.05 for all parameters). No oxidative damage was observed among subjects. Past history of not engaging with any physical activities at the age of 45 to 54 years old increased risk of prostate cancer by approximately three folds (Adjusted OR 2.9(95% CI = 0.8-10.8)) (p < 0.05). In conclusion, low fat diet, high intake of fruits, vegetables and lycopene rich foods and being physical active at middle age were found to be protective. Thus, it is essential for Malaysian men to consume adequate fruits and vegetables, reduce fat intake and engage in physical activity in order to reduce prostate cancer risk.

**Keywords:** Prostate cancer - food intake - physical activity - oxidative DNA damage - Lycopene

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### Introduction

Prostate cancer represents the second common cancer in men (after lung cancer) in both the United Kingdom and European Union and is the most common cancer in men in the United States. With over 20,000 new cases distinguished in the United Kingdom every year (and 134,000 in Europe), the cancer has an important effect on the national health (Bowsher & Carter 2006). In Malaysia,

there was a total of 735 cases of prostate cancer in 2006, making it the fourth most common cancer among man after colorectal, lung and nasopharync cancer. It was found to be the highest among the Indians (13.7 per 100,000) followed by Chinese (11.5 per 100,000) and Malays (9.2 per 100,000) (NCR, 2006). The cause of prostate cancer was largely unknown (Kolonel et al., 2000). Nutritional epidemiology of prostate cancer have been intensively studied because diet appears to be the only composite

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factor that could explain the striking international variability in the incidence of clinical prostate cancer and the mortality from this disease (Kolonel et al., 2000). Mediterranean diet, which is rich in vegetables and fruits, including tomatoes, has been suggested to be responsible for the lower cancer rates in that region (La Vecchia, 1997). These observations support the evidence that diets rich in fruits and vegetables are associated with a reduced risk of numerous chronic diseases.

Oxidative DNA damage might also play an important role in the process of carcinogenesis (Valko et al., 2006). At high concentration, reactive oxygen species were important mediators to the damage of cell structures, nucleic acids, lipids and proteins (Valko et al., 2006). Due to this, consumption of fruits and vegetables containing a mixture of natural antioxidant and phytochemical compounds are linked to the protection of biological system from the oxidative DNA damage and further reduced prostate cancer risk. The World Cancer Research Fund and the American Institute for Cancer Research (WCRF/AICR, 2007) concluded that food containing lycopene, as well as selenium or food containing it, probably protect against prostate cancer. However, there are limited evidences of fatness especially at the abdominal, physical activity and energy intake with risk of prostate cancer (WCRF/AICR 2007). An inverse relationship between oxidative DNA damage with intake of total fruits, vegetables and lycopene and breast cancer risk has been reported (Suzana et al., 2008).

Physical activity may have an inverse association with prostate cancer risk, however, the epidemiologic evidence is currently inconsistent and the magnitude of the risk reduction observed was small (Jian et al. 2005). Another large cohort study in Washington State by Littman et al., (2006) reported that recreational physical activity was not associated with prostate cancer risk, except in subgroups defined by age, obesity and screening history.

Therefore, the aim of this study was to comprehensively investigate the association between diet, lifestyle, physical activity and oxidative DNA damage with prostate cancer risk among men in Klang Valley of Malaysia. This study also aimed to specifically evaluate the role of fruits, vegetables and consumption of lycopene rich food with of prostate cancer among Malaysian men.

## Materials and Methods

This is a case control comparative study on 35 prostate cancer patients (cases) and 70 healthy men (controls) conducted from March to December 2009 at Kuala Lumpur Hospital and Universiti Kebangsaan Malaysia Medical Centre in the area of Klang Valley of Malaysia. Cases were newly diagnosed prostate cancer patients (as diagnosed using biopsy), not at the fourth stage of prostate cancer, not undergoing chemotherapy or radiation, not severely stressed as determined using Hospital Anxiety and Depression Score test (HADS) (Montazeri et al., 2003) and age between 40 to 80 years old. Controls were patients with benign prostate hypertrophy (BPH) without past medical history of prostate cancer, not suffering from any unstable chronic diseases and age 40 to 80 years old.

Cases and controls were matched according to age ( $\pm 5$  years) and ethnicity. Sample size was calculated with 95% confidence interval and 80% study power following the method of Sample Size Determination in Health Studies (Lwanga & Lemeshow 1991).

Socio-demographic data, health status and medical history, diet history, fruits and vegetables intake and lifetime physical activity were obtained through interview based questionnaire. In addition, anthropometric measurements including weight, height, waist and hip circumferences were also carried out on subjects. In a subsample of 76 subjects, a total of 3 mL fasting venous blood sample was collected using heparinized tube for genotoxicity analysis using the Alkaline Comet Assay. The study has been approved by the Research and Medical Research Ethical Committee of the Universiti Kebangsaan Malaysia and Ministry of Health of Malaysia. Written informed consent has been obtained from subjects.

### Dietary assessment

Food intake was assessed through a face-to-face interview using a validated Diet History Questionnaire (DHQ). Estimated lycopene intake was obtained using a semiquantitative food frequency questionnaire (FFQ) consists of 13 vegetables and fruits that are high in lycopene (Charoensiri et al., 2009) commonly consumed by the Malaysian population. Cases were requested to report their eating habits before diagnosis. The interview using DHQ included details for every meal or snack through the use of open-structured questions. With respect to the FFQ, pictures of fruits and vegetables were shown to the subjects to help in portion size estimation. Participants were asked to describe the frequency of consuming a particular food per day, per week, per month or per year over the past one year. Nutrient was analyzed using the Food Works (2007) software based on the Malaysian Food Composition Table (Tee et al., 1997) for calories, fat, protein, carbohydrate, vitamin A, and C and  $\beta$ -carotene. For estimation of lycopene intake, composition from Charoensiri et al., (2009) and USDA food database (USDA, 2003) were used. Fruits and vegetables consumed were quantified according to the Atlas of Food Exchanges & Portion Sizes (Suzana et al., 2009). One serving of vegetables is equal to half cup of cooked dark green vegetables with edible stem, root or sweet potatoes. Whilst one serving of fruits equal to half cup or half medium size guava, one slice papaya, watermelon and one medium banana, orange or apple.

### Anthropometric measurements

Anthropometric measurements including weight, height, waist and hip circumferences were carried out on subjects. The weight and height of subjects were measured by a calibrated TANITA digital scale (TANITA, Japan) and a portable stadiometer (Leicester height measure, Germany) to the nearest 0.1 kg and 0.1 cm, respectively. Measuring tape (Rockton, USA) was used to measure waist and hip circumferences to the nearest decimal.

### Physical activity

The short version of the International Physical Activity

Questionnaire (IPAQ) was used to assess physical activity level. The IPAQ classifies physical activity level into three categories which are low, moderate and high. In this study, moderate and high physical activity were combined into one category (high) (International Physical Activity Questionnaire Committee 2005). Whilst, the lifetime physical activity questionnaire modified from the Breast Cancer Comprehensive Questionnaire (University Temple, 1998) was used to assess physical activity pattern.

#### Alkaline Comet Assay

The alkaline comet assay was conducted in this study to determine oxidative DNA damage. This method was modified according to the method previously described (Singh et al., 1988). All of the steps were performed in the dark. A total of 100  $\mu$ l 0.6% normal melting point (NMA) agarose was spread on top of each frosted slides. The slides were immediately covered with cover slips and kept at room temperature for 5 minutes to allow the agarose gel to solidify. Fresh whole blood of 10  $\mu$ l was mixed with 80  $\mu$ l of low melting point (LMA) agarose to form a suspension. The cover slips were gently removed and the suspension was gently pipetted onto the first layer of agarose, then covered with cover slips again and kept on ice for 5 minutes to solidify. After removal of the cover slips, the slides were immersed in cold lysing solution (2.5M NaCl, 10  $\mu$ M Na2EDTA, 10mM Tris, pH 10) with Triton X-100 and 10% DMSO prepared one hour before used. After one hour, the slides were removed from the lysing solution, drained and placed in electrophoresis tank. Electrophoresis tank was then filled with freshly prepared electrophoresis solution (1mM Na2EDTA and 10N NaOH, pH 13) to cover all slides. Before electrophoresis, the slides were left in the solution for 20 minutes to allow unwinding of DNA double helix. Electrophoresis was conducted at 25 volt, 300 mA, and 20 minutes. After electrophoresis, the slides were taken out of the tank and neutralized using neutralizing buffer (0.4M Tris, pH 7.5) for 5 minutes and repeated three times. Onto each slide, 35  $\mu$ l ethidium bromide (EtBr 10  $\mu$ g/ml) was added and covered with a cover slip. All slides were placed in a humidified airtight container to prevent drying of the gel and analyzed the very next day. A total of 100 cells were captured by Leica Leitz Laborlux S, Germany and analyzed by Comet Score™.

#### Statistical Methods

Statistical tests were conducted using Statistical Packages for Social Sciences (SPSS) Version 16.0. Descriptive data were presented as mean and percentage between cases and controls. In order to investigate the difference of lymphocyte oxidative DNA damage, macronutrients, fruits and vegetables and lycopene intake and physical activity level, Independent Sample t-test were used. Chi squared test was used to analyze categorical data. The relationship between oxidative DNA damage and consumption of fruits and vegetables and lycopene was analyzed using Pearson Correlation Coefficient. Adjusted odd ratio was analyzed using binary logistic regression with age, ethnic, family history of cancer and energy intake as confounding factors or covariates.

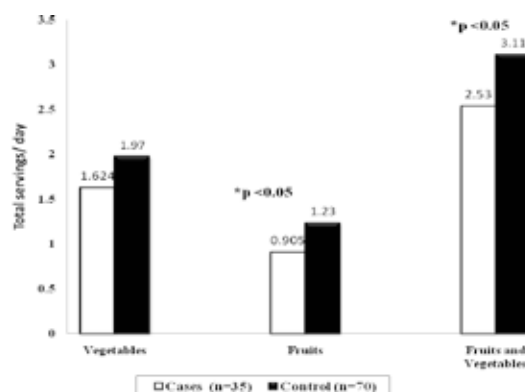
**Table 1. Socio-demographic and Health-related Characteristics of Cases and Controls**

Characteristic	Cases (%)		Controls (%)		P value
	n = 35	n = 70	n = 35	n = 70	
Age group	<60 years	3	4		0.59
	$\geq$ 60 years	97	96		
Race	Malay	38	38		
	Chinese	51	51		
	Indian	11	11		
Marital status	Single	3	6		0.072
	Married	97	94		
Family history of prostate cancer	Yes	27	23		0.62
	No	73	77		
Education level	Lower	60	42		0.06
	Higher	40	58		
Waist circumference	$\geq$ 90 cm	53	64		0.28
	< 90cm	47	36		
Waist Hip Ratio	$\geq$ 0.95	38	52		0.18
	< 0.95	62	48		
Ever use tobacco	Yes	68	53		0.12
	No	32	47		
Alcohol intake	Yes	14	17		0.71
	No	86	83		
Body Mass Index		23.8 $\pm$ 3.3	25.8 $\pm$ 3.9		0.01*
Waist Hip Ratio		0.95 $\pm$ 0.1	0.95 $\pm$ 0.1		
Education, years		8.2 $\pm$ 5.2	9.2 $\pm$ 4.0		0.28

% values; \*p < 0.05, Independent sample t-test

## Results

One hundred and five men aged 40 to 80 years, consisted of 35 prostate cancer patients and 70 controls participated in this study. The ethnic composition of both cases and controls was 38% Malays, 51% Chinese and 11% Indians as shown in Table 1. The mean age of cases (67.63  $\pm$  4.72 years) was comparable with controls (67.76  $\pm$  4.58 years). The mean body weight of cases and controls were 65.0  $\pm$  10.9kg and 69.5  $\pm$  10.5kg, respectively; height 164.6  $\pm$  5 cm and 163.8  $\pm$  5.7 cm. Mean BMI in cases (23.8  $\pm$  3.28kg/m<sup>2</sup>) was lower than controls (25.8  $\pm$  3.94kg/m<sup>2</sup>) (p < 0.05) (Table 1). The mean energy intake for cases (1620  $\pm$  252 kcal/day) were not significantly different as compared to controls (1614  $\pm$  296 kcal/day). However, energy intake from fat were significantly higher among cases (27.7 $\pm$ 5.5 %) compared to controls (25.1 $\pm$ 5.9 %) (p<0.05) (Table 2).



**Figure 1. Mean ( $\pm$  SD) Servings of Fruits and Vegetables Consumed among Cases and Controls. p < 0.05, Independent sample t-test**

**Table 2. Macronutrient Intake and Energy Percentage from Macronutrients**

Characteristic	Cases (35)	Controls (70)	P value
Energy (kcal/day)	1620 ± 252	1614 ± 296	0.912
Carbohydrate (g/day)	228.9 ± 54.3	237.7 ± 53.6	0.434
Energy from C (%)	56.0±7.6	58.8±7.1	0.064
Protein (g/day)	64.2 ± 13.9	63.0 ± 14.	0.682
Energy from Protein (%)	16.0±3.7	15.7±2.8	0.612
Fat (g/day)	49.3 ± 9.6	45.0 ± 13.1	0.092
Energy from fat (%)	27.7±5.5	25.1±5.9	0.032*

mean±SD values; \*p<0.05 using independent samples t-test

Figure 1 showed that the mean intake as expressed by serving size per day of fruits and vegetables (3.11 + 1.01 servings/d)(p<0.05), fruits (1.23 + 0.59 servings/d) (p<0.05) and vegetables (1.97+0.94 servings/d) were higher in controls than cases (2.53 + 1.01, 0.91 + 0.69, 1.62 + 0.82 servings/d). The Malaysian Dietary Guideline (NCCFN 1999) suggested that intake of fruits and vegetables of more than three serving per day, however, 71% of cases did not met the recommendation compared to only 34% of controls (p<0.05)[OR 4.79 (95% CI 1.9-11.59)]. It was found that subjects consumed at least three servings of fruits and vegetables a day have a reduced risk of prostate cancer up to 6.5 times [Adjusted OR 6.52 (95% CI 2.3-17.8)] (p<0.05).

The mean of lycopene intake among cases (2339 + 1312 mcg/d) were lower compared to controls (3881 + 3120mcg/d) (p< 0.01). Estimated lycopene intake of less than 2498 mcg/day (50th percentile) increased prostate cancer risk by double [Adjusted OR 2.5 (95%CI 0.99-6.31)]. As shown in Table 3, intake of tomatoes, watermelon, guava, pomelo, papaya (p<0.05), mango, oranges, dragon fruit, carrot, tomato sauce (p< 0.05) and barbeque sauce were higher in controls compared to cases(p<0.05). Intake of tomato sauce of more than 2.24g/d (25th percentile), papaya more than 22.7g/d (50th percentile) and oranges more than 19.1g/d (50th percentile) would reduce prostate cancer risk by 7.40 times [Adjusted OR 7.4 (95% CI 1.17-46.77)], 2.7 times [adjusted OR 2.75 (95% CI 1.03-7.39)] and 2.6 times [adjusted OR 2.6 (95% CI 1.01-6.67)].

DNA damage was analyzed in a subsample of 22 cases and 52 controls. The mean DNA damages expressed by

tail moment (TM ) (cases 1.85 ± 1.29, controls 1.78 ± 1.53) and % DNA damage (TD) (cases 1.56 ± 0.97%, controls 1.57 ± 1.31%) were lower than the references for oxidative stress (TM>5.0, % TD>10%)(%) (Olive et al 1990) indicating that there was no obvious oxidative stress among subjects. However, in cases subjects, lycopene intake was inversely correlated with DNA damage as expressed by TM (r = -0.43, p<0.05).

The mean of total MET min per week for physical activity in cases and controls were 1454.6±1939.9 and 1811.3±3526.5 minutes per week, respectively. With respect to physical activity throughout lifetime, vigorous physical activity category was combined with moderate physical activity to facilitate analysis. In this study, 83% of cases and 89% of controls have engaged in physical activity throughout lifetime, with controls were more active than cases. A significant association was noted for physical activity at the age of 45 to 54 years, with a higher percentage of cases (89%) compared to controls (69%) did not engage with any physical activity during the age category [Adjusted OR 2.9(95% CI =0.8-10.8)] (p<0.05)(Table 4). Among those engaged with physical activity during this age criteria, brisk walking was the most commonly reported activity.

## Discussion

In this study, a higher percentage of energy from fat was found to be associated with prostate cancer. Sources of fat intake among subjects in this study include animal sources and also cooking method (deep frying and usage of coconut milk). An early study by Giovannucci et al., (1993) reported that fat intake from animal sources was associated with the increase of prostate cancer risk. While in another study, energy derived from animal products, animal fat and non-fat milk has a weak correlation with fatal prostate cancer (Grant et al., 2004). However a study by Crowe et al., (2008) stated that there was no association between fat intakes with prostate cancer risk. Contradicting findings on studies on dietary intake might be due to the difficulties in estimating dietary intake especially in a case control study design such as this study.

This study also found that consumption of fruits and vegetables of less than three servings of fruits and

**Table 3. Mean (± SD) intake of types of fruits and vegetables frequently consumed among cases and controls**

Type of food	Case (n)	Serving/week	g/week	Control (n)	Serving/week	g/week	P value
Tomato	33	0.84 ± 0.76	54.6 ± 49.4	62	1.21 ± 1.91	78.6 ± 124.2	0.18
Watermelon	30	0.64 ± 0.60	21.1 ± 79.8	55	1.08 ± 1.62	143.6 ± 215.5	0.08
Guava	23	0.36 ± 0.35	114.5 ± 111.3	40	0.48 ± 0.85	152.6 ± 270.3	0.52
Pomelo	16	2.46 ± 4.95	95.9 ± 193.1	37	6.02 ± 14.17	234.8 ± 552.6	0.33
Papaya	33	1.23 ± 1.09	195.6 ± 173.3	65	2.44 ± 2.85	387.9 ± 453.2	0.01*
Mango	30	5.56 ± 7.8	822.9 ± 1154	53	6.26 ± 9.73	926.5 ± 1440	0.72
Orange	30	1.21 ± 1.53	102.9 ± 130.1	57	1.92 ± 2.23	163.2 ± 189.6	0.13
Apple	31	2.35 ± 3.62	263.2 ± 405.4	56	1.87 ± 1.97	209.4 ± 220.6	0.42
Dragonfruit	12	0.35 ± 0.31	42 ± 37.2	37	0.38 ± 0.61	45.6 ± 73.2	0.86
Carrot	26	1.54 ± 1.74	147.8 ± 167	57	1.64 ± 1.85	157.4 ± 177.6	0.80
Tomato Sauce	13	1.74 ± 1.78	31.3 ± 32.0	25	3.78 ± 3.75	68 ± 67.5	0.01*
Barbeque Sauce	5	1.03 ± 0.94	11.3 ± 10.3	6	1.17 ± 2.62	12.9 ± 28.8	0.92
Bake bean	14	2.38 ± 3.86	35.7 ± 57.9	24	1.05 ± 2.7	15.8 ± 40.5	0.23

\*p < 0.05, Independent sample t-test

**Table 4. Lifetime Vigorous/Moderate Physical Activity of Cancer Cases and Controls**

Activity	Cases (35)		Controls (70)		Crude OR (95% CI)	Adjusted OR <sup>b</sup> (95% CI)
	N	%	N	%		
Lifetime physical activity						
No	6	(17)	8	(11)	1.6 (0.5-5.0)	1.4 (0.37-5.6)
Yes	29	(83)	62	(89)	P=0.543	P=0.598
History of physical activity during high school						
No	9	(26)	19	(27)	0.9 (0.4-2.3)	0.8 (0.3-2.3)
Yes	26	(74)	51	(73)	P=0.876	P=0.710
History of physical activity 18-24 years old						
No	21	(60)	37	(53)	1.3 (0.6-3.0)	1.8 (0.7-4.8)
Yes	14	(40)	33	(47)	P=0.488	P=0.251
History of physical activity during 25-34 years old						
No	21	(60)	42	(60)	1.0 (0.4-2.3)	1.1 (0.4-3.0)
Yes	14	(40)	28	(40)	P=1.00	P=0.792
History of physical activity during 35-44 years old						
No	31	(89)	51	(73)	2.9 (0.9-9.3)	3.0 (0.8-11.1)
Yes	4	(11)	19	(27)	P=0.066	P=0.110
History of physical activity during 45-54 years old						
No	31	(89)	48	(69)	3.6 (1.1-11.3)	2.9 (0.8-10.8)
Yes	4	(11)	22	(31)	P=0.025*	P=0.114
History of physical activity during 55 years and above						
No	22	(63)	40	(57)	1.3 (0.6-2.9)	1.0 (0.4-2.7)
Yes	13	(37)	30	(43)	P=0.575	P=0.957

\*p<0.05 using chi-squared test; <sup>b</sup>Adjusted for confounding factors age, family history, education level, BMI and total energy intake per day

vegetables per day may increase risk of prostate cancer by 6.5 times. Similar observations were noted in other case control (Kolonel et al., 2000; Cohen et al., 2000) and cohort studies (Mills et al., 1989; Giovannucci et al., 1995). However, some other studies (Villeneuve et al., 1999; Hayes et al., 1999) did not found positive association between fruits and vegetables consumption with prostate cancer risk. Phytochemicals found in fruits and vegetables can affect the free radical damage processes by several mechanisms. Free radical damage which induces oxidative stress can cause DNA damage, which in turn can lead to base mutation, DNA cross-linking, and chromosomal breakage and rearrangement. This damage may be limited by dietary antioxidants in fruits and vegetables through modulation of detoxification enzymes, scavenging of oxidative agents, stimulation of the immune system, hormone metabolism, and regulation of gene expression in cell proliferation and apoptosis (Pool-Zobel et al., 1998; Singh et al., 1988). For example, tomatoes are high in lycopene that exert two times higher ability than  $\beta$ -carotene and one time higher than  $\alpha$ -tocopherol to quench singlet oxygen (Agarwal & Rao 2000). In this study lycopene intake in cases were inversely related to DNA damages.

In contrast to previous study among breast cancer women in Malaysia (Suzana et al., 2008), DNA oxidative damage did not differ between cases and controls probably due to the fact that the status of DNA damages in this study were lower than the cut of points of oxidative damages (TM>5.0, %DNA >10%) (Olive et al., 1990). Other studies have reported that oxidative stress was not a contributing factor for prostate cancer (Lockett et al., 2006). Discrepancy of findings in DNA damages may be

due to the selection of controls in this study. The controls were BPH patients, which is a form of chronic disease that may increase oxidative stress and DNA damages. It was reported that BPH patients with both decreased antioxidant enzyme activities and increased levels of DNA lesions might be at risk of developing prostate cancer (Olinski et al., 1995). However other study showed that oxidative damage was high in prostate cancer patients compared to BPH patients (Landers et al. 2005). Therefore, it is best to select controls from non BPH patient in future studies.

In this study, the classification of food that high in lycopene might deepened the horizon of study on prostate cancer. Estimated lycopene intake was higher among controls as compared to cases. It was also found that lycopene intake from papaya and tomato sauce were significantly higher in controls compared to cases (p<0.05). Other study found that consumption of 400 g/day papaya for two weeks increased antioxidant level in healthy male subjects (Rahmat et al., 2004). Thus, papaya and tomatoes are good source of lycopene for Malaysian men.

Physical activity is considered as a global health aspect that needs to be given special attention, however there is no standard method to evaluate physical activity. Therefore, international comparison and global surveillance is difficult (Booth 2000). In this retrospective case-control study, it appeared that the effect of past history of lifetime physical activity was more evident at the age group of 45 to 54 years old. These findings were comparable to a study by Le Marchand et al., (1991) which stratified the study population into men aged less than 70 years and 70 or more years and found no effect of physical activity at younger age but a 60 percent borderline significant increased risk of prostate cancer at older age. However, Villeneuve et al., (1999) reported decreased risk of prostate cancer among those who performed strenuous activity during early adulthood. Giovannucci et al., (1998) also observed a decreased risk associated with the highest level of physical activity among men with metastatic prostate cancer. Thus, physical activity may have a differential effect on prostate cancer risk dependent on numerous factors including age, stage of disease, and type and intensity of activity (Friedenreich et al., 2004). There is an underlying biologic rationale to support an etiologic role for physical activity in prostate carcinogenesis. At least four plausible mechanisms exist that might explain how activity influences prostate cancer risk. These mechanisms include alterations in endogenous hormones, energy balance, immune function, and antioxidant defense mechanisms. Men who were physically active may have lower endogenous androgen levels, decreased body fat, enhanced immune function, and better antioxidant defense mechanisms than inactive men (Freidenreich & Thune 2001). Thus, further studies aiming in investigating physical activity level and prostate cancer should also incorporate other biomarkers including androgen hormone, immune factor and antioxidant status. It should be noted that as in any case control design that assesses exposure after onset of disease, differential dietary recall between case and control participants could impose bias in this study.

In conclusion, this study suggested that low fat diet and consumption of fruits and vegetables of specific family groups and types and a total serving of more than three serving per day might protect against oxidative DNA damage and further reduced the risk of prostate cancer. Further larger population study need to be conducted to investigate the effects of dietary pattern, particularly low in fat and high in fruits, vegetables and lycopene in reducing prostate cancer risk.

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