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Abdominal Obesity Increased Breast Cancer Risk

RABETA MOHD SALLEH, SUZANA SHAHAR, FATIMAH ARSHAD,
AHMAD ROHI GHAZALI, NORMAH HARON & NOR FADILAH RAJAB

ABSTRAK

Kajian kes-kawalan ini dijalankan untuk mengkaji hubungan adipositi dan komposisi tubuh terhadap risiko kanser payudara di kalangan 70 orang wanita yang baru didiagnos kanser payudara dan 138 orang kawalan. Parameter antropometri yang merangkumi tinggi, berat, ukuran pinggang dan ukuran pinggul dan aras glukosa darah berpuasa serta tekanan darah diukur di kalangan subjek. Komposisi tubuh ditentukan menggunakan analisis bioimpedans (Maltron 906). Hasil kajian menunjukkan Indeks Jisim Tubuh (IJT) kumpulan kes adalah 26.0 ± 4.8 kg/m² dan 25.3 ± 4.5 kg/m² bagi kumpulan kawalan (p > 0.05). Seramai 71% subjek dari kumpulan kes dan 40% subjek kumpulan kawalan mengalami obesiti abdominal (ukurlilit pinggang ≥ 80 cm) [OR = 3.4 (95% CI =1.7-6.9] (p < 0.05). Wanita pra menopaus berisiko sebanyak empat kali untuk mendapat kanser payudara dengan [Adjusted OR = 4.3 (95% CI = 1.8-10.3)]. Peratus lemak tubuh adalah tinggi di kalangan kes (36.4 ± 4.7%) berbanding kawalan 35.3 ± 4.4% tetapi perbezaan ini adalah tidak signifikan. Jisim Tubuh Tanpa Lemak (JTTL) menunjukkan nilai min 38.8 ± 5.7 kg bagi kawalan dan 38.9 ± 5.5 kg pada kes. Korelasi positif yang lemah ditunjukkan di antara umur dan IJT (r = 0.179, p = 0.010), ukuran pinggang (r = 0.218, p = 0.002), nisbah pinggang-pinggul (NPP) (r = 0.233, p = 0.001) dan peratus lemak tubuh (r = 0.330, p = 0.000). Kesimpulannya, obesiti abdominal meningkatkan risiko kanser payudara, terutama di kalangan wanita pra menopaus. Obesiti jenis ini dan peratus lemak tubuh adalah meningkat dengan pertambahan usia. Adalah penting bagi wanita untuk mengekalkan ukuran pinggang yang sihat melalui gaya hidup sihat bagi mengurangkan risiko kanser payudara.

Kata kunci: Kanser payudara, obesiti abdominal, komposisi tubuh, kajian kes-kawalan

ABSTRACT

A case-control study was carried out to examine the association between adiposity and body composition with risk of breast cancer among 71 newly diagnosed breast cancer cases and 138 controls. Anthropometric parameters

included height, weight, waist and hip circumferences, fasting blood glucose and blood pressures were measured on the subjects. Body composition was measured using bioelectrical impedance analysis (Maltron BF906). Results showed that the mean body mass index (BMI) among cases were 26.0 ± 4.8 kg/m² and 25.3 ± 4.5 kg/m² for control group (p > 0.05). A total of 71% of the cases and 40% of the control had abdominal obesity (waist circumference ≥ 80 cm) [OR = 3.4 (95% CI = 1.7-6.9)] (p < 0.05). Pre menopausal women have four times higher risk [Adjusted odds ratio OR = 4.3 (95% CI = 1.8-10.3)]. Percent of body fat was slightly higher in cases (36.4 ± 4.7%) compared to controls (35.3 ± 4.4%) but the difference was not significant. The mean of fat free mass (FFM) in controls was 38.8 ± 5.7 kg and 38.9 ± 5.5 kg in cases. A weak positive correlation was shown between age and BMI (r = 0.179, p = 0.010), waist circumference (r = 0.218, p = 0.002), waist hip ratio (WHR) (r = 0.233, p = 0.001) and percent body fat (r = 0.330, p = 0.000). In conclusion, abdominal obesity increased breast cancer risk, especially among premenopausal women. This type of obesity and percentage of body fat was also found to increase with age. It is essential for women to maintain a normal waist line through healthy lifestyle in order to reduce breast cancer risk.

Key words: Breast cancer, abdominal obesity body composition, case-control study

INTRODUCTION

In year 2000, 3825 new cases of breast cancer were reported in Malaysia and deaths from the disease were 1707 (Abdullah & Yip 2003). In 2003, there were 3738 breast cancer cases that were reported, making it the most commonly diagnosed cancer in women and accounted for 31.0% of newly diagnosed cancer cases (Second Report of the National Cancer Registry 2004). One in 16 Chinese women, 1 in 16 Indian women and 1 in 28 Malay women will develop breast cancer in her lifetime (Yip 2006).

Breast cancer causes personal, family and socio-economics burden and impose added cost on health (Hejar et al. 2004). Although the management of breast cancer worldwide has evolved with many fundamental changes toward breast conservation and minimally invasive breast surgery, among the Malaysian population application of the new approaches has been impeded by the advanced presentation of breast cancer and not the least, by the social-cultural perception of the disease (Abdullah & Yip 2003).

Data from WHO's Global Database on Obesity and Body Mass Index in Adults from 1999-2000, showed that the global prevalence of obesity (BMI ≥ 30 kg/m²) was 8.7% (Florentino 2002). The Malaysian Second National Health Morbidity Survey data in year 1996 revealed that in adults, 20.7% were overweight and 5.8% obese (Lim et al. 2000). The prevalence of pre-obesity and obesity

among women was higher than men for every age group (Khor et al. 1999). Human obesity has also been recognized as one of major risk factors in cancer. A growing number of epidemiologic literature has investigated the association between behavioral and lifestyle variables and breast cancer (Lemon et al. 2004). Previous studies showed that, even after adjustment for other risk factors, overweight people have a greater risk (about one and a half times) of developing cancer than those of normal weight in both genders (Lee et al. 2002). Increased body mass index (BMI) was protective in pre menopausal women [OR = 0.4, CI (0.2-0.6)], but not in postmenopausal women, for whom it is a risk factor for cancer [OR = 1.5 CI (1.0-2.3)] (Tailoli et al. 1995).

In recent years, bioelectrical impedance (BIA) has become an increasingly popular modality in the assessment of body composition and the acceptance of the technique has been related partly due to the ease of use of the equipment (Andrew & Nuala 1998). Impedance measurements are extremely simple, rapid, safe and portable, they are potentially useful in epidemiologic settings (Willet 1998). The use of fat-free mass (FFM) and body fat mass (BFM) allows the tracking of the effects of illness, treatment, or aging in individuals and groups because they can be interpreted as absolute values or by classifying individuals or groups of individuals as normal or abnormal (low and high) (Kyle et al. 2003).

Little information exists regarding factors that are associated with breast cancer in Asian women (Norsa'adah et al. 2005). Previous case-control studies in Malaysia had investigated the association between dietary fibre and cancer (Suzana et al. 2004), breast cancer and lifestyle risks among Chinese women (Hejar et al. 2004) and also among women in Klang Valley (Rozanim et al. 2006). However, a specific study investigating adiposity and body composition using BIA method on breast cancer risk is scarce. Therefore, this study was done to examine the effect of body composition on risk of breast cancer.

MATERIALS AND METHODS

This is a retrospective case-control study involving pathologically confirmed newly diagnosed breast cancer cases in Klang Valley, with 80% study power to investigate between adiposity and body composition with breast cancer risk. Sample size was calculated by Power and Sample Size Program versi 2.1.31. The cases were outpatients and inpatients of Kuala Lumpur General Hospital, Hospital Universiti Kebangsaan Malaysia, Hospital Selayang and National Cancer Society from January 2005 until Jun 2006. Whereas, the controls matched with cases for age ± 5 years and menopause status were volunteers recruited using convenience sampling from National Cancer Society, Dewan Bandaraya Kuala Lumpur Jalan Raja Laut, Universiti Kebangsaan Malaysia, Universiti Putra Malaysia, China Press, Ho Association Jalan Ipoh, Taman Bukit Ampang and Section 5 Bandar Baru Bangi. This study has obtained ethical approval from the Ministry of Health

of Malaysia [KKM/JEPP/Jld. 11 (148)] and Hospital Universiti Kebangsaan Malaysia (UKM 1.5.3.5/244/PPP2). Informed consent was also obtained from the subjects. The study was conducted from January 2005 till June 2006.

The inclusion criteria for cases were newly diagnosed breast cancer (Stage I to III) who had not undergone any therapy for cancer, had no other chronic diseases such as hypertension and diabetes, good cognitive function, not pregnant or lactating, and not having menses for pre menopausal subjects. The control group comprised of women, who were healthy, had not been diagnosed with cancer and other chronic diseases, not pregnant or lactating, and not in menstruation at the time of data collection. Postmenopausal status was defined as the absence of menstrual bleeding for at least 12 months before participation in this study. Demographic data and health habits were obtained through a standardized pre-tested questionnaire by trained interviewers.

The weight and height of the subjects were measured by a calibrated TANITA HD-309 digital scale and a portable stadiometer (Leicester height measure) to the nearest 0.1 kg and 0.1 cm, respectively. During measurement, subjects were asked to remove their shoes and empty their pockets. Body mass index (BMI) was calculated based on the weight and height measurement. Measuring tape (Figure Finder Novel Products Rockton, IL USA) was used to measure waist and hip circumferences to the nearest decimal in standing condition. Waist to hip ratio (WHR) was calculated. Fasting blood glucose from venous blood was measured by a glucometer (Accu-Chek Advantage III) while blood pressure was assessed using BP Set (OMRON Model T5) for screening.

Body composition was measured by bioelectrical impedance analysis (BIA) namely Maltron BF 906 (Maltron International Ltd. Essex, UK) in weight-stable subjects. The measurements were taken from right side of the body, in supine position on non-conductive surface in a normal ambient temperature. Subjects were instructed to fast for at least 8 hours prior to measurement. BIA measurements should not be performed within several hours of moderate-to-strenuous exercises and the dehydration associated with physical activity should be completely corrected before the measurements are taken (National Institutes of Health Technology Assessment Conference Statement).

Data was analyzed using SPSS software version 12.0. Independent samples t-test was used to compare means of all variables measured. Bivariate correlations with two-tailed test of significance using Pearson coefficients were done to compare between two variables. The *p* value less than 0.05 were considered as statistically significant. Chi-squared test was used to investigate associations between categorical variables. The Crude Odds Ratio (OR) was also calculated using 2 by 2 table, without adjusting for other risk factors. Multivariate analysis, ie. logistic regression was used to calculate Adjusted Odds Ratio by controlling for confounding factors.

RESULTS

A total of 75 eligible subjects were identified, however, five subjects refused to partipate (response rate 93.3%). This study involved 70 newly diagnosed breast cancer patients and matched with 150 controls for age and menopausal status. The mean age of cases and control were 47.1 ± 7.9 and 46.2 ± 6.5 years, respectively. The age ranged was 29 to 65 years. About 54 cases (76%) were in 40-59 years age group. Table 1 presents the socio-economic profile of the subjects according to group. The ethnic compositions of the cases were 61% Malays, 17% Chinese and 22% Indians. The ethnic composition of the controls were 57% Malays, 32% Chinese and 11% Indians. Out of 70 cases of breast cancer, it was observed that 10 (14%) of them were single or widowed. More than 96% of the subjects received formal education. It was found that most of the subjects were still working but the percentage of women who were not working in cases only about 8% lower than those who were still working. Monthly household income of most of the subjects ranged from RM1500-3000.

TABLE 1. Sociodemographic profile of cases and controls

Variables	Cases (N = 70)		Control (N = 138)	
	No	(%)	No	(%)
Race				
Malays	43	(61)	79	(57)
Chinese	12	(17)	44	(32)
Indian	15	(22)	15	(11)
Marital status				
Single/Widowed	10	(14)	20	(14)
Married	60	(86)	118	(86)
Educational status				
Not schooling	3	(4)	1	(1)
Primary school	25	(36)	18	(13)
Secondary school	32	(46)	87	(63)
Higher institution	10	(14)	32	(23)
Employment				
Yes	38	(54)	105	(76)
No	32	(46)	33	(24)
Monthly Household Income				
< 1,500	15	(21)	27	(19)
1500-3000	37	(53)	63	(46)
> 3000	18	(26)	48	(35)

Table 2 shows the lifestyle and non-diet factors and health status of the subjects that are associated with breast cancer risk. Only 4% of cases used to

consume alcohol and the differences between cases and control were not significant. As shown in Table 2, a total of 71% of the cases and 40% of the control had abdominal obesity (waist circumference ≥ 80 cm). Women with abdominal obesity revealed four times higher risk [OR 3.8 (95% CI = 2.0-7.0)]. After adjusting for confounding variables (ie. Family history, alcohol, smoking and working status), the risk is still high [3.8 (95% CI = 2.0-7.3)] compared to those who were not ($p < 0.05$). Similar trend was noted for waist to hip ratio. High waist-to-hip ratio increased risk of breast cancer at 3.3 times [OR 3.3 (95% CI 1.8-6.1)] using univariate analysis. The adjusted odds ratio was 3.2 (95% CI 1.7-6.0). BMI more than 25 kg/m^2 did not appear to be the risk of breast cancer.

TABLE 2. Lifestyle and non-diet risk factors of breast cancer in cases and controls

Variables	Cases (N = 71) No	(%)	Control (N = 138) No	(%)	Crude OR	95% CI	p value
Smoking							
Yes	2	(3)	4	(3)	1.0	0.1-5.5	0.987
No	68	(97)	134	(97)			
Alcohol							
Yes	3	(4)	10	(7)	0.6	0.1-2.1	0.410
No	67	(96)	128	(93)			
Family history							
Yes	11	(16)	20	(14)	1.1	0.5-2.5	0.815
No	59	(84)	118	(86)			
Menstrual status							
Pre menopausal	49	(70)	93	(67)	0.9	0.5-1.7	0.703
Postmenopausal	21	(30)	45	(33)			
Waist classification							
More 80 cm	50	(71)	55	(40)	3.8	2.0-7.0	0.000*
Less 80 cm	20	(29)	83	(60)			
WHR							
More 0.85	37	(53)	35	(25)	3.3	1.8-6.1	0.000*
Less 0.85	33	(47)	103	(75)			
BMI							
More 25 kg/m^2	36	(52)	71	(51)	1.0	0.6-1.8	0.889
Less 25 kg/m^2	34	(48)	67	(49)			

*$p < 0.05$ using chi-squared test

Table 3 revealed that in both univariate (OR = 4.8, 95% CI = 2.3 to 10.1) and multivariate analysis (adjusted OR = 4.7, 95% CI = 2.2 to 10.1), pre menopausal women faced approximately four to five times risk of breast cancer if they had abdominal obesity as measured using waist circumference. The risk as measured using waist hip ratio was also noted in both pre-and postmenopausal women.

Table 4 shows that the mean ± SD of body composition profile in cases and controls and its correlation with age. It indicates that mean body mass index

TABLE 3. Crude odd ratio and adjusted odd ratio of waist classification relation to breast cancer risk in pre- and postmenopausal women

	Premenopause	N = 143	Postmenopause	N = 66
	Univariate analysis	Multivariate analysis#	Univariate analysis	Multivariate analysis#
Waist classification	OR = 4.8 95% CI = 2.3-10.1) P = 0.000*	OR = 4.7 95% CI = 2.2-10.1 P = 0.000*	OR = 2.8 95% CI = 0.8-9.8 P = 0.100	OR = 2.9 95% CI = 0.7-12.2 P = 0.161
Waist hip ratio	OR = 3.9 95% CI = 1.8-8.5) P = 0.000*	OR = 3.5 95% CI = 1.6-7.8 P = 0.002*	OR = 3.4 95% CI = 1.1-10.4 P = 0.031*	OR = 4.4 95% CI = 1.2-16.2 P = 0.026*

*$p < 0.05$ using chi-squared test
Multivariate analysis, adjusted for family history, smoking, alcohol and working status

TABLE 4. Mean ± SD of body composition profile in cases and controls and its correlation with age

Variables	Cases (N = 74) Mean ± SD	Controls (N = 136) Mean ± SD	r value	p value
BMI (kg/m^2)	26.0 ± 4.8	25.3 ± 4.5	0.179	0.010[b]
Waist circumference (cm)	86.0 ± 11.6	78.4 ± 10.4	0.218	0.002 [a,b]
WHR	0.9 ± 0.1	0.8 ± 0.1	0.233	0.001[a,b]
% Body fat	36.9 ± 5.3	35.3 ± 4.5	0.330	0.000[b]
FFM (kg)	38.9 ± 5.5	38.8 ± 5.7	0.044	0.527
% Total water	46.4 ± 3.7	47.3 ± 3.2	-0.284	0.000[b]

[a]Significant differences with $p < 0.05$ using independent samples t-test
[b]Significant differences with $p < 0.05$ using Pearson correlation

(BMI) among cases of 26.0 ± 4.8 kg/m^2 and controls of 25.3 ± 4.5 kg/m^2 was not statistically significant. There was a positive weak correlation of BMI with age ($r = 0.179$, $p = 0.010$). Whilst, the correlation of BMI with waist circumference was higher ($r = 0.798$, $p < 0.0001$). BMI values have been shown to indicate health risks and result in variations in body fat and fat-free mass (FFM). The mean of waist circumference of the cases (86.0 ± 11.6 cm) was higher than controls 78.4 ± 10.4 cm) ($p < 0.05$) (Table 4). Waist circumference was highest in Indian women compared to other ethnics (86.2 ± 11.8 cm). Malays had 81.4 ± 10.6 cm of waist circumference and Chinese 77.0 ± 11.6 cm. The WHR of cases was significantly higher (0.85 ± 0.1) as compared to control 0.80 ± 0.1 ($p < 0.05$). Body fat percent was higher in cases compared to control which is 36.4 ± 4.7% and 35.3 ± 4.5% but the difference in both group was not significant ($p > 0.05$). Body fat percent was

highest in Indian (38.4 ± 4.3%) followed by Malays (35.9 ± 4.3%) and Chinese (33.9 ± 4.2%). FFM assessment showed mean value of 38.8 ± 5.7 kg for control and 38.9 ± 5.5 kg for cases ($p > 0.05$). The mean of total body water was higher in control (47.4 ± 3.3%) than cases (46.1 ± 4.1%) ($p < 0.05$). A positive correlation was shown between age and waist circumference ($r = 0.218$, $p = 0.002$), WHR ($r = 0.233$, $p = 0.001$), percent body fat ($r = 0.330$, $p = 0.000$) and percent of total water ($r = -0.284$, $p = 0.000$).

DISCUSSION

The mean age of the cases (47 ± 7.9) and the findings that most of the cases were in the age range of 40 to 59 years were consistent with the figure reported in the Second Report of The National Cancer Registry in 2003 (2004), of which 64.1% of the cases diagnosed were in women between 40 and 60 years of age. In Malaysia, the mean age of breast cases was 48.1 years in Malays, 51.4 years in Chinese and 52.3 years in Indian (Yip et al. 2006). However, the ethnic compositions of the cases were not comparable to those reported by Second Report of the National Cancer Registry 2003 (2004). The case subjects in this study was mostly Malays (61%), whilst, the latter report indicated that Chinese had the highest incidence with age-standardized incidence rate (ASR) of 59.7 per 100,000 population followed by Indian women with an ASR of 55.8 per 100,000 population and Malay women with an ASR of 33.9 per 100,000 population. The dissimilarity in ethnic composition was probably because the cases were mostly recruited from the Kuala Lumpur General Hospital, the government hospital of which the patients were predominantly Malays.

Although this study has not find any association between family history, other studies had reported that family history constitutes the strongest known risk factor for development of breast cancer (Charpentier & Aldaz, 2002; Silvera et al. 2005). Therefore, this factor has been included as confounding factors, together with age at first pregnancy and working status in the multivariate analysis. No association between smoking and alcohol consumption and breast cancer risk was noted in this study probably due to the small number of smokers and alcohol drinker. Cigarette smoking has been suggested as a cause of breast cancer, but many studies addressing the relationship have yielded inconsistent results (Burton & Sulaiman 2000). A recent study has reported that the incidence of breast cancer among current smokers was slightly higher than that among non-smoker [OR 1.32 (95% CI = 1.10-1.57)] (Reynolds et al. 2004).

The proportion of storage fat in males and females is relatively constant being 12% of total body weight in males and 15% in females (Mirnalini et al. 2007). Relatively consistent findings about the relationships between body size and shape and breast cancer risk have been emerging in recent years. Women with abdominal obesity as assessed using waist circumference revealed four

times higher risk [OR 3.8 (95% CI = 2.0-7.0)]. After adjusting for confounding variables (ie. Family history, smoking, alcohol and working status), the risk is still high [3.8 (95% CI = 2.0-7.3)] compared to those who were not. Similar trend was noted for waist to hip ratio. High waist-to-hip ratio increased risk of breast cancer at 3.3 times [OR 3.3 (95% CI 1.8-6.1)] using univariate analysis and at 3.2 times [OR 3.2 (95% CI 1.7-6.0)] using multivariate analysis. Waist circumference remained strongly and directly associated with all-cause mortality when adjusted for total body fat in middle-aged men and women, suggesting that the increased mortality risk related to excess body fat is mainly due to abdominal adiposity (Bigaard et al. 2005). According to Bigaard et al. (2005), waist circumference accounted for the mortality risk associated with excess body fat and not fat-free mass, such as breast cancer in this present study. The mechanisms by which body weight effects breast cancer outcome probably involve a complex relationship between obesity, breast physiology and tumor biology (Rose et al. 2002).

Obesity is a worldwide problem which impacts on the risk and prognosis of some of the more common forms of cancer but also provides us with one of the few preventive interventions capable of making a significant impact on the cancer problem (Rose et al. 2004). BMI more than 25 kg/m^2 did not appear to be the risk of breast cancer. This result did not consistent with study done by Norsa'adah et al. (2005). They reported that overweight as assessed using high BMI ($\geq$ 25 kg/m^2) was one of the factors contributing towards increased risk of breast cancer (OR 2.1, 95% CI = 1.1-3.9). However, their study did not measure waist circumference. The discrepancy may be due differences in subjects characteristics and sample size.

This study also found that menopausal status is an important factor influencing the association between adiposity and the occurrence of breast cancer. In both univariate (OR = 4.8, 95% CI = 2.3 to 10.1) and multivariate analysis (adjusted OR = 4.7, 95% CI = 2.2 to 10.1), pre menopausal women faced approximately four to five times risk of breast cancer if they had abdominal obesity as measured using waist circumference. The risk as measured using waist hip ratio was also noted but only when the associate being investigated using univariate analysis. In the Western countries, it was reported that adiposity among the post menopausal women is a greater risk factor of breast cancer than their premenopausal counterpart (Tailoli et al. 1995). A major development has been the growing recognition of overweight as a risk factor for cancers of the colon, endometrium, kidney and, in postmenopausal women, of the breast (Riholi et al. 2002). The dissimilarity finding in this study compared to West was probably because the cases were mostly aged between 40-49 years old. Breast cancer in Malaysian women occurs more commonly in younger women, aged between 40 and 49 years, compared to the West, where the peak prevalence is in the 50-to-59-year-old age group (Abdullah & Yip 2004). This discrepancy may also be due to the generally short stature in this population compared to West that a higher

percentage of body fat especially at the abdominal may exist even though the BMI is not too high. Furthermore, it was reported that adiposity and the peak prevalence of increasing BMI among Malaysian women were below 60 years old in all ethnic group in Malaysia (Ismail et al. 2002).

The human body frequently been considered as two compartments: adipose (storage fat) and lean tissue (fat-free mass) (Willet 1998). This study revealed that cases had a higher waist circumference and waist hip ratio as compared to controls. Among cases their percentage of body fat was higher, lean body mass and total body water was lower than the controls. Indicators of obesity in this study were also found to be age associated.

The etiology of obesity involves a complex interaction of various factors, such as genetics, physical activity, diet, social, environment and health (Zalilah et al. 2006). The extent to which obesity reduces breast cancer survival because it impedes early detection, as opposed to it having a causal association with an aggressive, potentially highly metastasis, tumor phenotype, remains an unresolved issue (David et al. 2002). Other mechanisms may also account for the relationship between obesity and breast cancer risk (Charpentier & Aldaz, 2002). Obesity has a complicated relationship to both breast cancer risk and other established chronic diseases (Stephenson & Rose, 2003).

CONCLUSION

It is concluded that abdominal obesity was found to be associated with breast cancer risk, especially among premenopausal women. A stronger association between waist circumference and breast cancer risk was noted as compared to waist hip ratio. Maintaining a healthy waistline through healthy lifestyle may contribute to decreasing breast cancer risk.

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Rabeta Mohd Salleh
Suzana Shahar
Normah Haron
Department of Nutrition and Dietetics
Faculty of Allied Health Sciences
Universiti Kebangsaan Malaysia
Jalan Raja Muda Abdul Aziz
50300 Kuala Lumpur

Fatimah Arshad
International Medical University
No. 126, Jalan 19/155B,
Bukit Jalil 57000 Kuala Lumpur

Ahmad Rohi Ghazali
Nor Fadilah Rajab
Department of Biomedical Sciences
Faculty of Allied Health Sciences
Universiti Kebangsaan Malaysia
Jalan Raja Muda Abd. Aziz
50300 Kuala Lumpur