

The Study of Nutrition Pattern That Influences Risk of Colorectal Cancer in Thai Population

Watcharapol Khoonin, MSc¹, Bunchorn Siripongpreeda, MD²

¹ Nutrition Division, Chulabhorn Hospital, HRH Princess Chulabhorn College of Medical Science, Chulabhorn Royal Academy, Bangkok, Thailand

² Faculty of Medicine and Public Health, HRH Princess Chulabhorn College of Medical Science, Chulabhorn Royal Academy, Bangkok, Thailand

Background: A diet including vegetables and fruit is suggested to be a part of a healthy diet associated with a low colorectal cancer (CRC) risk. However, consumption of vegetables and fruit varies in daily life. Therefore, we determined whether the intake of vegetables and fruit is associated with the CRC risk in the Thai population.

Materials and Methods: This cross-sectional study enrolled participants (n=1,172) who underwent CRC screening and completed a food frequency questionnaire (FFQ). Information on food items, which focused on vegetables and fruit, was analyzed to elucidate the association with colonoscopy findings.

Results: Consumption of fresh fruit was related to a lower risk of CRC. Consuming sweet and mildly sweet fruits more than once a week revealed odds ratios (ORs) of 0.63 (0.43 to 0.92) and 0.63 (0.41 to 0.98), respectively, in patients with polyps and CRC. Conversely, processed canned fruit increased the risk with OR 4.68 (1.56 to 14.03) in the high risk group with CRC.

Conclusion: The protective benefits of vegetable and fruit involved appropriate food processing, consumption quantity, and frequency. The processing involved adding sugar and calories, which increased the risk of developing CRC.

Keywords: Colorectal cancer, Nutrition, Vegetable and fruit intake, Thai population

J Med Assoc Thai 2021;104(Suppl2): S61-7

Website: <http://www.jmatonline.com>

By 2030, the global burden of colorectal cancer (CRC) is expected to increase by 60%⁽¹⁾. The highest rate of CRC is found in developed countries, while developing countries such as Asia and Africa have relatively lower rates of CRC⁽²⁾. The reason might be a sedentary lifestyle, lack of physical activity, smoking, alcoholic drinking, high consumption of red and processed meats, and low consumption of whole grains, fiber, fruit, and vegetable⁽³⁾. In Thailand, CRC is the third leading cause of cancer-related deaths for both men and women. CRC is the third leading cause of cancer-related death in men and the fourth leading cause of cancer-related death in women⁽⁴⁾.

Regarding the factors, a diet that promotes inflammation appears to affect the risk of CRC⁽⁵⁾. A conventional diet with vegetable and fruit confers a low risk of CRC and because of anti-inflammatory effects⁽⁶⁾. Updated evidence of WCRF-AICR on food and beverages and

CRC risk found a significant association between fruit and vegetable intake of less than 300 g per day and elevated CRC risk^(7,8).

Studying CRC screening outcomes and diet information among Thai volunteers may elucidate an association. Thus, we determined whether intake of vegetable and fruit is associated with CRC risk.

Materials and Methods

Study participants

All participants were recruited from the colorectal screening program of Chulabhorn Hospital during July 2009 to June 2010. The volunteers in the present study were 50 to 65 years of age with no history of CRC. A total of 1,172 individuals had completed dietary data collection. The Ethical Committee of Human Research of Chulabhorn Hospital approved this study (EC No. 04/2556).

Diagnosis of CRC

Physicians performed colonoscopies for all subjects. The colonoscopic outcomes in each section were documented and evaluated for their risk of CRC. The pathology confirmed that all cases presented with abnormal mucosal findings. Cases were divided into malignant (CRC), high risk adenoma, low risk adenoma, and non-adenomatous polyps. Malignant cases were identified by staging using the Seventh edition of the Union for International Cancer Control TNM Classification of Malignant Tumours⁽⁹⁾. All CRC patients were treated in accordance with the NCCN Guidelines⁽¹⁰⁾.

Correspondence to:

Siripongpreeda B.

Faculty of Medicine and Public Health, HRH Princess Chulabhorn College of Medical Science, Chulabhorn Royal Academy, Bangkok 12120, Thailand.

Phone: +66-2-1054669

Email: bunchorn.sir@pccms.ac.th

How to cite this article:

Khoonin W, Siripongpreeda B. The Study of Nutrition Pattern That Influences Risk of Colorectal Cancer in Thai Population. J Med Assoc Thai 2021;104 (Suppl2): S61-7.

doi.org/10.35755/jmedassocthai.2021.S02.12603

Data collection

To assess dietary intake, we examined data obtained from a food frequency questionnaire (FFQ) used in a population-based cross-sectional study of the Thai population who enrolled in the colorectal screening project. The Human Research Ethical Committee of Chulabhorn Research Institute had approved the research protocol of the CRC screening and data collection. The participants acknowledged further analysis of their information with a multiple screening questionnaire including diet history.

Assessment of vegetable and fruit intake

The FFQ was adapted to the Thai population, which included 19 groups of food and beverages related to CRC risk⁽¹¹⁾. Food figures were available with printed figures illustrating the portion size of food in household units of a spoon, ladle, and cup. The questionnaire also asked to provide the frequency of each food item consumption. The participants were asked about food items in terms of quantity and average consumption frequency during the past 12 months. Trained field interviewers conducted all screening questionnaires at local hospitals upon appointments.

Odds ratios (ORs) with 95% confidence intervals (CIs) were used to determine associations between vegetable and fruit consumption and CRC risk. Statistical analysis was performed with STATA version 12.1. In our analyses, vegetable and fruit consumption was categorized into three groups: 1) ≤ 1 times/month; 2) ≥ 1 time/week; 3) 2 to 3 times/month. CRC risks were separately analyzed in four groups: 1) non-any polyp+CRC; 2) any polyp+CRC; 3) adenoma polyps+CRC; 4) high risk+CRC. Participants with high risk adenoma presented with one of the following colonoscopic and pathological criteria: ≥ 1 cm in size, ≥ 3 adenomas, or tubulovillous, villous adenoma or high grade dysplasia⁽¹⁰⁾. Logistic regression analysis was used to examine associations between vegetable and fruit consumption and CRC risk. Logistic regression analyses were conducted to compare different risk groups with each other. The following covariates were included in adjusted ORs: sex, age, BMI, first family history CRC, alcohol consumption, and smoking.

Results

Among the 1,404 participants who underwent a colonoscopy in the CRC screening program, 1,172 agreed to participate in this study. After allowance for sex, age, BMI, first family history of CRC, alcohol consumption, and smoking history, the demographics of participants are shown in Table 1. The selected food items were vegetable and fruit groups.

Among discordant cases, colorectal cancer risk was increased with an increase in consumption of raw green leafy vegetable at 2 to 3 times per month (OR for any polyps+CRC versus non-any polyps+CRC: 1.97; 95% CI: 1.11 to 3.50). The ORs were somewhat higher for participants with adenoma polyps+CRC (OR: 2.44; 95% CI: 1.31 to 4.52), and high risk group+CRC (OR: 5.39; 95% CI: 2.09 to

Table 1. Distribution of cases of CRC by sex, family history, alcohol consumption, smoking, and colonoscopic outcomes in terms of mean age and BMI

Variables	n	%
Sex		
Male	356	30.4
Female	816	69.6
Age (years)	62 \pm 4.3	
BMI (kg/m ²)	24.7 \pm 3.9	
Family history of CRC in a first-degree relative		
SAbsent	1,073	91.6
Present	99	8.4
Alcohol consumption		
None history of consumption	926	79.0
Former history of consumption	47	4.0
Occasionally	104	8.9
Actively	95	8.1
Smoking		
Non-smoker	1,033	88.1
Former history of smoking	103	8.8
Actively smoking	36	3.1
Colonoscopic outcomes		
CRC	3	0.26
High risk group	78	6.66
Low risk group	174	14.85
Hyperplastic polyp	155	13.23
Other	13	1.11
Normal	749	63.91

13.90). Findings were similar in terms of the additional consumption frequency of more than once a week (OR: 2.21; 95% CI: 1.10 to 4.42) (Table 2).

We categorized fresh fruit into sweet and mildly sweet of which both appeared to decrease the CRC risk. Sweet fresh fruits decreased risk by consuming at least once per week as shown by the OR of 0.63 (95% CI: 0.43 to 0.92) in the any polyps+CRC group, OR of 0.55 (95% CI: 0.36 to 0.84) in the adenoma polyps+CRC group, and OR of 0.43 (95% CI: 0.23 to 0.79) in the high risk group+CRC. Similarly, the OR of mildly sweet fruit was 0.63 (95% CI: 0.41 to 0.98) in the any polyps+CRC group and 0.59 (95% CI: 0.37 to 0.95) in the adenoma polyps+CRC group (Table 3).

A great concern was the possible elevated risk found in the processed fruit category. Patients with a high-risk+CRC had an OR of 3.63 (95% CI: 1.24 to 10.65) of consuming fermented fruit and OR of 4.68 (95% CI: 1.56 to 14.03) of sweet canned fruits when consumed 2 to 3 times per month (Table 4).

Table 2. Odds ratios (ORs) and 95% confidence intervals (CIs) of CRC risk by categories of vegetable

Food	Any polyps+CRC			Adenoma polyps+CRC			High risk group+CRC		
	Any polyps +CRC (n=423)	Non-any polyps+CRC (n=749)	Adjusted OR* (95% CI)	Adenoma polyps+CRC (n=255)	Non-adenoma polyps+CRC (n=917)	Adjusted OR* (95% CI)	High risk group+CRC (n=81)	Non-high risk group+CRC (n=1,091)	Adjusted OR* (95% CI)
Cooked green leafy vegetables									
≤1 time/month	13 (3.07)	25 (3.34)	Ref.	6 (2.35)	32 (3.49)	Ref.	2 (2.47)	36 (3.30)	Ref.
2 to 3 times/month	7 (1.65)	8 (1.07)	1.56 (0.45 to 5.44)	2 (0.78)	13 (1.42)	0.78 (0.13 to 4.48)	2 (2.47)	13 (1.19)	2.97 (0.35 to 24.83)
≥1 time/week	403 (95.27)	716 (95.59)	1.08 (0.53 to 2.18)	247 (96.86)	872 (95.09)	1.55 (0.62 to 3.85)	77 (95.06)	1,042 (95.51)	1.46 (0.32 to 6.63)
Raw green leafy vegetables									
≤1 time/month	102 (24.11)	203 (27.10)	Ref.	53 (20.78)	252 (27.48)	Ref.	10 (12.35)	295 (27.04)	Ref.
2 to 3 times/month	31 (7.33)	29 (3.87)	1.97 (1.11 to 3.50)	21 (8.24)	39 (4.25)	2.44 (1.31 to 4.52)	10 (12.35)	50 (4.58)	5.39 (2.09 to 13.90)
≥1 time/week	290 (68.56)	517 (69.03)	1.05 (0.79 to 1.40)	181 (70.98)	626 (68.27)	1.33 (0.94 to 1.88)	61 (75.31)	746 (68.38)	2.21 (1.10 to 4.42)

* Adjusted by sex, age, BMI, first family history of CRC, alcohol consumption, and smoking

Table 3. Odds ratios (ORs) and 95% confidence intervals (CIs) of CRC risk by categories of fresh fruit

Food	Any polyps+CRC			Adenoma polyps+CRC			High risk group+CRC		
	Any polyps +CRC (n=423)	Non-any polyps+CRC (n=749)	Adjusted OR* (95% CI)	Adenoma polyps+CRC (n=255)	Non-adenoma polyps+CRC (n=917)	Adjusted OR* (95% CI)	High risk group+CRC (n=81)	Non-high risk group+CRC (n=1,091)	Adjusted OR* (95% CI)
Sweet fruit e.g., rambutan, longan, ripen durian, ripen jackfruit, ripen mango, sapodilla plum, and pineapple									
≤1 time/month	61 (14.42)	70 (9.35)	Ref.	41 (16.08)	90 (16.08)	Ref.	17 (20.99)	114 (10.45)	Ref.
2 to 3 times/month	45 (10.64)	42 (5.61)	1.30 (0.74 to 2.28)	26 (10.20)	61 (6.65)	0.98 (0.54 to 1.79)	13 (16.05)	74 (6.78)	1.32 (0.58 to 3.01)
≥1 time/week	317 (74.94)	637 (85.05)	0.63 (0.43 to 0.92)	188 (73.73)	766 (83.53)	0.55 (0.36 to 0.84)	51 (62.96)	903 (82.77)	0.43 (0.23 to 0.79)
Mildly sweet fruit e.g., rose apple, guava, and watermelon									
≤1 time/month	45 (10.64)	49 (6.54)	Ref.	30 (11.79)	64 (6.98)	Ref.	10 (12.35)	84 (7.70)	Ref.
2 to 3 times/month	27 (6.38)	31 (4.14)	0.98 (0.50 to 1.92)	14 (5.49)	44 (4.80)	0.67 (0.31 to 1.43)	6 (7.41)	52 (4.77)	1.00 (0.33 to 3.04)
≥1 time/week	351 (82.98)	669 (89.32)	0.63 (0.41 to 0.98)	211 (82.75)	809 (88.22)	0.59 (0.37 to 0.95)	65 (80.25)	955 (87.53)	0.68 (0.33 to 1.40)

* Adjusted by sex, age, BMI, first family history CRC, alcohol consumption, and smoking

Table 4. Odds ratios (ORs) and 95% confidence intervals (CIs) of CRC risk by categories of processed vegetable and fruit

Food	Any polyps+CRC			Adenoma polyps+CRC			High risk group+CRC		
	Any polyps +CRC (n=423)	Non-any polyps+CRC (n=749)	Adjusted OR* (95% CI)	Adenoma polyps+CRC (n=255)	Non-adenoma polyps+CRC (n=917)	Adjusted OR* (95% CI)	High risk group+CRC (n=81)	Non-high risk group+CRC (n=1,091)	Adjusted OR* (95% CI)
Fermented fruit									
≤1 time/month	406 (95.98)	732 (97.73)	Ref.	244 (95.69)	894 (97.49)	Ref.	74 (91.36)	1,064 (97.53)	Ref.
2 to 3 times/month	11 (2.60)	9 (1.20)	1.49 (0.59 to 3.80)	9 (3.53)	11 (1.20)	2.19 (0.87 to 5.55)	6 (7.41)	14 (1.28)	3.63 (1.24 to 10.65)
≥1 time/week	6 (1.42)	8 (1.07)	0.98 (0.32 to 3.01)	2 (0.78)	12 (1.31)	0.41 (0.09 to 1.95)	1 (1.23)	13 (1.19)	0.55 (0.06 to 4.76)
Dried fruit									
≤1 time/month	408 (96.45)	724 (96.66)	Ref.	246 (96.47)	886 (96.62)	Ref.	75 (92.59)	1,057 (96.88)	Ref.
2 to 3 times/month	6 (1.42)	14 (1.87)	0.66 (0.24 to 1.79)	5 (1.96)	15 (1.64)	1.12 (0.40 to 3.17)	3 (3.70)	17 (1.56)	2.21 (0.60 to 8.14)
≥1 time/week	9 (2.13)	11 (1.47)	1.06 (0.42 to 2.69)	4 (1.57)	16 (1.74)	0.70 (0.22 to 2.17)	3 (3.70)	17 (1.56)	1.61 (0.44 to 5.96)
Sweet canned fruit									
≤1 time/month	409 (96.69)	734 (98.00)	Ref.	224 (95.69)	899 (98.04)	Ref.	74 (91.36)	1,069 (97.98)	Ref.
2 to 3 times/month	9 (2.13)	10 (1.34)	1.40 (0.55 to 3.57)	8 (3.14)	11 (1.20)	2.43 (0.95 to 6.19)	5 (6.17)	14 (1.28)	4.68 (1.56 to 14.03)
≥1 time/week	5 (1.18)	5 (0.67)	1.63 (0.46 to 5.76)	3 (1.18)	7 (0.76)	1.54 (0.39 to 6.08)	2 (2.47)	8 (0.73)	3.52 (0.71 to 17.49)

* Adjusted by sex, age, BMI, first family history CRC, alcohol consumption, and smoking

Discussion

Vegetable and fruit provide a natural source of fiber and lower inflammation in the bowel⁽¹²⁾. However, fresh produce can carry toxic substances such as pesticides. The effect of pesticides has a major role in CRC prevalence. A study of organochlorine pesticides in sera of 42 CRC patients compared with 30 healthy subjects revealed significantly higher malondialdehyde and total antioxidant capacity in the patient group than in the control group. The study concluded that higher levels of organochlorine pesticides in CRC patients along with hypermethylation of the p16 promoter gene corresponded to CRC initiation and development⁽¹³⁾. Therefore, consumption of fresh green leafy vegetable may include pesticides if the preparation process is insufficient. The residues of post-harvest insecticides can be removed by processing such as washing and heat treatment⁽¹⁴⁾. Proper washing with 12 L running tap water at for 3 minutes reduces in pesticide residue in green lettuce by 16.5% to 76.6%⁽¹⁵⁾. Even though the present study did not examine residual pesticides on local vegetable, it would be a great challenge to further study Thai agriculture to develop policy regarding food chain quality.

Consumption of fresh fruit did not increase CRC risk in all groups of colonoscopy outcomes. A contradictory effect was found in processed fruits as evidence by higher ODs. The reason may be additional ingredients and processing that enhance inflammation⁽¹⁶⁾. Added sugars such as sucrose and fructose to food is associated with all types of cancer initiation and progression⁽¹⁷⁾. Sucrose consisting of glucose and fructose affects cancer as evidenced by a significant increase in the activities of the enzymes related to inflammation⁽¹⁸⁾. Food processing often involves fructose rather than sucrose in the form of high fructose corn syrup with 42% to 90% of sugar⁽¹⁹⁾. Fructose is metabolized in a different manner to glucose in the liver and may have unique adverse effects on health as clinically evidenced by a fatty liver⁽²⁰⁾. Most reports on sugars and cancer have been case-control studies, which suggest that sugars incorporated in foods and beverages may be related to higher risks of some cancers⁽²¹⁻²³⁾. The World Cancer Research Fund and American Institute for Cancer Research's (AICR) Second Expert Report expressed limited suggestive due to epidemiological studies that fructose and sucrose were linked to the risk of colorectal cancer⁽²⁴⁾. The report suggested that sugary food and beverages result in obesity and accumulation of body fat, which are major contributors to inflammation⁽²⁵⁾. Therefore, receiving high amounts of sugar might play a role in obesity and local initiation of inflammation^(18,25).

Conclusion

Regular consumption of vegetable and fruit lowers the risk of developing CRC and its progression. The protective benefits of vegetable and fruit involve appropriate food handling processes and consumption quantity for the optimum nutritional requirement.

What is already known on this topic?

Fruit and vegetable are known for their health benefits to prevent CRC. Moreover, the carbohydrate contents in vegetable and fruits can be both simple and complex. Oligosaccharides and fiber in the form of soluble and insoluble fibers are potentially beneficial to the local intestinal environment. Consumption of excessive simple sugar can relate to elevated risk of noncommunicable disease including cancer.

What this study adds?

Raw green leafy vegetable intake may predispose to risk of colorectal polyp and cancer more than the cooked one. Fresh fruit intake had lower risk of advanced colorectal neoplasm than taking in chemically preserved form.

Acknowledgements

The present study was supported by HRH Princess Chulabhorn College of Medical Science, Chulabhorn Royal Academy Chulabhorn Royal Academy.

Potential conflicts of interest

The authors declare no conflict of interest.

References

1. Arnold M, Sierra MS, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global patterns and trends in colorectal cancer incidence and mortality. *Gut* 2017;66:683-91.
2. Favoriti P, Carbone G, Greco M, Pirozzi F, Pirozzi RE, Corcione F. Worldwide burden of colorectal cancer: a review. *Updates Surg* 2016;68:7-11.
3. Murphy N, Moreno V, Hughes DJ, Vodicka L, Vodicka P, Aglago EK, et al. Lifestyle and dietary environmental factors in colorectal cancer susceptibility. *Mol Aspects Med* 2019;69:2-9.
4. Virani S, Bilheem S, Chansaard W, Chitapanarux I, Daoprasert K, Khuanchana S, et al. National and subnational population-based incidence of cancer in Thailand: assessing cancers with the highest burdens. *Cancers (Basel)* 2017;9:108.
5. Keum N, Giovannucci E. Global burden of colorectal cancer: emerging trends, risk factors and prevention strategies. *Nat Rev Gastroenterol Hepatol* 2019;16:713-32.
6. Levi F, Pasche C, La Vecchia C, Lucchini F, Franceschi S. Food groups and colorectal cancer risk. *Br J Cancer* 1999;79:1283-7.
7. Makarem N, Lin Y, Bandera EV, Jacques PF, Parekh N. Concordance with World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) guidelines for cancer prevention and obesity-related cancer risk in the Framingham Offspring cohort (1991-2008). *Cancer Causes Control* 2015;26:277-86.
8. Norat T, Aune D, Chan D, Romaguera D. Fruit and vegetable: updating the epidemiologic evidence for the WCRF/AICR lifestyle recommendations for cancer prevention. In: Zappia V, Panico S, Russo GL, Budillon

- A, Ragione FD, editors. *Advances in nutrition and cancer*. Berlin, Heidelberg: Springer; 2014. p. 35-50.
9. Sobin LH, Gospodarowicz MK, Wittekind C. *Stomach*. In: Sobin LH, Gospodarowicz MK, Wittekind C, editors. *TNM classification of malignant tumours*. 7th ed. New York: Wiley-Blackwell; 2009. p. 73-7.
10. National Comprehensive Cancer Network. *NCCN Guidelines: Colorectal cancer, Version 1.2010*. Plymouth Meeting, PA: NCCN; 2010.
11. Sriamporn S, Parkin DM, Pisani P, Vatanasapt V, Suwanrungruang K, Kamsa-ard P, et al. A prospective study of diet, lifestyle, and genetic factors and the risk of cancer in Khon Kaen Province, northeast Thailand: description of the cohort. *Asian Pac J Cancer Prev* 2005;6:295-303.
12. Terry P, Giovannucci E, Michels KB, Bergkvist L, Hansen H, Holmberg L, et al. Fruit, vegetables, dietary fiber, and risk of colorectal cancer. *J Natl Cancer Inst* 2001;93:525-33.
13. Abolhassani M, Asadikaram G, Paydar P, Fallah H, Aghaee-Afshar M, Moazed V, et al. Organochlorine and organophosphorous pesticides may induce colorectal cancer; A case-control study. *Ecotoxicol Environ Saf* 2019;178:168-77.
14. Kaushik G, Satya S, Naik SN. Food processing a tool to pesticide residue dissipation—A review. *Food Res Int* 2009;42:26-40.
15. Kwon H, Kim TK, Hong SM, Kim CS, Baeck M, Kim DH, et al. Removal of pesticide residues in field-sprayed leafy vegetable by different washing method. *Korean J Pestic Sci* 2013;17:237-43.
16. Itzkowitz SH, Yio X. Inflammation and cancer IV. Colorectal cancer in inflammatory bowel disease: the role of inflammation. *Am J Physiol Gastrointest Liver Physiol* 2004;287:G7-17.
17. Franceschi S, Dal Maso L, Augustin L, Negri E, Parpinel M, Boyle P, et al. Dietary glycemic load and colorectal cancer risk. *Ann Oncol* 2001;12:173-8.
18. Das UN. Sucrose, fructose, glucose, and their link to metabolic syndrome and cancer. *Nutrition* 2015;31:249-57.
19. Wartman AM, Spawn TD, Eliason MA. Relationship between density, temperature and dry substance of commercial corn syrups, high-fructose corn syrups, and blends with sucrose and invert sugar. *J Agric Food Chem* 1984;32:971-4.
20. Le MT, Frye RF, Rivard CJ, Cheng J, McFann KK, Segal MS, et al. Effects of high-fructose corn syrup and sucrose on the pharmacokinetics of fructose and acute metabolic and hemodynamic responses in healthy subjects. *Metabolism* 2012;61:641-51.
21. Aune D, Chan DS, Lau R, Vieira R, Greenwood DC, Kampman E, et al. Carbohydrates, glycemic index, glycemic load, and colorectal cancer risk: a systematic review and meta-analysis of cohort studies. *Cancer Causes Control* 2012;23:521-35.
22. Key TJ, Spencer EA. Carbohydrates and cancer: an overview of the epidemiological evidence. *Eur J Clin Nutr* 2007;61 Suppl 1:S112-21.
23. Wang Z, Uchida K, Ohnaka K, Morita M, Toyomura K, Kono S, et al. Sugars, sucrose and colorectal cancer risk: the Fukuoka colorectal cancer study. *Scand J Gastroenterol* 2014;49:581-8.
24. World Cancer Research Fund and American Institute for Cancer Research. *Food, nutrition, physical activity and the prevention of cancer: A global perspective*. Washington, DC: AICR; 2007.
25. John BJ, Irukulla S, Abulafi AM, Kumar D, Mendall MA. Systematic review: adipose tissue, obesity and gastrointestinal diseases. *Aliment Pharmacol Ther* 2006;23:1511-23.