

Study the Correlation between Fecal Occult blood, C-Reactive Protein and Gastro-Intestinal Tract Cancer among Iraqi Patients

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Abstract

Background: Early detection of gastro-intestinal tract cancer (GIT) is necessary in order to increasing survival. Fecal occult blood test (FOBT) is a screening inexpensive test used to evaluate whether or not the upper digestive tract should be examined when the fecal occult blood test is.

Objective: The objective of the project was to investigate the prevalence rate of GI tumor among the population of Al- Najaf city and study correlation between Fecal Occult Blood Test (FOBT), C - reactive protein (CRP) and Gastro-Intestinal Tract Cancer (GIT).

Patients and Methods: Eighty patients with GIT cancers (16-80) years old. Samples were taken from Al –Sader Medical City Hospital in Al- Najaf city complaining from GIT cancers cases around the period Oct/ 2016 to the end of May/ 2017. Estimation of CRP, FOBT and body mass index (BMI) compared with 30 apparently healthy volunteers as control group who have no history or clinical evidence for any other chronic disease. All patients were exposed for questionnaire.

Results: The result was observed that the mean age was 45.500 ± 15.602 with ratio female to male was $23:17 = 1.35$. The prevalence of positive FOBT was 18(45%), CRP was 17(42.5%), while the mean of BMI was 44.90 ± 14.31 with high significant p value (0.0001)

Conclusion: The percentages of colon and stomach cancer were higher than other types of GIT cancer cases. Prevalence of positive result of FOBT was (40.9%) of colon cases and stomach cancer (50%). Majority of GIT patients were females with female to male ratio 23:17.

Keywords: GIT cancer, FOBT, BMI, CRP.

دراسة العلاقة بين الدم المخفي البرازي ، البروتين النشط سي وسرطانة القناة المعوية لدى مرضى عراقيين

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الخلاصة

الخلفية: من الضروري التحري المبكر عن سرطانة القناة المعوية لأجل عيشة المرضى. أن اختبار فحص الدم المخفي البرازي FOBT هو فحص تقصي رخيص يستخدم لتقييم الحالات الجزء العلوي من القناة الهضمية فيما يتطلب الأمر إجراء فحص أم لا.

الهدف: أن الغاية من هذا المشروع هو التحري عن مدى انتشار الأورام في مجتمع مدينة النجف ومدى العلاقة بين فحص الدم المخفي البرازي ، البروتين النشط سي CRP وسرطانة الجهاز المعوي.

المرضى والطرائق: أخذت العينات من ثمانين مريضاً بسرطانة الجهاز المعوي تتراوح أعمارهم ما بين 16-80 سنة. جمعت العينات من مستشفى مدينة الصدر الطبية في مدينة النجف من حالات سرطانة الجهاز المعوي ضمن الفترة من أكتوبر/ 2016 الى نهاية مايس / 2017. احتساب أو تخمين FOBT ، CRP ومؤشر كتلة الجسم (BMI) مقارنة بثلاثين عينة تعود لأصحاء متطوعين كمجموعة سيطرة ممن ليس لديهم تاريخ طبي أو سريري لأي حالة مرضية مزمنة. كل المرضى خضعوا لأستبيان

النتائج: النتائج الملحوظة تشير الى ان معدل اعمار المرضى هو 45.500 ± 15.602 سنة وبنسبة أنثى الى ذكور هي 23:17 = 1.35 . أن إيجابية فحص FOBT كانت 18(45%) ، CRP 17 (42.5%) بينما كان مؤشر كتلة الجسم للمرضى هو 14.31 ± 44.90 وبمعنوية عالية جداً مقارنة بالأصحاء (0.0001).

الاستنتاجات: إن النسبة المئوية لسرطانتى القولون والمعدة كانت الأعلى من بقية سرطانات الجهاز الهضمي . أن نسبة إيجابية فحص FOBT كانت (40.9%) لحالات سرطانة القولون و (50.0%) لسرطان المعدة. معظم المرضى من النساء ونسبة إناث : ذكور هي 1.35 .

الكلمات المفتاحية: سرطان الجهاز المعوي GIT ، فحص الدم المخفي البرازي FOBT ، مؤشر كتلة الجسم BMI البروتين النشط سي CRP .

Introduction

Gastrointestinal cancers are complex diseases. Each patient's cancer is different, behaving differently in the bodies. Gastrointestinal cancer is a term for the group of cancers that affect the digestive system. This includes cancers of the oesophagus, gallbladder, liver, pancreas, stomach, small intestine, bowel (large intestine or colon and rectum), and anus. Cancer can affect any part of the GIT, and rarely in the small intestine where most digestion occurs. The cause of the disease is mysterious but there are many risk factors for gastrointestinal cancer vary among the different types of cancer location such as excessive alcohol consumption, increasing age, smoking, chronic pancreatitis, genetic aspects and infections such as, Epstein-Barr virus or *Helicobacter pylori* and pernicious anemia[1,2].

The patients to be survival must be used chemotherapy compared to the well supportive care; however the optimal treatment is unclear [3].

Overall, the GIT and the accessory organs of digestion (pancreas, liver, and gall bladder) are responsible for more cancers and more deaths from cancer than any other system in the body.[4,5] .There is geographic variation significantly in the rates of various gastrointestinal cancers [1]. The common symptoms of GIT cancer relate to the organ affected and can include obstruction leading to difficulty swallowing, abdominal pain, discomfort, bloating, bleeding of rectal, loss of appetite, nausea/vomiting and fatigue.

The diagnoses of the cancer depend on, imaging tests, endoscopy, biopsies of suspect tissue, and, laboratory tests such as complete blood picture to look for anemia [6]. A fecal occult blood test may be done to look for stool containing blood. Once cancer is confirmed, the stage of the cancer is then identified and a treatment regimen is developed. The common methods of treating gastrointestinal cancer depend on the location and the types of the cancer include surgery (most commonly used) chemotherapy and radiation therapy [2].

Materials and Methods

Data and blood samples were collected from forty patients chosen from Al –Sader Medical City Hospital complaining from GIT cancer cases performed under the supervision of consultant physician during the period from the Oct/ 2016to the end of May/ 2017. The patients' age (16-80) years. C-Reactive Protein (CRP), Fecal Occult Blood were detected and estimation of body mass index (BMI), then the results of investigations were compared with the 30 apparently healthy volunteers as a control group (HC).

Methods

- Calculation of Body Mass Index was performed by using the following formula:

$$\text{BMI} = \frac{\text{Weight (Kg)}}{[\text{Height in meter}]^2}$$

In general, the higher the number, the more body fat a person has.

- Underweight: BMI is less than 18.5
- Normal weight: BMI is 18.5 to 24.9
- Overweight: BMI is 25 to 29.9
- Obese: BMI is 30 or more [7]

C - reactive protein test: this test done by latex agglutination test qualitative and semi-quantitative by serial dilutions

Fecal Occult Blood Test

Principle: Fecal Occult blood test consists of phenolphthalein swam by al zinc, in found of oxygen water and peroxidase blood cell. Oxidation of phenolphthalein leads to give red to pink color according blood concentration in the stool (Meyer Kastle method).

Statistical Analysis: All the results had been analyzed statistically using SPSS program by applied t-student test, chi-square and Fisher test [8].

Demographical Descriptive Picture of the studied Groups

The demographical picture for the studied groups showed that the mean of patients' ages was (45.5 ± 15.60) years. Moreover, the table revealed that the incidence with cancer was higher among females (23 females vs.17 males) and the mean of BMI very high (44.90 Kg/m^2) in comparison with control group (28.4 Kg/m^2) with highly significant difference ($P = 0.0001$).

Recently it was demonstrated that obesity plays a crucial role in many diseases and cancer development as breast and colorectal cancer [9,10]. These facts were recruited by the result of this study.

Table (1): Demographical Picture (basic characteristics) of studied groups

Parameters	Patients	Control	P value
Age (Mean \pm SD)	45.500 \pm 15.602	37.63 \pm 10.640	0.040 S
Age of disease onset. (Mean \pm SD)	40.4100 \pm 16.02	.0000 \pm 0.0	0.000 HS
F:M ratio	23:17 = 1.35		
BMI Kg/ m ² (Mean \pm SD)	44.90 \pm 14.31	28.4080 \pm 4.81199	0.0001 HS
Smoking: No. (%)	20 (50%)	18 (60%)	0.186 NS
Alcoholism: No. (%)	1(2.5%)	0 (0.0)	
Fecal Occult Blood: No. (%)	18(45%)	0 (0.0%)	0.000 HS
C-Reactive Protein: No. (%)	17(42.5%)	. 0000 \pm 0.0	0.000 HS
Location of Tumor:			
Gastric	12 (30%)		
Colon	22 (55%)		
Colorectal	1 (2.5%)		
Pancreas	4 (10%)		

Family History Positivity (%)	7%	0.0%	0.000 HS
Diabetes Mellitus: No. (%)	32(80%)	13 (43.3%)	>0.05 NS
Hypertension: No. (%)	31(77.5%)	19 (63.3%)	1.000 NS
Total	40	30	

Number: No, high significant: HS

Body mass index is often used as a screening tool to decide if your weight might be putting you at risk for health problems such as heart disease, diabetes, and cancer [10]. Also it is used to broadly define different weight groups in adults 20 years old or older. The same groups apply to both men and women [11].

The interpretation of this association may be attributed to increased density of fats and muscles which make the detection and recognition of tumor development is difficult and thereby its' diagnosis will be late. Additionally, gain of weight may be enhances after menopause among females which perhaps explains the high incidence among female rather than males which agreed with other study [12].

Many risk factors play a crucial role in initiation of cancer such as smoking and alcoholism. However, the present study showed no significant differences between patients and control group particularly in smoking. Although 50% of patients were observed to be smokers, 60% of control group was cigarette smokers too. The current results were matched the other studies [13-15]. However, the frequency of Iraqi smokers was less that of abroad.

Distribution of the studied groups according to age groups

Table 2 showed the distribution of patients according to age groups. The table revealed that the majority of patients were at age 40-49 years (i.e. at age of menopause for females) with significant difference ($P < 0.05$).

Table (2): Distribution of the studied groups according to age groups

Age – Groups (years)	Patient Group		Control Group		P- Value
	No.	(%)	No.	(%)	
<20 – 29	4	10.0	9	30.0	(t = 2.147) P< 0.05 (S)
30 – 39	10	25.0	8	26.7	
40 – 49	11	27.5	8	26.7	
50 – 59	5	12.5	3	10.0	
60 +	10	25.0	2	6.7	
Total	40	100.0	30	100.0	

This stage of lifespan may enhance so many disorders due to hormonal disturbances among female or the immune system became weak and susceptible for many infections which act as a trigger and inducer for mutagenesis in cells as the viral or bacterial infections. [16].

Distribution of patients according to gender

Table 3 below showed that most of cancer cases were among females (57.5% females Vs. 42.5% males); majority of them were complain of colon and stomach cancer; particularly colon cancer (32.5% for females Vs. 22.5% males) and stomach cancer (20% females Vs. 10% males). The explanation for these results may be attributed that most cancer cases are originated from a chronic inflammatory disease such as autoimmune diseases which elevated among female since the progesterone and estrogen hormones activated T helper cells and thus most of these diseases flare up among females and progress to tumorigenesis by time. Additionally, majority of those females at menopause age in which there is a disturbance in hormonal state that may lead to development of cancer. [17-19].

Table (3): Distribution of patients according to type of cancer & Gender

Type of cancer	Gender: No. / (%)		Total
	female	Male	
Colon	13 (32.5%)	9(22.5%)	22 (55.0%)
Pancreas	5.0% (2)	5.0%(2)	10.0%(4)
Rectum	0 (0.0%)	1(2.5%)	1(2.5%)
Small intestine	0 (0.0%)	1(2.5%)	1(2.5%)
Stomach	8 (20.0%)	4 (10.0%)	12 (30.0%)
Total	23 (57.5%)	17 (42.5%)	40 (100.0%)

Table 3 showed that the highest percentage of cancer cases was among colon cancer (55%) and stomach carcinoma cases (30%). These high frequencies may be related to high incidence with inflammatory bowel diseases which perhaps, may be considered as inducer for bowel bleeding, in addition to *H. pylori* infection which regarded as trigger for stomach carcinoma that highly distributed among patients. [20,21].

Detection of the Studied Parameters among the Studied Groups

The current study indicated to proportional relationship between FOB, CRP and cancer development as shown in Table 4. It was observed that there was highly significant difference between patients (45%, 42.5%) and control group (0.0, 0.0%) respectively with p value (0.04, 0.0001) respectively.

In the positivity of the type of tumors parameter particularly that (70%) of the tumors cases were malignants. Many evidences suggested that febrile inflammatory diseases may be involved in the initiation of cancer development. These facts recruit the present results. [22-24].

Table (4): Positivity of the studied parameters among the studied groups

Parameters	Patients	Control	P value
Fecal Occult Blood	18(45%)	0 (0.0%)	0.040 S
C-Reactive Protein	17(42.5%)	.0000±0.0	0.0001 H S
Type of Tumors: Benign Malignant	12 (30%) 28 (70%)	0 0	0.0001 HS
Location of Tumor: Gastric Colon Colorectal Pancreas	12 (30) 22 (55) 1 (2.5) 4 (10)	-	
Total	40	30	

Table 4 revealed that malignancy cases were higher among GIT cases (70%) in comparison with (30%) of benign cases. These results resemble the data of others. [25-27]

The interpretations of these results relate too many factors enhance metastasis and act to alter benign tumor into malignant one such as genetic factor, exposure to depleted uranium and others. [28,29]

Relation between Occult Blood Test and Types of Cancer

Table 5 showed that out of 22 colon cancer cases nine (40.9%) were positive for fecal occult blood while, (50%) of gastric carcinoma were positive. Other GIT cancer cases showed low positivity. Therefore, this test should recommend as a screening method for GIT cancer.

Table(5): Distribution of patients according to type of cancer & occult blood positivity

Type of cancer	Fecal Occult blood		Total
	(-) ve	(+) ve	
Colon	13 (32.5%)	9 (40.9%)	22 (55.0%)
Pancreas	2 (5.0%)	2 (50%)	4 (10%)
Rectum	1 (100%)	0 (0.0%)	1 (2.5%)
Small intestine	0 (0.0%)	1 (100%)	1(2.5%)
Stomach	6 (50%)	6 (50%)	12 (30.0%)
Total	22 (55.0%)	18 (45.0%)	40 (100.0%)

The explanation of these results attributed to bleeding that occurs in colon and gastric carcinomas. [30].

Relation between CRP and Types of Cancer

It is clear from Table 6 that positivity of CRP was lower than its negativity, although the highest positivity was noticed among colon and stomach cancers cases (17.5% for each). Moreover, almost; all positive fecal occult blood cases were positive for CRP. These data were similar to that of other study. [31]

Table (6): Percentage of Positive CRP among different cancer cases

Type of cancer	C-reactive protein		Total
	Negative (-)	Positive (+)	
Colon	15 (37.5%)	7 (17.5%)	22 (55.0%)
Pancreas	2 (5.0%)	2(5.0%)	4 (10.0%)
Rectum	1(2.5%)	0 (.0%)	1 (2.5%)
Small intestine	0 (.0%)	1 (2.5%)	1 (2.5%)
Stomach	5 (12.5%)	7 (17.5%)	12 (30.0%)
Total	23 (57.5%)	17 (42.5%)	40 (100.0%)

Role of diabetes mellitus in GIT Cancer Type Development

Table 7 showed the frequency of diabetes mellitus (DM) among different GIT types. This table evoked that the majority of colon and stomach cancer complained from DM. These results are quietly compatible with that of previous studies. [32-35].

Table (7): Distribution of Cancer cases according to DM

Type of cancer	Diabetes mellitus		Total
	No	Yes	
Colon	3 (7.5%)	19 (47.5%)	22(55.0%)
Pancreas	1(2.5%)	3 (7.5%)	4(10.0%)
Rectum	0(0.0%)	1(2.5%)	1(2.5%)
Small intestine	0(0.0%)	1(2.5%)	1(2.5%)
Stomach	4 (10.0%)	8 (20.0%)	12 (30.0%)
Total	8 (20.0%)	32 (80.0%)	40 (100.0%)

Role of Obesity on the Development of Cancer

Table 8 showed that most of colon (50%) patients were obese. In addition to colon, gastric carcinoma patients were also characterized by obesity (22.5%). On the contrary, there was low percentage (0.0%) of rectal and small intestine cancer patients were overweight.


Table (8): Distribution of patients according to BMI

Type of cancer	Body mass index		Total
	Over weight(25-30)	Obese(>30)	
Colon	2 (5.0%)	20(50.0%)	22(55.0%)
Pancreas	0 (0.0%)	4(10.0%)	4(10.0%)
Rectum	0 (0.0%)	1(2.5%)	1(2.5%)
Small intestine	0 (0.0%)	1(2.5%)	1(2.5%)
Stomach	3 (7.5%)	9 (22.5%)	12 (30.0%)
Total	5 (12.5%)	35 (87.5%)	40(100.0%)

These results may be attributed to low frequency of pancreatic, rectum and small intestine case due to sample size. [36-39].

The conclusions of this study was that majority of patients were females with females to males ratio of 23:17. The percentages of colon and stomach cancer were higher than other types of GIT cancer cases. It was noticed that most colon (40.9%) cases and stomach cancer cases (50%) were positive for fecal occult blood test.

References

1. Yamada T, Alpers DH. *et al.* Textbook of gastroenterology (5th Ed.). Chichester, West Sussex: Blackwell Pub. pp. 603, 1028. 2009.
2. O'Connor A, McNamara D, O'Moráin CA. "Surveillance of gastric intestinal metaplasia for the prevention of gastric cancer". The Cochrane database of systematic reviews. 9: 2013. CD009322.
3. Wagner AD, Syn NLX, Moehler M, *et al.* *Cochrane Database of Systematic Reviews*. John Wiley & Sons, Ltd. (2017-08-29).
4. "Cancer (Fact sheet N°297)". World Health Organization. February 2009. <http://www.who.int/mediacentre/factsheets/fs297/en/>. Retrieved 2009-05-11. 2009.
5. "What Are The Risk Factors For Stomach Cancer(Website)". American Cancer Society. http://www.cancer.org/docroot/cric/content/cric_2_4_2x_what_are_the_risk_factors_for_stomach_cancer_40.asp. Retrieved 2010-03-31.
6. Nicki R. Colledge; Brian R. Walker; Stuart H. Ralston, eds. (2010). *Davidson's principles and practice of medicine. Illustrated by Robert Britton (21st ed.)*. Edinburgh: Churchill Livingstone/Elsevier. ISBN 978-0-7020-3085-7. OCLC 455157186.
7. MacKay, N.J. "Scaling of human body mass with height: The body mass index revisited". *Journal of Biomechanics*. (2010). 43 (4): 764–66. [arXiv:0910.5834](https://arxiv.org/abs/0910.5834) . [Bibcode:2009arXiv0910.5834M](https://doi.org/10.1016/j.jbiomech.2009.10.038). doi:10.1016/j.jbiomech.2009.10.038. PMID 19909957
8. Sorlie DE: Medical Biostatistics & Epidemiology: Examination & board review." 1st Ed. Norwalk, Connecticut Appleton & Lange: (1995) pp: 47-88.
9. Renehan AG, Soerjomataram I, Tyson M, *et al.* Incident cancer burden attributable to excess body mass index in 30 European countries. *Int. J. Cancer*. 2010 Feb 1;126(3):692-702. doi: 10.1002/ijc.24803. 2010.
10. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. *Lancet*; 16; 371(9612):569-78. doi: 10.1016/S0140-6736(08)60269-X. (2008) .
11. Shimazu T, Tsuji I, Inoue M. *et al.* "Alcohol Drinking and Gastric Cancer Risk: An Evaluation Based on a Systematic Review of Epidemiologic Evidence among the Japanese Population". *Japanese Journal of Clinical Oncology* 38 (1): 8–25. doi:10.1093/jjco/hym152. PMID 18258712.(2008).
12. Sung, NY, Choi, KS, Park, EC, *et al.* "Smoking, alcohol and gastric cancer risk in Korean men: the National Health Insurance Corporation Study". *British Journal of Cancer* 97 (5): 700–4. (2007). doi:10.1038/sj.bjc.6603893. PMC 2360367. PMID 17637680. <http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pmcentrez&artid=2360367>.(2007).
13. Labmedica International staff writers Fecal Blood Test Predicts Lower Gastrointestinal Lesions Labmedical 2011.

14. Carolin T, Markus S, Konrad K, Gero N. Fecal pyruvate kinase isoenzyme type M2 for colorectal cancer screening: A meta-analysis. World J Gastroenterol. 14; 18 (30):4004-Renée MN11. 2012.
15. Renée MN, Stephanie M, Michael M: Fecal DNA testing for Colorectal Cancer Screening: the ColoSure™ test. Evidence on Genomic Tests March 22, 2011.
16. Marc JG, Rachael S-S, Amanda JC, *et al*: A Prospective Study of Serum C-Reactive Protein and Colorectal Cancer Risk in Men. *Cancer Res.*; 66(4): 2483-7.2006
17. Shemesh T, Rowley KG, Jenkins A, Brimblecombe J, Best JD, O'Dea K. "Differential association of C-reactive protein with adiposity in men and women in an Aboriginal community in northeast Arnhem Land of Australia." *Int. J. Obes. (Lond).* 31(1):103-8. 2007.
18. Chung DC, Yoon SS, Lauwers GY, Patel D. Case records of the Massachusetts General Hospital. Case 22-2007. A woman with a family history of gastric and breast cancer. *N Engl J Med.* Jul 19 2007;357(3):283-91.
19. Bresciani C, Perez RO, Gama-Rodrigues J. Familial gastric cancer. *Arq Gastroenterol.*;40(2): 114-7. 2003.
20. El-Serag H, Hampel H, Javadi F. The association between diabetes and hepatocellular carcinoma: a systematic review of epidemiologic evidence. *Clin. Gastroenterol. Hepatol.*;4:369–80. 2006.
21. McFarland MSh, Cripps R.: Diabetes Mellitus and Increased Risk of Cancer: Focus on Metformin and the Insulin Analogs. *Pharmacotherapy.* 2010;30(11):1159-1178.
22. Yu-Xiao T, Hennessy S, Lewis JD.: Insulin therapy and colorectal cancer risk among type 2 diabetes mellitus patients. *Gastroenterology*; 127(4): 1044–1050. 2004. Clinical-alimentary tract <http://dx.doi.org/10.1053/j.gastro.2004.07.011>.
23. Erwin B: Portal hypertension & Gastrointestinal Bleeding: Diagnosis, Prevention & Management. *World J Gastroenterol.* ; 19(31): 5035–5050. Aug 21, 2013 published online Aug 21, 2013. doi: 10.3748/wjg.v19.i31.5035.
24. Jane G, Gabriela C, Gillian R, Joanna W, *et al*. Menopausal hormone therapy and risk of gastrointestinal cancer: nested case–control study within a prospective. *Int. J. Cancer*: 130, 2387–2396 (2012) VC 2011 UICC.
25. Chao L, Pengyuan Z. The relationship of helicobacter pylori infection and the risk of colon neoplasia based on meta-analysis. *Int J Clin Exp Med* 2016;9(2):2293-2300.
26. "Proceedings of the fourth Global Vaccine Research Forum". Initiative for Vaccine Research team of the Department of Immunization, Vaccines and Biological. WHO. April 2004. http://www.who.int/vaccine_research/documents/en/gvrf2003.pdf. Retrieved 2009-05-11. "Epidemiology of *Helicobacter pylori* and gastric cancer...".
27. Dong SM, Traverso G, Johnson C, *et al*.: Detecting colorectal cancer in stool with the use of multiple genetic targets. *J. Natl. Cancer Inst.* 93:858-865. 2001.

28. Calistri D, Rengucci C, Bocchini R, *et al.*: Fecal multiple molecular tests to detect colorectal cancer in stool. Clin. Gastroenterol. Hepatol., 1:377-383.2003.
29. Tagore KS, Lawson MJ, Yucaitis JA, *et al.*: Sensitivity and specificity of a stool DNA multitarget assay panel for the detection of advanced colorectal neoplasia. Clin. Colorectal Cancer, 3:47-53. 2003.
30. Syngal S, Chung D, Willet C, *et al.*: The loss of stool DNA mutation abnormalities in colorectal neoplasia after treatment. Gastroenterol Suppl, 124:A5. 2003.
31. Muller HM, Oberwalder M, Fiegl H, *et al.*: Methylation changes in fecal DNA: a marker for colorectal cancer screening? Lancet, 362:1283-1285. 2004.
32. Brand RE, Shuber AP, Laken SJ, *et al.*: Reliability of a stool DNA mutation specific assay for colorectal cancer. Gastroenterol Suppl, 122: A-479. 2002.
33. Song K, Fendrick AM, Ladabaum U: Fecal DNA testing compared with conventional colorectal cancer screening methods: a decision analysis. Gastroenterology, 126:1270-1279. 2004.
34. Jie W, Qiuyin C, Honglan L, *et al.* Circulating C-reactive protein and colorectal cancer risk: a report from the Shanghai Men's Health Study. Carcinogenesis. 2013 Dec; 34(12): 2799–2803.
35. Mao Y, Yan C, Lu Q, *et al.* Genetically predicted high body mass index is associated with increased gastric cancer risk. Eur J Hum Genet. 2017 Sep;25(9):1061-1066. doi: 10.1038/ejhg.2017.103. Epub 2017 Jun 21.
36. Ooi CH, Ivanova T, Wu J, *et al.* Oncogenic pathway combinations predict clinical prognosis in gastric cancer. *PLoS Genet*. 5(10):e1000676. Oct 2009.
37. Tae YR, Jiyoung P, and Philipp ES. Hyperglycemia as a Risk Factor for cancer progression. J Diabetes Metab 2014 Oct; 38(5): 330–336.
38. Biadgo B, Abebe M. Type 2 Diabetes Mellitus and Its Association with the Risk of Pancreatic Carcinogenesis: A Review. Korean J Gastroenterol. 2016 Apr 25;67(4):168-77. doi: 10.4166/kjg.2016.67.4.168.
39. Church TR, Yeazel MW, Jones RM, *et al* : A randomized trial of direct mailing of fecal occult blood tests to increase colorectal. Cancer screening J Natl. Cancer Inst. 96:770-780.2004.