

Role of Immunological Method of Fecal Occult Blood Test for Screening Colorectal Diseases

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Abstract:

Background: Colorectal diseases specially colorectal carcinoma is one of the major health problems throughout the world. Therefore, early diagnosis of these diseases is mandatory. There are various screening methods are used for early diagnosis of colorectal diseases. Among them fecal occult blood test is the most widely used screening test. **Objectives:** The objectives of the present study were to find out the role of immunological method of fecal occult blood test for screening colorectal diseases. **Methods:** This was a prospective study consisted of 110 patients suspected to have colorectal diseases of both sexes attending in Gastroenterology and Clinical Pathology department of Bangabandhu Sheikh Mujib Medical University. Stool samples of all the patients were examined by immunological method of fecal occult blood test and then advised for colonoscopy and histopathology for confirmatory diagnosis. The results of immunological method of fecal occult blood test and the colonoscopic findings were compared. **Results.** Of 110 patients, 87 (79%) cases were positive and 23 (20.9%) cases were negative by immunological method of fecal occult blood test. According to colonoscopy and histopathology, 65(32.5%) cases were found to have colorectal diseases and 45(22.5%) cases had no pathology. Diseases detected by colonoscopy in occult blood test positive patients, 18(16.4%) colorectal polyp, 24(21.8%) colonic ulcer, 8(7.3%) colorectal cancer, 5(3.5%) inflammatory bowel disease, 7(6.4%) haemorrhoids and fissure, 2(1.8%) colonic diverticulum and 1(0.9%) proctitis. Among the 65(32.5%) lesions detected by colonoscopy, 62(95.3%) cases were positive by immunological method of fecal occult blood test where as only three(3) lesions were found in occult blood test negative cases. The sensitivity, specificity, PPV and NPV of immunological method of fecal occult blood test (IFOBT) for detection of occult bleeding were 95.4%, 44.4%, 71.3% and 87.0% respectively. **Conclusion:** It can apparently be concluded from this study that the role of immunological method of fecal occult blood test for colorectal diseases is promising in Bangladesh.

Key words: Colorectal diseases, Fecal occult blood test, Immunological method.

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Introduction:

Screening is very much helpful to reduce the morbidity and mortality from colorectal diseases specially colorectal carcinoma. Among the screening modalities colonoscopy is gold standard because of high sensitivity and specificity. But this procedure is invasive, requires expertise and preparation of patient, carries risk for perforation or any other complication as well as it is a costly procedure. In this perspective fecal occult blood test is widely acceptable because it is simple, cheap and easy to interpret. There are different methods to detect occult blood in the stool. Among them guaiac based test (GFOBt) is being used world wide for many years. But many studies reported that, as a screening test it is not very much helpful because of its low sensitivity, low compliance rate, high false

positive and false negative results. So, it is necessary to identify a better method than chemical method which has wide acceptance and has higher validity and reliability. The immunological test based on immunochromatographic technique which was introduced in 1984, employs a more complex reaction that uses monoclonal or polyclonal antibodies that detect the intact globin protein portion of human hemoglobin. The problem of dietary restriction is solved by the use of immunological method of fecal occult blood test since they do not react with non human hemoglobin or with uncooked fruits and vegetables that may contain peroxidase. The method has high sensitivity, minimum error and a single sample examination is sufficient¹. Several advantage of immunological FOBT over chemical method has been demonstrated. An average healthy person passes up to 2.0 ml of blood per 150 gm of stool into the GI tract daily. The conventional chemical fecal occult blood test usually picks up a daily blood loss

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of about 10 ml (about two teaspoonfuls), where as the sensitive immunological test picks up as little as 0.05 mg hemoglobin/g dry stool². The main negative feature of chemical FOBT is low sensitivity, around 40% for cancer and 24% for the detection of advanced adenoma or in situ carcinoma. Where as several studies using immunological tests, showed a sensitivity above 75% for the detection of advanced adenoma and even higher for cancer. Various study in U.S. U.K, Japan, Australia and Israel concluded that immunological FOBT had a higher sensitivity and specificity for the detection of occult bleeding ranged from 81.1% to 91.4% and 89.4% to 98.5% respectively³. On the other hand the sensitivity and specificity of chemical FOBT (done in 3 consecutive samples) have been reported as 30% to 64% and 87% to 90.6% respectively⁴. The aim of the present study was to see the efficacy of immunological method of fecal occult blood test based on immunochromatographic technique for screening colorectal diseases. Thus to reduce the incidence and mortality from GIT bleeding disorders by early diagnosis and further management of the patient.

Methods:

This cross sectional study was carried out in the department of Clinical Pathology, BSMMU, Dhaka during the period October, 2008 to August, 2009. For this purpose a total number of 110 patients suspected to have occult bleeding were included from inpatient and out patient department of Gastroenterology, BSMMU. Referred cases from other areas of Dhaka city were also included. Stool samples of all patients were examined by immunological method. In this study, HEXAGON OBTI test device from HUMAN, Germany were used for immunological test. The device has been designed as a rapid immunological test for qualitative detection of human hemoglobin in stool samples. The test is based on an immunochromatographic technique, featuring immobilized monoclonal antibodies and a coloured particular reagent. Due to use of monoclonal antibodies the test is highly specific for human hemoglobin and is not affected by animal proteins, vitamin, drugs etc. The patients were then advised for colonoscopy for detection of any pathological lesions in lower GI tract. Tissue was taken from these lesions and histopathological examination done.

Data were evaluated by standard statistical methods. Analysis was done by SPSS (Statistical package for social science) by applying appropriate formula. Sensitivity & specificity of immunological method of FOBT were calculated in diagnosing occult lower GIT bleeding considering colonoscopy and

biopsy as gold standard. 95% confidence interval was calculated for sensitivity and specificity. Positive and negative predictive values were calculated.

Results:

Out of 110 patients, 18 Colonic polyps were detected by colonoscopy, all of which were positive primarily by immunological test method. No polyps were found in IFOBT negative patients. The result is shown in Table I. The sensitivity, specificity, PPV and NPV of I-FOBT for detection of colonic polyp were 100.0%, 42.4%, 20.7% and 100% respectively (Table-V).

Table-I

Comparison between I-FOBT and colonoscopy for identification of Colonic polyp (n=110).

		Colonoscopy	
		Colonic polyp	Normal
I-FOBT	Positive (n=87)	18	69
	Negative (n=23)	0	43
	Total (n=110)	18	102

Chi value = 10.33, p value=0.001 degree of freedom(df) =1 (I-FOBT)

Table-II

Comparison between I-FOBT and colonoscopy for identification of Colorectal cancer (n=110).

		Colonoscopy	
		Colorectal cancer	Normal
I-FOBT	Positive (n=87)	7	2
	Negative (n=23)	1	22
	Total (n=110)	8	102

Chi value = 0.33, p value=0.470 degree of freedom(df)

Table-III

Comparison between I-FOBT and colonoscopy for identification of Ulcerative lesions (n=110).

		Colonoscopy	
		Ulcerative lesions	Normal
I-FOBT	Positive (n=87)	27	60
	Negative (n=23)	2	21
	Total (n=110)	29	81

Chi value = 4.68, p value=0.031 degree of freedom (df)

Table-IV

Comparison between colonoscopy and I-FOBT for identification of any pathology (n=110).

	Colonoscopy	
I-FOBT Positive (n=87)	62	25
Negative (n=23)	3	20
Total (n=110)	65	45

Chi value = 25.51, p value=0.001 degree of freedom (df)

In this study, eight(8) colorectal cancer were diagnosed by colonoscopy, out of which seven(7) cases were found to be positive by I-FOBT. Only one (1) colorectal cancer was diagnosed in I-FOBT negative cases. . The result is shown in Table II. The sensitivity, specificity, PPV and NPV of I-FOBT for detection of colorectal cancer were 87.5%, 47.1%, 10% and 96% respectively (Table V).

Table-V

Sensitivity, specificity, positive and negative predictive values I-FOBT for identification of Colorectal cancer, Colonic polyp and ulcerative lesions (n=110).

Validity test	I-FOBT(%)		
	Colorectal cancer	Colonic polyp	Ulcerative lesions
Sensitivity	87.5	100.0	93.1
Specificity	47.1	42.4	44.4
PPV	10.0	20.7	31.0
NPV	96.0	100.0	91.3

In this study, 29 ulcerative lesions were detected by colonoscopy, out of which 27 cases were found to be positive by I-FOBT. Only two (2) ulcerative lesions were detected in I-FOBT negative cases. The result is shown in Table III. The sensitivity, specificity, PPV and NPV of I-FOBT for detection of ulcerative lesions were 93.1% ,44.1%,31.0% and91.3% respectively (Table V).

Out of 110 patients, 65 patients were found to be disease positive and 45 cases were disease negative in colonoscopy. Among 65disease positive cases, 62 cases were found to be positive by immunological method. Only three (3) lesions were detected by colonoscopies which were negative by I-FOBT. The result is shown in Table IV.

The overall sensitivity, specificity, Accuracy, PPV and NPV of IFOBT for detection of occult bleeding were 95.4%, 44.4%, 74.5%, 71.3% and 87.0% respectively. The result is shown in Table VI.

Discussion:

Diseases causing occult gastrointestinal bleeding specially colorectal carcinoma are important public health concern in the world. With 655,000 deaths worldwide per year, it is the second most common form of cancer and the second leading cause of cancer-related death in the Western world⁵. In recent years an increase in incidence of these diseases have been recognized. While various colorectal examinations are available, the fecal occult blood test believed to be the most acceptable, in that no pain is inflicted on the patients⁶. However, conventional fecal occult blood tests need dietary restrictions, produce false positive and false negative results, and hence it has less reliability. The usefulness of new method of fecal occult blood test (IFOBT) have been reported by various investigators. In the present study, stool samples of one hundred and ten (110) patients suspected to have occult bleeding were examined by immunological method of fecal occult blood test and then undergone colonoscopy for detection of any pathology in lower GIT. According to colonoscopic findings 45 (40.9%) cases were found normal i.e. no pathology in lower GIT. It may be explained by the fact that the lesion might be in upper GIT which could be detected by upper GI endoscopy. On the other hand various types of diseases were found in the rest sixty five (65) patients. The diseases detected by colonoscopy in OBT positive patients were 18(16.44%) colonic polyp, 24(21.8%) colonic ulcers, 8(7.3%) colorectal cancer, 5(3.5%) inflammatory bowel disease, 7(6.4%) haemorrhoids and fissure, 2(1.8%) colonic diverticulum and 1(0.9%) proctitis. Guittet et al.⁷ identified 21 (3.3%) colorectal cancers and 149 (23.1%) patients adenomas among 644 IFOBT positive patients who underwent colonoscopies for final diagnosis. Otto and Dobrossy⁸ described a study to find out the role of immunological fecal occult blood test to demonstrate the feasibility and validity of the test in screening context, in addition to social acceptance and impact on early cure. Among 243(65%) patients, colorectal cancer were detected and histologically confirmed in 12 cases (5% of all test positives) and 59 cases (20%), adenomatous polyps were found⁸. A prospective study was conducted by Kemppainen M et al.⁹to investigate whether an immunological fecal occult blood test can be used in screening patients with symptoms suggestive of colonic or rectal origin in primary health care. Total 523 patients were included in that study, among them 71 IFOBT positive patients were investigated with colonoscopy and this group had 13 cancers, 8 adenomas and one hyperplastic polyp. The IFOBT negative patients had no malignant colorectal tumors in the mean follow-up period

of 2.2 years according to hospital records⁹. Hughes et al.¹⁰ described the colonoscopic outcome of 89 IFOBT positive patients among 1,219 asymptomatic average risk population in Australia. Among 89 cases there were 2(2.4%) colorectal cancer, 26(31.7%) other adenoma, 10(12.2%) hyperplastic polyp, 9(11%) diverticular disease, 2(2.4%) haemorrhoid and 3(3.7%) had no pathology in colonoscopy.

In this study, we calculated individually the accuracy of IFOBT for detection of colonic polyp, colorectal cancer and ulcerative lesions in the colon. Although in developing country, the prevalence of colorectal cancer is low (1/100,000), the incidence is increasing day by day due to change in life style, dietary habit and huge urbanization. The relative risk of developing colorectal carcinoma in Bangladesh is also high. In this perspective, it is necessary to screen colorectal cancer among our asymptomatic average risk population of our country to reduce its incidence and prevalence rate. Although polyps and ulcerative lesions are benign but it is proved that in time they may progress to invasive cancers. Polyps, specially larger (>1cm.) polyps become colorectal cancer at a rate of roughly 1% per year.² By screening, if we can detect these benign lesions and treat in this stage obviously it will decrease the incidence of invasive disease². Patients with ulcerative colitis or Crohn's disease also have an increased risk of colonic epithelial dysplasia and carcinoma. Ulcerative colitis patients have a colon cancer risk at least three times higher than that in the general population. Crohn's disease patients with at least 30% of the colon involved with disease may have an increased risk of colorectal dysplasia and cancer. Considering this fact we had evaluated the performance characteristics of IFOBT for detection of polyp and ulcerative lesions in colon.

In the present study we found the sensitivity of IFOBT for detection of colonic polyp, colorectal cancer and ulcerative lesions in the colon were 87.5%, 100% and 93.1% respectively. These findings are nearly similar to the findings noted by Simon¹¹ where higher sensitivity of IFOBT (75% to over 90%) were found. This study recommended that the newer generation of test such as immunological test would undoubtedly proved even better in practice. Morikawa et al.¹² also found higher sensitivity of IFOBT in a study among 21805 Japanese population. Allison et al.² found that the sensitivity of IFOBT for detecting the colorectal cancer was 82%, substantially higher. Although there were differences in results (ranged from 66% to 98%) the sensitivity of IFOBT in many published studies^{13,14} was much higher, which suggested

that the method would show improved performance in screening programmes.

Regarding specificity, in this study we found the specificity of IFOBT for detecting colorectal cancer, colonic polyp, and ulcerative lesions were 47.1%, 42.4%, 44.4% respectively. The higher specificity of IFOBT was also noted by Burch et al.³ who reported the eight diagnostic case control studies regarding comparison of two methods. Among these 8 studies, IFOBT had higher specificities in four studies, another four studies founded comparable specificity of both methods. Although James et al.¹⁵ reported much higher specificity of than our study, it was obvious that IFOBT had greater specificity. The specificity of Hemeselect i.e. IFOBT were 94.4% and 95.2% for detection of carcinoma and polyp respectively. In another study conducted by Allison et al.² it was concluded that IFOBT had higher sensitivity and specificity for detecting colorectal cancer. Young et al.¹⁶ founded around 95% specificity of IFOBT for detection of colonic neoplasia. The IFOBT's sensitivity for hemoglobin is also much greater at 0.05 mg hemoglobin per gram of stool. The increased sensitivity of the IFOBT makes intermittent tumor bleeding a less significant issue¹⁷. An additional advantage is the IFOBT has fewer false positives because the globin protein is denatured in the upper GI tract. The IFOBT therefore is specific for bleeding in the lower GI tract¹⁸.

In the present study we had analyzed the positive and negative predictive value of IFOBT for detection of colorectal cancer, polyps and ulcerative lesions. The PPV of IFOBT were 10%, 20.7% and 31% for detection of colorectal cancer, polyps and ulcerative lesions respectively. NPV of IFOBT were 96%, 100% and 91.3% for detection of colorectal cancer, polyps and ulcerative lesions respectively. Our findings were different from the study conducted by James et al.¹⁵ where the PPV of IFOBT for detection of carcinoma and polyp were slightly lower. They also found higher PPV if both conventional and immunological tests were done simultaneously. Guittet et al.⁷ also observed higher (8.7% vs 7.3%) PPV of IFOBT for detection of polyp and (49.2% vs 27.2%) for detection of colorectal neoplasia.

The overall sensitivity, specificity, accuracy, PPV and NPV of IFOBT were 95.4%, 44.4%, 74.5%, 71.3% and 87% respectively. Ranshoff¹⁹ found the sensitivity of IFOBT 95.9%, and specificity 59.2%, resulting in a 30% reduction of colonoscopy use. This findings is very much consistent with our findings. A multicenter prospective case control study by Lohsiriwat²⁰ in Thailand found the overall

sensitivity, specificity, positive predictive value, and negative predictive value of IFOBT for CRC detection were 91.0% 93.8%, 95.8% and 87.0% respectively, which supported the present study.

The potential usefulness of IFOBT was being considered by several organizations. The American Cancer Society recommended that in comparison with guaiac-based tests for the detection of occult blood, immunological tests were more patient friendly and were likely to be equal or better in sensitivity and specificity. The World Health Organization and the World Organization for Digestive Endoscopy have also endorsed the use of immunological test because population cannot be relied on to comply with the dietary and drug restrictions necessary for guaiac-based tests².

Conclusion:

From this study, we may conclude that immunological method of fecal occult blood test is very much helpful for screening colorectal diseases for its high compliance rate, sensitivity, specificity, PPV and NPV. This study provided us with an opportunity to evaluate the accuracy of immunological method of fecal occult blood test, thereby find out a better screening method to get an idea about incidence and prevalence of colorectal diseases in Bangladesh.

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