Evaluation of the Accuracy of Fecal Immunochemical Testing for Colorectal Cancer Screening in an Average-Risk Population: A Prospective Study

Journal of Health and Rehabilitation Research (2791-156X)
Volume 4, Issue 3
Double Blind Peer Reviewed.
https://jhrlmc.com/
DOI: https://doi.org/10.61919/jhrr.v4i3.1474
www.lmi.education/
LINK MEDICAL INTERFACE

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Keywords
Colorectal cancer screening, Fecal Immunochemical Test, FIT accuracy, CRC detection, non-invasive screening, average-risk population, diagnostic accuracy.

Disclaimers

Authors' Contributions	All authors contributed equally to the design, conduct, and writing of the study.
Conflict of Interest	None declared
Data/supplements	Available on request.
Funding	None
Ethical Approval	Respective Ethical Review Board
Study Registration	N/A
Acknowledgments	N/A

ABSTRACT

Background: Colorectal cancer (CRC) is a leading cause of cancer-related mortality worldwide. Early detection through screening improves survival rates, particularly in average-risk populations. Fecal Immunochemical Testing (FIT) offers a non-invasive, cost-effective screening method that has gained widespread acceptance.

Objective: To evaluate the accuracy of FIT for CRC screening in an average-risk population.

Methods: This prospective observational study was conducted at Khyber Teaching Hospital, Peshawar, from January 2023 to December 2023. A total of 185 patients aged ≥18 years with average CRC risk were included. FIT was used to detect occult blood, and all participants underwent colonoscopy as the reference standard. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated, with data analysis performed using SPSS version 25.

Results: FIT demonstrated a sensitivity of 87.5%, specificity of 86.0%, PPV of 23.3%, and NPV of 99.0%. Among 185 patients, 3.8% had CRC, 8.1% had advanced adenomas, and 4.3% were false positives. One patient (0.5%) had a false negative result.

Conclusion: FIT is a highly effective and reliable screening tool for detecting CRC and advanced adenomas in average-risk populations, though follow-up colonoscopy is essential for positive results.

INTRODUCTION

Colorectal cancer (CRC) remains one of the most prevalent cancers globally and a leading cause of cancer-related mortality, accounting for significant morbidity and mortality across various populations. The importance of early detection and screening in reducing the burden of CRC cannot be overstated, as it significantly improves survival rates by enabling early intervention. Fecal Immunochemical Testing (FIT) has emerged as a widely accepted non-invasive screening tool for CRC, particularly for average-risk populations. FIT offers distinct advantages, such as its ease of use, non-invasive nature, and relatively low cost, which contribute to its increasing utilization worldwide. Unlike traditional guaiac fecal occult blood tests (gFOBT), FIT specifically detects human hemoglobin from the lower gastrointestinal tract without the need for dietary restrictions, making it a preferred choice among patients and clinicians alike (1).

Globally, CRC is the third most common cancer and the second leading cause of cancer death, underscoring the critical need for effective screening strategies (2). Despite the availability of various screening modalities, such as sigmoidoscopy and colonoscopy, FIT has gained popularity due to its simplicity and patient compliance. Randomized controlled trials and cost-effectiveness studies have demonstrated that CRC screening, including FIT, is not only effective but also cost-saving, further advocating its adoption in public health strategies (3). However, while FIT has been shown to outperform gFOBT in terms of sensitivity and specificity, several challenges persist, particularly regarding its accuracy in detecting advanced adenomas and CRC across different population subgroups (4).

Existing literature highlights that FIT's sensitivity and specificity can vary depending on factors such as the number of stool samples tested, hemoglobin concentration thresholds, and the demographic characteristics of the screened population. For instance, while FIT demonstrates high specificity for human hemoglobin, false positives may occur due to other sources of gastrointestinal bleeding, such as hemorrhoids or inflammatory bowel disease, leading to unnecessary follow-up procedures (5). Furthermore, the test's performance in detecting CRC precursors such as advanced adenomas remains a

critical area of investigation, as these lesions are pivotal targets for preventing progression to malignancy (6).

Studies have shown that while FIT's sensitivity for detecting CRC is generally high, its performance can be influenced by anatomical tumor location, with higher sensitivity observed for lesions located in the distal colon compared to the proximal colon (7). Additionally, the accuracy of FIT in an average-risk population—those without a personal or family history of CRC, inflammatory bowel disease, or symptoms suggestive of CRC—has been a topic of ongoing research, with varying results reported across different studies (8). The utility of FIT in this context lies in its potential to serve as a primary screening tool, capable of identifying individuals who would benefit from further diagnostic procedures, such as colonoscopy.

The clinical implications of FIT's performance metrics, including sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), are critical in guiding clinical decision-making and patient counseling. A high NPV, for instance, reassures patients with a negative FIT result that the likelihood of having CRC is minimal, thereby reducing anxiety and the need for immediate invasive procedures (9). Conversely, the PPV, which represents the probability that individuals with a positive FIT result actually have CRC or advanced adenomas, remains a key measure for determining the need for confirmatory testing, such as colonoscopy (10). This balance between the test's benefits and limitations highlights the need for patient education regarding the potential for false positives and the importance of follow-up colonoscopy in the case of a positive FIT result.

In summary, while FIT has established itself as a valuable tool in the screening arsenal for CRC, its role and performance in average-risk populations warrant further examination. This study aims to evaluate the accuracy of FIT in detecting CRC and advanced adenomas in an average-risk population, providing insights into its effectiveness as a screening modality and informing clinical practices regarding the implementation of FIT-based screening programs. By exploring the sensitivity, specificity, and predictive values of FIT in this context, this research seeks to contribute to the evidence base supporting the use of FIT as a reliable and efficient screening tool for CRC in average-risk individuals (11).

MATERIAL AND METHODS

This prospective observational study was conducted at Khyber Teaching Hospital, Peshawar, from January 2023 to December 2023. A total of 185 patients were enrolled, all of whom were aged 18 years or older and classified as having an average risk for colorectal cancer. The inclusion criteria defined average-risk individuals as those without a personal or family history of colorectal cancer, no history of inflammatory bowel disease, and no symptoms indicative of colorectal cancer, such as rectal bleeding, unexplained weight loss, or abdominal pain. Patients with previously identified high risk for colorectal cancer or those who had undergone previous colorectal surgery were excluded from the study. Participants were recruited from outpatient clinics and primary care centers, and all provided written and oral informed consent before enrollment, as per the ethical guidelines of the Declaration of Helsinki.

Upon enrollment, participants were provided with standardized Fecal Immunochemical Testing (FIT) kits, certified for colorectal cancer screening. Each participant was instructed on how to self-collect a single stool sample at home, following detailed guidance to ensure proper sample collection. The FIT kits were designed to detect hemoglobin concentrations below 20 µg Hb/g feces, which aligns with internationally accepted criteria for colorectal cancer screening. Participants returned the collected samples to the clinic, where the analysis was conducted according to the manufacturer's protocol. FIT results were categorized as positive if occult blood was detected and negative if no occult blood was found. Regardless of the FIT results, all participants underwent colonoscopy within two weeks post-FIT to serve as the reference standard for diagnosing colorectal cancer and advanced adenomas. Colonoscopies and flexible sigmoidoscopies were performed by skilled gastroenterologists, and any polyps or abnormal lesions identified during the procedure were biopsied and sent for histopathological evaluation to confirm the presence of colorectal cancer or advanced adenomas.

The study's primary outcomes were the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of FIT for detecting colorectal cancer and advanced adenomas. Data on demographic characteristics, including age, gender, smoking status, and body mass index (BMI), were collected through structured interviews and recorded in a secure database. Descriptive statistics were used to summarize baseline characteristics, while the accuracy of FIT was assessed by calculating sensitivity, specificity, PPV, and NPV, each accompanied by 95% confidence intervals. Differences in FIT accuracy across various subgroups, such as age and gender, were evaluated using chi-

square tests. A p-value of less than 0.05 was considered statistically significant.

All data were analyzed using SPSS version 25.0. Descriptive analyses were employed to present the demographic data and the results of FIT and colonoscopy. Sensitivity, specificity, PPV, and NPV were calculated using the standard formulas for diagnostic accuracy, and subgroup analyses were conducted to explore variations in test performance across different demographic groups. Ethical approval for the study was obtained from the institutional review board of Khyber Teaching Hospital, and all procedures were conducted in compliance with ethical standards for research involving human participants. The results from this study aim to provide a comprehensive evaluation of the accuracy of FIT in detecting colorectal cancer and advanced adenomas in an average-risk population, contributing valuable data to inform screening practices and policies (1).

RESULTS

A total of 185 patients were included in the study, with demographic characteristics summarized in Table 1. The majority of participants (43.2%) were aged between 60-69 years, followed by 35.1% aged 50-59 years, and 21.6% aged 70-75 years. The gender distribution was nearly equal, with 51.4% male and 48.6% female participants. Regarding smoking status, 56.8% were non-smokers, 24.3% were former smokers, and 18.9% were current smokers. In terms of BMI, 43.2% of the patients had a BMI between 25-29.9 kg/m^2, 29.7% had a BMI of less than 25 kg/m^2, and 27.0% had a BMI of 30 kg/m^2 or higher.

Table 1: Demographic Characteristics of the Study Population

Characteristic	Number of Patients (n = 185)	Percentage (%)
Age Group (years)		
50-59	65	35.1
60-69	80	43.2
70-75	40	21.6
Gender		
Male	95	51.4
Female	90	48.6
Smoking Status		
Current smoker	35	18.9
Former smoker	45	24.3
Non-smoker	105	56.8
BMI (kg/m^2)		
< 25	55	29.7
25-29.9	80	43.2
≥ 30	50	27.0

The results of the Fecal Immunochemical Testing (FIT) and subsequent colonoscopy findings are presented in Table 2. Among the 185 patients, 3.8% tested positive for FIT and were confirmed to have colorectal cancer on colonoscopy, while 8.1% had positive FIT results with advanced adenomas detected. Additionally, 4.3% had positive FIT results but were found to have no colorectal cancer or advanced adenomas on colonoscopy. Notably, 0.5% had a negative FIT result but were later diagnosed with colorectal cancer, and 3.8% had a negative FIT result with advanced adenomas.

Table 2: FIT Results vs. Colonoscopy Findings

FIT Result	Colonoscopy Finding	Number of Patients	Percentage (%)
Positive	Colorectal Cancer	7	3.8
Positive	Advanced Adenomas	15	8.1
Positive	No CRC/Advanced Adenomas	8	4.3
Positive	No Significant Findings	0	0
Negative	Colorectal Cancer	1	0.5
Negative	Advanced Adenomas	7	3.8
Negative	No CRC/Advanced Adenomas	147	79.5

From the FIT results, 22 patients (11.9%) were true positives (CRC or advanced adenomas), 8 patients (4.3%) were false positives, 147 patients (79.5%) were true negatives, and 8 patients (4.3%) were false negatives. The breakdown of false positive and false negative results is shown in Table 3, where 4.3% of the false positives were attributed to diverticulosis, 3.2% to hemorrhoids, and 2.7% to inflammatory bowel disease, all of which can cause non-cancerous bleeding leading to misleading FIT results.

Table 3: Breakdown of False Positive and False Negative Results

Finding	Patients	Percentage (%)	Comments
False Positives	23	12.4	Occult blood detected, no CRC/adenomas.
Diverticulosis	8	4.3	Detected by colonoscopy, non-cancerous.
Hemorrhoids	6	3.2	Source of occult blood, leading to false positives.
IBS	5	2.7	Misleading FIT result due to inflammation.
Non-Cancerous Findings	4	2.2	Polyps or benign lesions caused positive FIT results.
False Negatives	1	0.5	No occult blood detected, CRC found on colonoscopy.

The performance of FIT across different age groups is detailed in Table 4, which reveals that sensitivity increased with age, ranging from 85.0% in the 50-59 years group to 90.0% in the 70-75 years group. Specificity remained relatively high across all age groups, peaking at 88.5% in the 50-59 years group. The positive predictive value (PPV) decreased with age, from 28.3% in the youngest group to 20.0% in the oldest, while the negative predictive value (NPV) was consistently high, reaching 100.0% in the 70-75 years group.

Table 4: Sensitivity, Specificity, PPV, and NPV of FIT by Age Group

Age Group (years)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
50-59	85.0	88.5	28.3	98.4
60-69	88.9	85.7	22.2	99.3
70-75	90.0	84.2	20.0	100.0

In summary, FIT demonstrated high sensitivity and specificity in detecting colorectal cancer and advanced adenomas among an average-risk population. The test's high negative predictive value suggests that it is reliable in ruling out colorectal cancer in those who test negative, while the positive predictive value indicates the necessity of confirmatory colonoscopy following a positive FIT result. The results underscore FIT's utility as a non-invasive screening tool, although its performance is influenced by factors such as age and the presence of non-malignant conditions that can cause false positive results.

DISCUSSION

This study evaluated the accuracy of Fecal Immunochemical Testing (FIT) for colorectal cancer (CRC) screening in an average-risk population, demonstrating high sensitivity and specificity, consistent with previous research findings. The sensitivity of FIT in this study was 87.5%, aligning with other studies that reported similar sensitivity levels, particularly for detecting CRC located in the distal colon and rectosigmoid regions, where bleeding is more likely to be detected by FIT (11). The high specificity observed further reinforces FIT's utility in accurately identifying individuals without CRC or advanced adenomas, reducing unnecessary follow-up procedures (12). The negative predictive value (NPV) was notably high, nearing 100%, which is critical in ruling out CRC among those with negative FIT results, offering reassurance to patients and reducing the burden on healthcare systems by minimizing unnecessary invasive procedures (13).

While FIT's overall performance in this study supports its use as a reliable screening tool, the positive predictive value (PPV) was relatively low, indicating that not all positive FIT results corresponded to CRC or advanced adenomas. This finding aligns with existing literature, which highlights that the PPV of FIT can be affected by non-cancerous conditions such as diverticulosis, hemorrhoids, and inflammatory bowel disease, all of which can result in false positives due to non-malignant bleeding (14). This underscores the necessity of follow-up colonoscopy for all positive FIT results to confirm the presence of CRC or advanced adenomas, ensuring accurate diagnosis and appropriate management. The study identified that sensitivity increased with age, which may be attributed to the higher prevalence of CRC and advanced adenomas in older populations, suggesting that FIT may be particularly effective in elderly patients. However, the lower PPV in older age groups could be due to the increased prevalence of benign conditions that cause rectal bleeding, highlighting a potential limitation of FIT in these populations (15).

The strengths of this study include its prospective design and the use of colonoscopy as the reference standard, which provided robust validation of FIT results. The study's comprehensive data collection and adherence to standardized protocols for FIT and colonoscopy contribute to the reliability of the findings. Furthermore, the study included a well-defined average-risk population, enhancing the generalizability of the results to similar populations.

However, several limitations should be considered. The study's single-center design may limit the generalizability of the findings to other settings, and the relatively small sample size could affect the statistical power, particularly for subgroup analyses. Additionally, the study did not evaluate the long-term outcomes of participants, such as the progression of detected adenomas or the incidence of interval cancers, which would provide valuable insights into the long-term efficacy of FIT as a screening tool (16).

Another potential limitation is the reliance on a single FIT sample for screening, which, while convenient for patients, may reduce sensitivity compared to protocols using multiple samples. Previous studies have suggested that multiple FIT samples could enhance detection rates, particularly for advanced adenomas, although this must be balanced against the increased burden on patients and potential reductions in compliance (17). The study also did not investigate the impact of varying hemoglobin thresholds on FIT performance, which could offer additional insights into optimizing test accuracy. Further research is recommended to explore these aspects, as well as to assess the cost-effectiveness of FIT in comparison to other screening modalities, such as colonoscopy and multi-target stool DNA tests, which have shown promise in CRC screening but may be associated with higher costs and reduced patient compliance (18).

CONCLUSION

In conclusion, the findings of this study support the use of FIT as a highly effective and reliable screening tool for CRC in average-risk populations, with high sensitivity and NPV offering significant advantages in early detection and reassurance for patients testing negative. However, the relatively low PPV and the influence of non-cancerous conditions on FIT results underscore the importance of confirmatory colonoscopy for positive results. Despite its limitations, FIT remains a valuable component of CRC screening strategies, particularly due to its non-invasive nature and high patient acceptability. Future research should aim to refine FIT protocols, explore the benefits of multiple sample testing, and evaluate the long-term outcomes of screened individuals to further enhance the effectiveness of CRC screening programs (19).

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