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An Audit Report on Mismatch Repair Deficiency Testing in Patients with Colorectal Cancer and Non-adherence to Testing Guidelines

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ABSTRACT

Background: Mismatch Repair (MMR) deficiency testing plays an important role in the management of Colorectal Cancer (CRC), particularly for identifying Lynch syndrome and guiding treatment decisions. Despite clear recommendations for universal testing, its use in routine practice remains inconsistent.

Objective: To assess the utilization of MMR deficiency testing in patients with colorectal cancer and to identify factors associated with nonadherence to testing guidelines.

Methods: This hospital-based audit included 117 patients with histologically confirmed CRC presenting between September 2025 and March 2026 at a tertiary oncology center. Clinical and demographic data were collected from medical records. The primary outcome was whether MMR/MSI testing was performed. Associations between patient characteristics and testing status were analyzed using appropriate statistical tests, with significance set at $p < 0.05$.

Results: MMR/MSI testing was performed in only 28.2% of patients, while 71.8% did not undergo testing. Younger and older age groups, socioeconomic status, education level, disease stage, and family history showed significant associations with testing status. The most common reason for not undergoing testing was financial constraint (38.5%), followed by lack of physician recommendation (14.5%) and non-availability of testing facilities (7.7%). A large proportion of patients presented with advanced-stage disease.

Conclusion: MMR deficiency testing remains underutilized in CRC patients in this setting. Financial barriers, limited access, and gaps in physician practice contribute to low testing rates. Addressing these issues is essential to improve adherence to guidelines and ensure appropriate patient care.

Keywords: Colorectal cancer; Mismatch repair deficiency; Microsatellite instability testing; Lynch syndrome; Guideline adherence/non adherence; Healthcare barriers

INTRODUCTION

Colorectal Cancer (CRC) remains one of the most frequently diagnosed malignancies in the world and is a major contributor to cancer-related deaths, ranking among the top causes in both men and women [1]. Defects in the Deoxyribonucleic Acid (DNA) Mismatch Repair (MMR) system are a defining feature of Lynch syndrome and are also identified in a proportion of sporadic CRC cases,

estimated at around 15%. These defects may result from inherited mutations in MMR genes, including *MLH1, MSH2, MSH6, and PMS2*, or from acquired epigenetic inactivation of *MLH1*. The resulting failure to correct errors in repetitive DNA sequences leads to genomic instability and increases susceptibility to several cancers, most notably CRC [2].

In the past, testing for MMR deficiency was largely restricted to patients considered at increased risk based on their clinical or family history. To aid in identifying such individuals, criteria such as the Amsterdam II criteria and the revised Bethesda guidelines were introduced, focusing on factors like age at diagnosis and familial cancer patterns, particularly in relation to microsatellite instability–high (MSI-H) tumors [3].

CRC occurring in younger individuals is more frequently associated with Lynch syndrome and *MSI-H* status. For this reason, clinical guidelines have long supported routine MMR testing in patients diagnosed before the age of 50. However, in practice, these recommendations have not always been consistently followed, leading to missed opportunities for identifying affected patients. The concept of universal MMR testing for all newly diagnosed CRC cases was proposed in 2008 and later incorporated into national guidelines in 2014. At present, universal screening is widely recommended by major professional organizations [4].

The present study evaluates current patterns of MMR deficiency testing in adults with CRC in an oncology center in Pakistan. It also explores the extent of underutilization in patients under 50 years of age, with the aim of identifying factors associated with non-adherence to established testing recommendations.

Objective

To evaluate the utilization of MMR deficiency testing in patients with colorectal cancer at a state-of-the-art oncology hospital, including both newly diagnosed and previously registered individuals presenting for treatment or follow-up, and to assess nonadherence to established testing guidelines in order to identify factors associated with gaps in the implementation of universal testing.

MATERIALS AND METHODS

This study was conducted at a state-of-the-art oncology hospital and included 117 patients with Colorectal Cancer (CRC) presenting between September 2025 and March 2026 in Gujranwala Institute of Nuclear Medicine and Radiotherapy (GINUM). Both newly diagnosed patients and previously registered patients attending for treatment or follow-up were included. Relevant clinical and demographic data were obtained from hospital records and patient files.

Patients of all ages and both sexes were considered. Individuals without a confirmed histologic diagnosis of CRC or with incomplete medical records were excluded to ensure data accuracy. Data collection focused on MMR deficiency testing status, patient demographics, tumor characteristics, and prior treatment history.

The study was conducted as a hospital-based audit and was approved by the institutional review board of the oncology center. As the analysis was performed on existing hospital records and deidentified patient information, no individual patient consent was required.

Study variables

The primary outcome variable was whether Mismatch Repair Deficiency (MMR) deficiency Microsatellite Instability (MSI/MMR) testing was completed for each colorectal cancer patient. Testing status was recorded as “Yes” or “No” based on documentation in the hospital record or pathology report, consistent with prior registry-based studies where MMR testing status was abstracted from medical records and pathology reports.

Demographic and patient-level variables included were age category (<30 years, 30–60 years, >60 years) ,gender (male; female) ,socioeconomic status (poor, middle class, good) ,family history of malignancy (present/absent) ,education level of patient or attendant (none, primary, matric, bachelor, master),clinical and tumor-related variables included: cancer stage at presentation (Stage I–IV), CRC diagnosis status (newly diagnosed *vs* previously registered patient presenting for treatment or follow-up), MMR testing result (performed *vs* not performed) .For patients who did not undergo MMR testing, reasons for non-testing were documented from clinical notes and hospital records, including categories such as not advised by clinician, lost advised testing paper, sample loss, inability to afford testing, inability to return for testing, and lack of availability of MMR/MSI testing at the hospital laboratory.

Additional variables were collected to explore potential correlates and risk factors for non-adherence to testing guidelines, including sociodemographic characteristics, clinical stage, and healthcare access factors.

Statistical analysis

The aim of this study was to assess the use of mismatch repair (MMR) deficiency testing in patients with Colorectal Cancer (CRC), including identifying factors associated with receipt of testing in older adults and evaluating underuse in younger patients.

All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) version 25. Descriptive statistics were used to summarize patient demographics, clinical characteristics, and MMR testing status. Categorical variables were presented as frequencies and percentages, with corresponding sample sizes (n).

Associations between categorical variables and MMR testing status were assessed using the chi-square (χ^2) test. For ordinal variables, the Cochran–Armitage trend test was applied where appropriate. The chi-square test statistic (χ^2 value) was calculated for each comparison, and corresponding p-values were reported.

Multivariable logistic regression analysis was performed to identify independent predictors of MMR testing among patients aged ≥60 years and factors associated with underutilization in younger patients (30-59 years). Adjusted Odds Ratios (ORs) with 95% Confidence Intervals (CIs) were calculated.

All statistical tests were two-tailed, and a p-value of <0.05 was considered statistically significant. The level of significance was predefined and consistently applied across all analyses.

RESULTS

A total of 117 patients were included in the analysis. Of these, 90 (76.9%) were male and 27 (23.1%) were female. With respect to age distribution, 20 patients (17.1%) were younger than 30 years, while 34 patients (29.1%) were older than 60 years. Age showed a statistically significant association with MMR testing status (p<0.002).

Most patients belonged to the middle socioeconomic group (69/117, 59.0%), followed by poor (38/117, 32.5%) and good (10/117, 8.5%) categories. Socioeconomic status was significantly associated with MMR testing (p-0.003).

Regarding disease stage at presentation, 47 patients (40.2%) were diagnosed at stage IV, 32 (27.4%) at stage II, 28 (23.9%) at stage III, and 10 (8.5%) at stage I. Stage at presentation was significantly associated with testing status (p<0.001) (Figure 1).

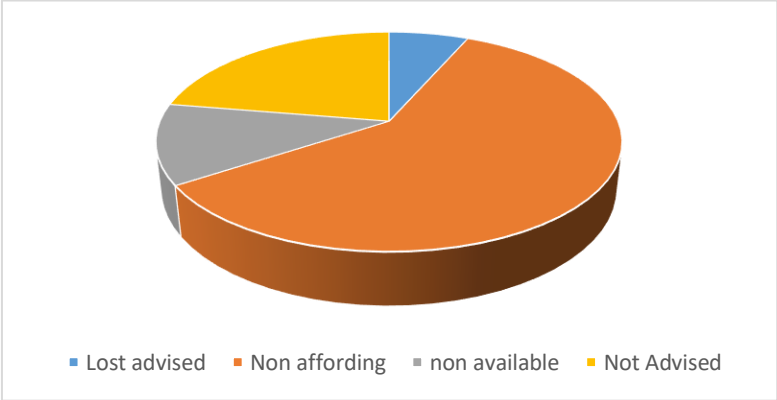

Figure 1: Reasons for non-performance of MMR/MSI Testing in Patients with Colorectal Cancer. This figure illustrates the distribution of reasons for non-performing of MMR/MSI testing among patients. Financial constraints were the most common cause, followed by lack of physician recommendation and limited availability of testing facilities.

Educational status also showed a significant association (p = 0.003), with 47 patients (40.2%) having matric-level education, 28 (23.9%) primary education, 16 (13.7%) bachelor's degree, and 6 (5.1%) master's degree, while 20 (17.1%) had no formal education.

MMR/MSI testing was performed in 33 patients (28.2%), whereas 84 patients (71.8%) did not undergo testing. Among those not tested, the most common reason was financial constraint (45/117, 38.5%), followed by lack of physician advice (17/117, 14.5%) and non-availability of testing facilities (9/117, 7.7%). These factors were significantly associated with non-testing (p<0.002).

A family history of malignancy was present in 12 patients (10.3%) and absent in 105 patients (90.0%), with a statistically significant association observed (p<0.001) (Table 1).

Variable	n(Percentage)	P value
Age		**<0.002**
<30	20(17.10%)	
>60	34(29.10%)	
Gender		**0.5**
Female	27(23.10%)	
Male	90(76.90%)	
Socioeconomic status		**0.003**
Good	10(8.50%)	
Middle class	69(59.00%)	
Poor	38(32.50%)	
Stage		**<0.001**
I	10(8.50%)	
II	32(27.40%)	
III	28(23.90%)	
IV	47(40.20%)	
Education		**0.003**
Bachelor	16(13.70%)	
Masters	6(5.10%)	
Matric	47(40.20%)	
No formal education	20(17.10%)	
Primary	28(23.90%)	
MMR Testing		**<0.01**
No	84(71.80%)	
Yes	33(28.20%)	
Cause of not testing		**<0.002**
Lost advised	5(1.70%)	
Non affording	45(38.50%)	
non available	9(7.70%)	
Not Advised	17(14.50%)	
Sample lost	4(3.40%)	
Unable to go to lab for testing again	4(3.40%)	
Family history		**<0.001**
No	105(90.00%)	
Yes	12(10.30%)	

Table 1: Association of patient and clinical characteristics with MMR testing status1

Categorical variables were analyzed using the chi-square (χ^2) test. P-values<0.05 were considered statistically significant.

DISCUSSION

In this study, MMR/MSI testing was performed in a relatively small proportion of patients (28.2%), showing clear underuse in our setting. Similar findings have been reported in previous studies, including the analysis from the National Cancer Database, where testing rates were also found to be low despite clear recommendations for routine use. This suggests that the problem is not limited to one region but reflects a broader gap between guidelines and actual practice [5,6].

One of the main factors associated with lack of testing in our patients was socioeconomic status. Patients from lower-income groups were less likely to undergo testing, and cost was the most commonly reported reason [7,8]. This is not surprising in our setting, where many patients pay out of pocket. Earlier studies have also shown that access-related factors, including financial limitations and healthcare coverage, significantly affect whether patients receive recommended testing [7,9].

Education level also appeared to play a role. Patients with lower educational background were less likely to undergo testing, which may be due to limited awareness or difficulty in understanding the importance of such investigations. This has been observed in other studies as well, where better-informed patients were more likely to receive guideline-based care [10,11].

Another important issue was that a number of patients were not advised testing at all. This points toward gaps at the physician level. Even though MMR testing is now widely recommended, it is still not being consistently incorporated into routine practice. Similar patterns have been described in larger datasets, where testing was underutilized even in eligible and high-risk patients [11,12].

Most of our patients presented at advanced stages, and stage was significantly associated with testing. In real-world practice, patients presenting late are often managed with priority given to immediate treatment, and additional testing may be overlooked or delayed. On the other hand, patients diagnosed earlier may be more likely to go through complete workup, including molecular testing [2].

Family history was also significantly associated, although only a small proportion of patients reported a positive history. This may reflect underreporting or lack of awareness about family history, which is common in our population [1,3,4].

Overall, the findings suggest that underutilization of MMR/MSI testing is due to a combination of factors, including cost, lack of awareness, limited access, and inconsistent clinical practice. Addressing these issues will require practical steps such as improving physician awareness, ensuring availability of testing, and reducing financial barriers so that more patients can benefit from appropriate evaluation [5].

LIMITATIONS

This study has a few limitations. It was conducted at a single center with a relatively small sample size, which may limit how widely the findings can be applied. Some of the data, particularly reasons for not undergoing testing, were based on patient reporting and may be subject to recall bias. In addition, we did not assess physician-related factors in detail, which could have provided further insight into why testing was not advised in some cases. Finally, as this was an observational study, causal relationships cannot be established.

CONCLUSION

MMR/MSI testing remains underutilized in patients with colorectal cancer in our setting. Financial constraints, lack of awareness, and inconsistent physician recommendation appear to be the main contributing factors. Efforts to improve access to testing, increase clinician awareness, and reduce cost barriers are needed to ensure that more patients receive appropriate evaluation and benefit from guideline-based care.

DECLARATIONS

Conflict of interest

The authors declare no conflict of interest.

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Author contributions

The authors contributed to the conception, design, analysis, interpretation, and writing of this manuscript.

Consent for publication

Not applicable.

Declaration of interest

The authors declare no conflicts of interest related to this work.

Availability of data and materials

All data generated or analysed during this study are included in this published article.

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