DOI:10.31557/APJCC.2026.11.4.583

RESEARCH ARTICLE

Identification of BRAF Variants and Their Frequency in Colorectal Cancer Patients from Iraq

Ayat Majeed Zeadan[1,2]* Tarek A.A. Mousaa[2], Ahmed Rushdi Abdullah[1]

[1]Botany and Microbiology Department, Faculty of Science, Cairo University, Egypt. [2]Microbiology Department, Collage of Medicine, Al-Iraqia University, Iraq.

Abstract

Introduction: Colorectal cancer (CRC) is a biologically heterogeneous disease characterized by diverse molecular alterations that influence tumor behavior and clinical outcomes. This study aimed to investigate BRAF gene alterations in Iraqi CRC patients. **Materials and Methods:** A total of 110 tissue biopsy samples were collected from CRC patients attending Ghazi Al-Hariri Specialized Surgery Hospital in Baghdad between November 2023 and August 2024, along with 36 tissue samples from individuals without colorectal cancer serving as controls. Genomic DNA was extracted from formalin-fixed paraffin-embedded (FFPE) tissues. A 209 bp fragment of the BRAF gene was amplified by PCR and analyzed using bidirectional Sanger sequencing. Identified variants were annotated using public databases (dbSNP and ClinVar). **Results:** Demographic analysis revealed no significant difference in gender distribution between cases and controls ($p > 0.05$), whereas age differed significantly ($p = 0.001$), with CRC patients being older. Tumors were most frequently located in the colon and rectum, and moderately differentiated adenocarcinoma represented the predominant histological subtype. Four BRAF variants were identified among CRC cases: two missense substitutions, AGT→AGG (p.Ser→Arg) and GAC→GTC (p.Asp→Val), and two intronic variants located outside the coding region. In addition, two single nucleotide polymorphisms (SNPs), rs2128998532 and rs2128998070, were examined in a subset of cases. The rs2128998532 T>C variant was observed predominantly in the heterozygous CT genotype (93.75%), while rs2128998070 (A>G) showed a heterozygous AG genotype frequency of 75% among analyzed samples. Two were missense coding variants resulting in amino acid substitutions, and two were intronic variants. All identified variants were previously reported in public databases. The affected cases included tumors from different anatomical sites and disease stages, with no evident clustering by stage or histological grade. **Conclusion:** Two common BRAF SNPs showed high prevalence in the limited subset analyzed; however, no association analysis with disease stage or risk was performed due to sample size limitations.

Keywords: Colorectal Cancer- BRAF- Mutation- SNPs

Asian Pac J Cancer Care, **11 (4)**, 583-590 Submission Date: 04/01/2026 Acceptance Date: 05/15/2026

Introduction

Colorectal cancer is the most common cancer of the gastrointestinal tract. Its mortality is expected to exceed heart disease mortality [1, 2]. Polyps are what these growths are called, and they can grow slowly for ten to twenty years before developing into cancer. The most prevalent kind is an adenoma or polyp that developed from granular cells, which line the walls of the large intestine with mucus [3].

Patients aged 20 to under 50 years had an increased incidence proportion (IP) of colorectal cancer (CRC) from 1.46 in 2000 to 4.36 per 100,000 people in 2019, representing an annual percentage change of 5.6%. In 2000 and 2019, the IP and APC for patients over 50 years of age increased from 12.7 to 40.59 per 100,000 population, respectively, from 3.69% in 2000 to 6.5% in 2019, the proportion of CRC cases to all malignancies in Iraq increased [4]. The assessment of RAS and BRAF mutational status is one of the main steps in the diagnostic and therapeutic algorithm of metastatic colorectal cancer (mCRC). Multiple mutations in the BRAF and RAS

Corresponding Author:
Dr. Ayat Majeed Zeadan
Microbiology Department, Collage of Medicine, Al-Iraqia University, Iraq. Botany and Microbiology Department, Faculty of Science, Cairo University, Iraq.
Email: ayat.m.zedan@aliraqia.edu.iq

pathway are described as a rare event, with concurrent variants in BRAF genes observed in approximately 0.05% of mCRC cases [5]. About 10–15% of CRCs have BRAF mutations, with BRAFV600E mutations being the most common. A mutation in BRAF causes constitutive activation of the MAPK signaling pathway. BRAF encodes a serine/threonine protein kinase, which is a downstream effector of the KRAS protein. From a molecular perspective, BRAF mutations may be a primary event for oncogenesis and represent an early stage in the carcinogenesis process that activates the MAPK pathway. BRAF mutations are associated with the location of CRC and have been found to be more common in females and right-sided, poorly differentiated tumors [6]. Only 2% of individuals with metastatic colorectal cancer had non-V600 BRAF mutations, which are extremely uncommon. Younger patients, primarily men, have these mutations. Tumors are more likely to have concurrent RAS mutations, are often well-differentiated, and are less usually found in the right colon. Patients with metastatic colorectal cancer who had either the RAS wild-type or the V600E BRAF mutation had better survival rates [7]. Women are more likely to have right-sided colon cancer, which also typically exhibits BRAF mutations and microsatellite instability. Men are more likely to develop left-sided colon cancer, which also exhibits KRAS mutations and chromosomal instability [8-10]. So, this study aimed to screening for BRAF genes mutation in CRC patients.

Materials and Methods

Study design: Case-control study

Patients and sampling

A total of 110 tissue biopsies samples were collected from Ghazi AL-Hariri Specialized Surgery Hospital/ Medical City Hospital, Baghdad Iraq, in period extended from November 2023 to August 2024. In addition, 36 tissue sample collected from patient free of colon cancer. Patients included in the present study were from different provinces in Iraq.

Classification of subjects and samples included in current study according to histopathological findings as patients was classified according to the site of tumor either in (colon, rectal, or rectosigmoid) and type of tumor either (poorly or moderate or well differentiated adenocarcinoma, or mucinous adenocarcinoma).

Patient cancer included both gender (male and female) aged from aged from 23 to 70 years old.

Control group included patient suffering from symptoms of digestive system problem especially on colon and rectal site with varies clinical cases including (celiac disease & autoimmune enteropathy, ulcerative colitis, congestion & edema, mild acute self-limited colitis, Hirschsprung disease [hypo ganglionic type], colonic polyps, or benign tumor), also blood and tissue samples were collected from both gender (male and female) aged from 6 to 69 years.

Five ml of venous blood were collected in gel tube from patients, placed at room temperature for 30min and then, centrifuged at 4000 r.p.m for 5 min. to separate the serum, stored at -20°C.

Tissue biopsy from included subjects were kept at -20°C for molecular analysis. Data were collected from each patient and control group included (name, age, gender, previous treatment). Histopathology findings of each patient were obtained from laboratory reports.

Included criteria: Patients with colon cancer.

Excluded criteria: patients missing of histopathological reports (patients' data).

Polymerase chain reaction

Patients DNA was extracted using Trans gene DNA from tissue block after soaked in ethanol for discard all paraffin waxes in tissue following manufacturer instructions. DNA was stored at -200C

Screening for BRAF genes was done by using specific primer in Table 1.

The PCR reaction for amplifying BRAF gene was prepared in a final volume of =25 µl=. The master mix included EasyTaq Master Mix, forward and reverse primers, and nuclease-free water, with =2 µl of DNA (100 ng) added to each reaction. A non-template control (NTC) was also prepared. PCR amplification was performed using a thermal cycling program consisting of initial denaturation, followed by 35 cycles of denaturation, annealing at 52°C, and extension, with a final extension at 72°C. The expected PCR product size was 209 bp. For verification, PCR products were run on a 1.5% agarose gelprepared in 0.5X TBE buffer and stained with RedSafe. After solidifying the gel, samples were loaded into wells and electrophoresed at 100 Vfor 90 minutes. The resulting bands were used to confirm successful amplification.

Control group DNA samples were not available for SNP genotyping due to insufficient DNA quantity and quality following extraction.

Next Generation Sequencing (NGS)

For the purpose of determining the sequence of nitrogenous bases using Next Generation Technology (NGS) for some colon cancer patients genotypes, for both BRAF and K-ras genes, 16 laboratory tubes were sent containing PCR products for each gene and sent to the Macrogen Inc. (Seoul, South Korea). Data obtained from the company were sequenced and analyzed using bioinformatics software. Sanger sequencing was performed on the amplified PCR fragments using an ABI3730XL automated DNA sequencer (Macrogen Corporation, Korea). Bioedit software showed the genotypes after aligning with a reference sequence in the Gene Bank. BioEdit is a software that is widely used in molecular biology research. It was initially designed as a Windows-only biological sequence alignment editor. It has various sequence alignment capabilities, such as easy hand alignment, split window view, user specified color, information-based shading, and auto interaction with other applications like Clustal W and Blast. However, it has been greatly improved in recent years to merge many additional features and functions

into valuable molecular tools for molecular biologists, such as many forms of hand alignment, plasmid drawing and annotation, restriction mapping, and much more. With its versatile molecular biology tools, it has become one of the most extensively used programs in molecular biology. Its shareware licensing, efficient, up-to-date modules and speedy ability to provide findings make it one of the most popular applications among molecular biologists today. rs2128998532 and rs2128998070 were genotyped in 16 CRC cases due to resource constraints. Allele frequencies were compared with published Middle Eastern and global population data (gnomAD, 1000 Genomes). DNA extraction from control samples yielded low concentration and fragmented DNA, which was inadequate for successful SNP sequencing despite repeated attempts.

Statistical analysis

Statistical Package for Social Sciences (SPSS) version 21 is used to interpret the data. The information is given in the form of a mean, standard deviation, and ranges. ANOVA was used to compare between tested mean. Continuous variables summarized as mean ± SD; categorical variables as counts and percentages. In addition, Hardy-Weinberg equilibrium (HWE) assessed for SNPs. While Odds ratios (ORs) with 95% confidence intervals (CI) could not be calculated without control genotype data.

Results

Patients demography

The study included 110 colorectal cancer (CRC) patients and 36 control individuals. The gender distribution in patients was 23 females (52%) and 21 males (48%), with no significant difference compared to controls ($p > 0.05$), indicating that gender is not a confounding factor. The mean age of patients was 50.6 ± 13 years (range 10–70), significantly higher than controls ($p = 0.001$). Most patients were aged 42–62 years, with a smaller proportion ≥63 years, indicating that older age is more common among CRC cases, Table 2.

Tumors were predominantly located in the colon (left-sided) and rectum, with smaller proportions in the right colon (cecum, appendix, ascending colon) and ileocecal valve. Histologically, moderate differentiation was the most common (56.8%), followed by well- and poorly differentiated adenocarcinomas, mucinous

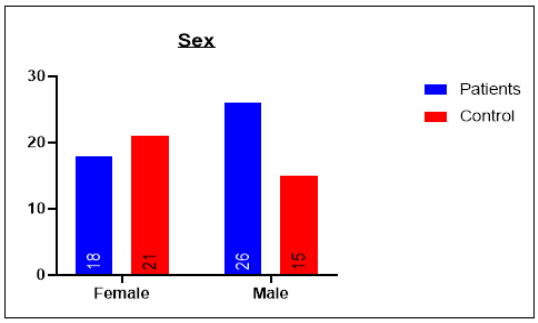

Figure 1. Gender Comparison between Patients and Control Groups

adenocarcinomas, and rare neuroendocrine tumors. TNM staging was available for a subset of patients (Stage I to T4, N0–N2). The colon was the most frequent site of tumor occurrence (18 cases, 40.9%), followed by rectal tumors (12 cases, 27.3%) and rectosigmoid lesions. Less common tumor sites included the appendix, ileocecal valve, ascending colon, and combined right colon–appendix locations (2.3% each). Due to incomplete clinicopathological annotation, tumors were not formally stratified into right-sided versus left-sided colorectal cancer categories, and no inferential analysis regarding tumor sidedness was performed. Therefore, these findings are presented descriptively. Occasional cases labeled as "colon from liver metastasis" reflect the biopsy source rather than the primary tumor origin and were included solely for anatomical documentation. Controls were patients with non-cancer digestive system disorders. The most frequent tissue site was the colon (47%), and the most common condition was colonic polyps (33.3%). Other conditions included mild inflammatory changes, autoimmune enteropathy, celiac disease, and benign tumors.

Histopathological examination revealed that moderately differentiated adenocarcinoma was the predominant tumor type, accounting for 25 cases (56.8%). Other adenocarcinoma subtypes included well-differentiated (4.5%) and poorly differentiated adenocarcinoma (2.3%). Mucinous neoplasms, including mucinous adenocarcinoma (6.8%) and low-grade appendiceal mucinous neoplasm (LAMN) (2.3%), constituted a smaller proportion of cases. Rare histological entities such as well-differentiated neuroendocrine tumors (2.3%) were also identified, reflecting histological heterogeneity within the cohort. The control group consisted of individuals with gastrointestinal disorders

Table 1. Primer Sequences for BRAF Gene

Primers	Primer Sequences	
BRAF	5′-AATGCTTGCTCTGATAGGAAAAT-3′	509 bp
	5′-TAATCAGTGGAAAAATAGCCTC-3′	

Table 2. Demographic Characteristics of Patients and Controls

GROUP	N	Male	Female	Mean Age ± SD	Age Range	p-value (Age)
Patient	44	21 (48%)	23 (52%)	50.6 ± 13	23–71	0.001
Control	36	17 (47%)	19 (53%)	41.2 ± 12	20-65	-

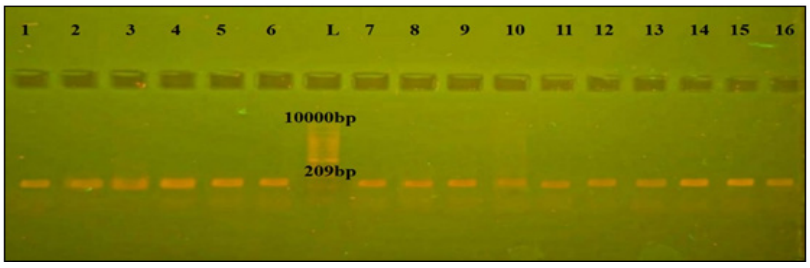

Figure 2. Agarose Gel Electrophoresis (1% agarose, 5 V/cm for 120min) for BRAF (amplified size 510 bp) of Colon Cancer Patients from Biopsy as Compared with (10000pb) DNA Ladder Lane (L). All lanes represent positive results to BRAF gene.

who were histologically negative for colorectal cancer. Control samples were primarily derived from colonic tissue (17 cases, 47.2%), followed by colonic biopsies (22.2%), as shown in Table 5. Histopathological diagnoses in the control group were heterogeneous, with colonic polyps representing the most frequent finding (33.3%). Other conditions included mild inflammatory changes such as congestion and edema, as well as a smaller proportion of inflammatory and autoimmune diseases (approximately 16.8%), including ulcerative colitis and celiac disease.

Genotypic analysis was performed by PCR using DNA extracted from tissue blocks. Amplified products of the BRAF gene were visualized at 209 bp using gel electrophoresis compared to a 100 bp DNA ladder. Representative bands are shown in Figure 2. All patient samples yielded clear amplification, confirming the quality of extracted DNA.

In the current study Sequence analysis reveals many mutations in BRAF gene in colorectal cancer in Iraqi patients, Figure 3, 4.

The mutations details in BRAF gene inpatients 13, 14, 15, 18 as follows: in patients 13 the site of mutation was chr7:140753320 causes change in normal code from AGT to AGG so change in amino acid, in patients 14the site of mutation was chr7:140753273 causes no change in normal code changes in intron. In patients 15 the site of mutation was chr7:140753375causes change in normal code from GAC to GTC so change in amino acid, while in in patients 14the site of mutation was chr7:140753442causes no change in normal code changes in intron, Table 3.

Sequence analysis for forward and reverse primers of BRAF showing the mutation sites in patients

Two single nucleotide polymorphisms (SNPs) in the BRAF gene were examined in this investigation in individuals with colon cancer:

rs2128998532 (T > C): Variant CT and Wild-type TT. Samples of patients: 1/16 (TT homozygous), 15/16 (CT heterozygous). rs2128998070 (A > G): Variant: AG and Wild-type: AA Samples of patients: 4/16 (AA homozygous) and 12/16 (AG heterozygous).

Because control group DNA samples were not available for SNP genotyping, no case–control comparison, odds ratio calculation, Hardy–Weinberg equilibrium testing, or allele frequency comparison could be performed. Accordingly, SNP genotype distributions are reported descriptively among CRC patients only. Among CRC cases, 93.75% were observed to carry the heterozygous CT genotype. No control comparison was available; therefore, these findings are descriptive only. while only 1 patient had the wild-type (TT). This suggests that the T > C variation may be prevalent in colon cancer cases, potentially influencing BRAF function. The impact of T > C variation in colon cancer is unclear, but it could affect BRAF expression levels, signaling efficiency, or interaction with other oncogenic pathways.

Table 3. Mutations in BRAF (HGVS) Gene

Patient	Amino Acid Change	Normal Code	Site	dbSNP ID	HGVS c. notation	HGVS p. notation	Variant Type
13	S > R	AGT → AGG	chr7:140753320	rs2128998223	c.123A>G	p.Ser41Arg	Missense
14	–	–	chr7:140753273	rs1586014199	c.IVS3+2A>G		Splice donor, intron
15	D > V	GAC → GTC	chr7:140753375	rs121913335	c.456A>T	p.Asp152Val	Missense
18	–	–	chr7:140753442	rs2128998636	c.IVS5-10C>T		Intron variant

Table 4. Clinicopathological Characteristics of Patients with Identified BRAF Mutation

Patient ID	Sex	Tumor location	Histology	Grade & TNM Stage	MSI/MMR Status
13	Male	Ileocecal valve	Poorly differentiated adenocarcinoma	T3 N2b MX	Not tested
14	Male	rectum	Moderate differentiated adenocarcinoma & desmoplastic stroma	PT3N1cMx	Not tested
15	Male	Sigmoid colon	Moderate differentiated glands & desmoplasia	-	Not tested
18	Male	Colon (liver metastasis)	Mucinous adenocarcinoma	Moderate to poorly	Not tested

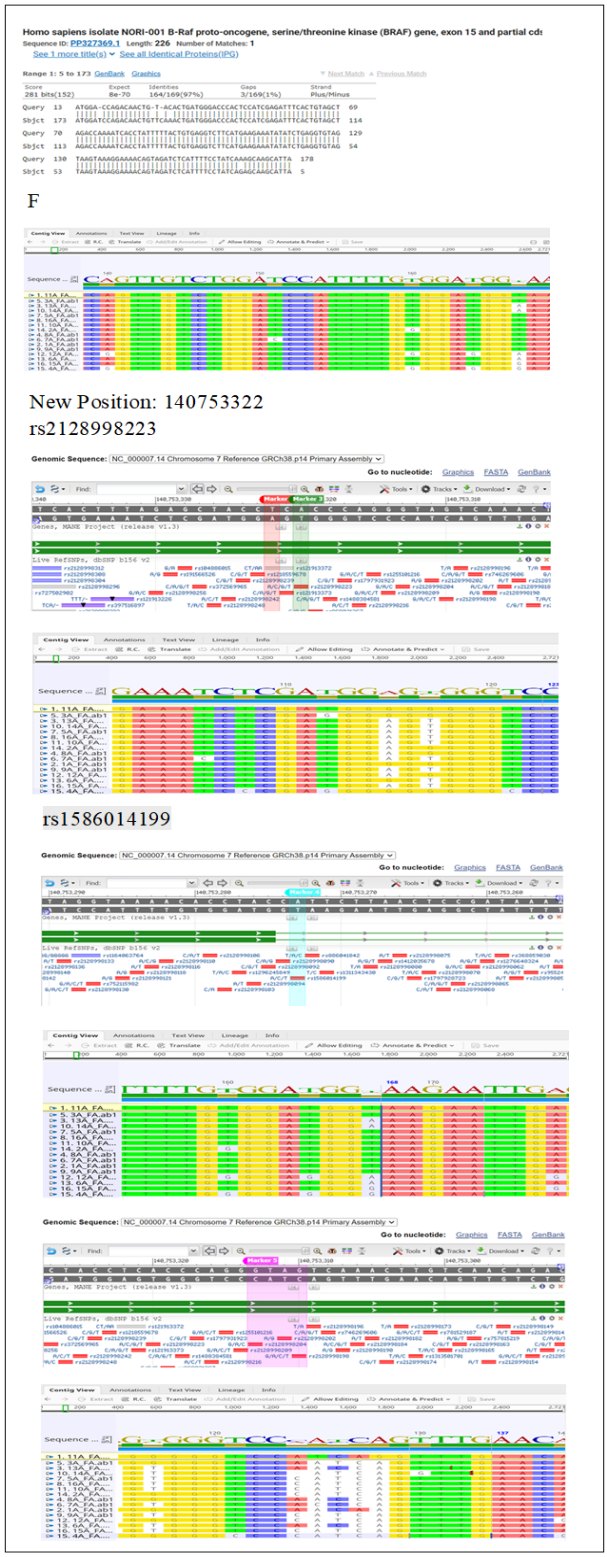

Figure 3. Sequence Analysis of Forward Primer of BRAF

For rs2128998070 (A > G) Shows a Mixed Pattern as 12 patients (75%) carried the AG heterozygous variant, while 4 patients (25%) had the wild-type AA genotype. The presence of A > G substitution may indicate a potential role in colon cancer, though further functional studies are needed to assess whether this SNP alters BRAF signaling activity, table 5, figure 5, 6, 7. Note: SNPs are reported descriptively; no statistical association with disease or functional impact has been analyzed in this study.

Discussion

In the current study male was more susceptible to get colon cancer than female especially in age more than 50 years. This may relate to differences in life style or sex hormone or diet habit such as eating spacy food or smoking with aging human body defenses become weak with recurrent infection and accumulation of inflammatory products may causes mutations thus progress of cancer. Men are more likely to have a diet high in red and processed meat, be heavier consumers of alcohol, and more likely to smoke [11, 12]. Men also have a greater propensity to deposit visceral fat which is associated with increased risk of CRC [13].

An epidemiological study for colon cancer in Iraq included 73 patients from 2014-2016, they found that males are more prone to get colon cancer than females between 50 and 60 years, and site of cancer was Right colon cancer is more prevalent [14]. Another Iraqi study in 2023 described the main symptoms and main characteristics of CRC on 79 patients, they found in spite of older people are more likely to develop CRC, but young people can be affected and both younger and older individuals both had similar symptoms and clinicopathologic features which is bleeding per rectum [15].

In the current study, highest site frequency was in colon (40%), followed by rectal with 27.3% but highest colon cancer type was moderate differentiated adenocarcinoma with frequency (56%), despite the fact that colon cancer is categorized based on whether it is rectal or colon, yet It has been observed that there are differences between colon and rectal cancer with regard to etiology, genetics, anatomy, clinical manifestation, biological characteristic, responsiveness to treatment, and clinical outcomes. Diet, smoking, and physical activity are examples of lifestyle factors that have distinct effects on colon cancer than on rectal cancer. Treatments for colon and rectal cancer vary based on TNM stage. Colon and rectal cancers in stages I and IV are often treated as one single entity [16].

The current study new mutation in BRAF gene was recorded in Iraqi patients may having a role in initiating of CRC. Mutation in BRAF gene having an important role in outcome of CRC that may be results inflammatory response accumulated in the aera thus development of CRC. The site and type of mutation was different according to aera and stage of tumor, age of patients, microbial infection, even may varies in one population to another.

In this study, BRAF variants were identified in 4 of 16 CRC patients (25%). The variants include two missense mutations (p.Ser41Arg and p.Asp152Val) and two intronic/splice region variants. These non-V600E variants are extremely rare in global CRC datasets. Tumor locations included rectal, sigmoid, ileocecal, and colon with liver metastasis. Functional significance of these variants cannot be determined based on the current data, and no clinical outcome data are available. Observed frequencies and variant types are descriptive and do not establish a causal role in CRC pathogenesis. Further functional studies and population comparisons are needed

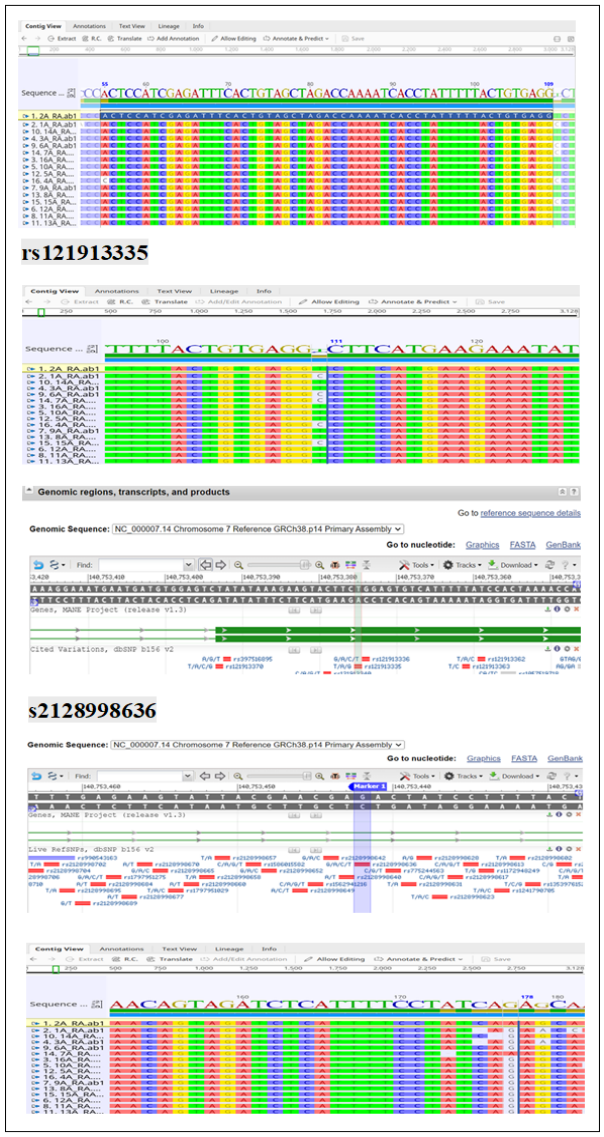

Figure 4. Sequence Analysis of Reverse Primer of BRAF

to assess potential pathogenicity.

It has been discovered that BRAF, an oncogene, is mutated in a notable percentage of tumors up to 10-15% of all CRC patients. With 98% of all BRAF gene mutations being BRAF V600, this mutation is the most common. Right-sided CRC is the primary site of observation for this mutation [17]. While 42% of BRAF-mutated colorectal cancer (CRC) tumors can be classified as belonging to this group, a significant fraction still belongs to other subtypes that are not immune-related. BRAF mutation-positive colorectal cancer tumors express a large number of genes related to antigen-presenting capabilities [18]. They were all members of the class of molecules known as major histocompatibility complex (MHC) II, which are mostly produced by lean antigen-presenting cells.

Mutations in the B-raf proto-oncogene (BRAF) gene are linked to the development of colon cancer. The encoded protein is a part of the signaling pathway known as mitogen-activated protein kinases/extracellular signal-regulated kinases (MAPK/ERK), which carries information from the external environment into the cell nucleus. The regulation of cell growth, migration, and proliferation is the primary role of the MAPK/ERK pathway. The V600E mutant (class I) is the result of the most frequent mutations in the BRAF gene. It is characterized by constant activation and signal transduction independent of external stimuli. Cancer patients with these mutations consequently have increased cell invasion and proliferation. Colon cancer and the V600E mutation have been connected [19]. The control group comprised patients with heterogeneous benign or inflammatory gastrointestinal conditions. This heterogeneity may confound comparisons with CRC cases and limits interpretation of mutation prevalence differences. A major limitation of this study is the absence of SNP genotype data for the control group. This prevented calculation of disease-association statistics such as odds ratios, relative risk, Hardy–Weinberg equilibrium testing, and allele frequency comparisons. Consequently, it cannot be determined whether the observed SNP distributions represent disease-associated variants or common population polymorphisms. Future studies including adequately genotyped control cohorts are required to validate these findings in accordance with epidemiological reporting standards.

In conclusion, BRAF variants were identified in a subset of Iraqi CRC patients, including coding and intronic changes, but functional significance and disease association remain unknown. Current data are descriptive, and no clinical recommendations can be made. Further functional studies and larger patient cohorts are needed to confirm whether these SNPs influence tumor progression, therapy resistance, or prognosis in colon cancer.

Table 5. SNPS on BRAF Gene among Colon Cancer Patients

BRAF Gene ID 673		
SNPs	rs2128998532	rs2128998070
Wild	TT	AA
Variation	T>C	A>G
Samples		
1A	CT	AG
2A	CT	AG
3A	CT	AA
4A	CT	AG
5A	CT	AG
6A	CT	AG
7A	CT	AA
8A	CT	AA
9A	CT	AG
10A	CT	AG
11A	CT	AG
12A	CT	AG
13A	CT	AG
14A	CT	AG
15A	CT	AG
16A	TT	AA

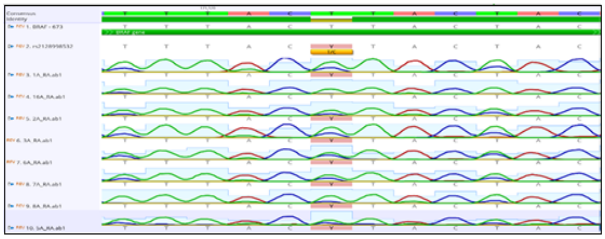

Figure 5. rs2128998070 SNP in BRAFA Gene

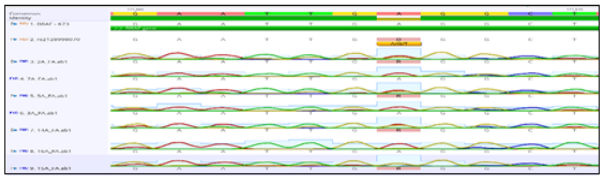

Figure 6. rs2128998532SNP in BRAFA Gene

Figure 7. Sequence Analysis for BRAF Gene

Declarations

Funding

This study was fully funded by Ayat Majeed Zeadan.

Clinical trial registration

Not applicable.

Conflicts of interest/Competing interests

Authors declare that they have no conflicts of interest.

Availability of data and material

The data sets used and/or analyzed during the current study are available from the corresponding authors per reasonable request.

Code availability

The custom code was used.

Authors' contributions

Ayat M. Zeadan contributed to the conception, design, and final drafting of the manuscript, contributed to data collection, contributed to the primary drafting of the manuscript. Mousaa A. A. and Ahmed R. supervised the study. All authors approved the final version for submission.

Ethics approval

This study was approved by ethical committee of the College of Medicine- AL-Iraqia University in Baghdad, (No. FM. SA/140- Date 1/10/2023)

Consent to participate

Written informed consent was obtained from all participants, and the trial was conducted in accordance with the Declaration of Helsinki.

Consent for publication

Written informed consent was obtained from all participants, and the trial was conducted in accordance with the Declaration of Helsinki.

Originality Declaration for Figures

All figures included in this manuscript are original and have been created by the authors specifically for the purposes of this study. No previously published or copyrighted images have been used. The authors confirm that all graphical elements, illustrations, and visual materials were generated from the data obtained in the course of this research or designed uniquely for this manuscript.

Acknowledgments

We extend our heartfelt gratitude to all the patients who generously contributed to this study.

References

1. Aljarshawi M, Albadree H, Bahar H, Al-Imam A. Misleading Presentation of Colorectal Cancer in an Otherwise Healthy Patient. Journal of the Faculty of Medicine Baghdad. 2020;62(4):132-138. https://doi.org/10.32007/jfacmedbagdad.6241800
2. Dhahir NK, Noaman AA. A Comparative Study of Colorectal Cancer Based on Patient's Age. Journal of the Faculty of Medicine Baghdad. 2021 07 13;63(2):70-73. https://doi.org/10.32007/jfacmedbagdad.6321825
3. Huck MB, Bohl JL. Colonic Polyps: Diagnosis and Surveillance. Clinics in colon and rectal surgery. 2016 Dec;29(4). https://doi.org/10.1055/s-0036-1584091
4. Ibrahem S, Ahmed H, Zangana S. Trends in colorectal cancer in Iraq over two decades: incidence, mortality, topography and morphology. Annals of Saudi medicine. 2022 08;42(4). https://doi.org/10.5144/0256-4947.2022.252
5. Zelli V, Parisi A, Patruno L, Cannita K, Ficorella C, Luzi C, Compagnoni C, et al. Concurrent RAS and RAS/BRAF V600E Variants in Colorectal Cancer: More Frequent Than Expected? A Case Report. Frontiers in oncology. 2022 04 07;12. https://doi.org/10.3389/fonc.2022.863639
6. Bellio H, Fumet JD, Ghiringhelli F. Targeting BRAF and RAS in Colorectal Cancer. Cancers. 2021 05 03;13(9). https://doi.org/10.3390/cancers13092201
7. Zarkavelis G, Boussios S, Papadaki A, Katsanos KH, Christodoulou DK, Pentheroudakis G. Current and future biomarkers in colorectal cancer. Annals of gastroenterology. 2017;30(6). https://doi.org/10.20524/aog.2017.0191
8. Kim SE, Paik HY, Yoon H, Lee JE, Kim N, Sung MK. Sex- and gender-specific disparities in colorectal cancer risk. World journal of gastroenterology. 2015 05 07;21(17). https://doi.org/10.3748/wjg.v21.i17.5167
9. Moretto R, Cremolini C, Rossini D, Pietrantonio F, Battaglin F, Mennitto A, Bergamo F, et al. Location of Primary Tumor and Benefit From Anti-Epidermal Growth Factor Receptor Monoclonal Antibodies in Patients With RAS and BRAF Wild-Type Metastatic Colorectal Cancer.

The oncologist. 2016 08;21(8). https://doi.org/10.1634/theoncologist.2016-0084
10. Benson AB, Venook AP, Cederquist L, Chan E, Chen YJ, Cooper HS, Deming D, et al. Colon Cancer, Version 1.2017, NCCN Clinical Practice Guidelines in Oncology. Journal of the National Comprehensive Cancer Network : JNCCN. 2017 03;15(3). https://doi.org/10.6004/jnccn.2017.0036
11. Chang LC, Wu MS, Tu CH, Lee YC, Shun CTt, Chiu HM. Metabolic syndrome and smoking may justify earlier colorectal cancer screening in men. Gastrointestinal endoscopy. 2014 06;79(6). https://doi.org/10.1016/j.gie.2013.11.035
12. Bates B, Cox L, Nicholson S, Page P, Prentice A, Steer T, et al. National Diet and Nutrition Survey: Results from Years 5 and 6 (combined) of the Rolling Programme (2012/2013–2013/2014). London: Public Health England; 2016.
13. White A, Ironmonger L, Steele RJC, Ormiston-Smith N, Crawford C, Seims A. A review of sex-related differences in colorectal cancer incidence, screening uptake, routes to diagnosis, cancer stage and survival in the UK. BMC cancer. 2018 09 20;18(1):906. https://doi.org/10.1186/s12885-018-4786-7
14. Meryud Abood A, Mohammud Habash M, Mohammed M J. Epidemiology of Colonic Cancer in Baghdad City, Iraq. Iranian Journal of War & Public Health. 2022;14 (3):331-337.
15. Farhad RM, Saleh ES, Alsammarraie AZ. Clinicopathological features of colorectal cancer in the Iraqi population focusing on age and early-onset of malignancy: A descriptive cross-sectional study. Al-Rafidain J Med Sci. 2023;5:86-91. https://doi.org/10.54133/ajms.v5i.158.
16. Doumouras AG, Tsao MW, Saleh F, Hong D. A population-based comparison of 30-day readmission after surgery for colon and rectal cancer: How are they different?. Journal of Surgical Oncology. 2016 09;114(3):354-360. https://doi.org/10.1002/jso.24334
17. Taieb J, Lapeyre-Prost A, Laurent Puig P, Zaanan A. Exploring the best treatment options for BRAF-mutant metastatic colon cancer. British Journal of Cancer. 2019 09;121(6):434-442. https://doi.org/10.1038/s41416-019-0526-2
18. Petrelli F, Tomasello G, Borgonovo K, Ghidini M, Turati L, Dallera P, Passalacqua R, et al. Prognostic Survival Associated With Left-Sided vs Right-Sided Colon Cancer: A Systematic Review and Meta-analysis. JAMA oncology. 2017 02 01;3(2):211-219. https://doi.org/10.1001/jamaoncol.2016.4227
19. Śmiech M, Leszczyński P, Kono H, Wardell C, Taniguchi H. Emerging BRAF Mutations in Cancer Progression and Their Possible Effects on Transcriptional Networks. Genes. 2020 Nov 12;11(11):1342. https://doi.org/10.3390/genes11111342