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The prevalence of HSV1 expression in Iraqi patients with colorectal cancer

Basim Mohammed Khashman[1], Hujaz Ismail Abdulrazzaq Alqirbi [2], Heba F. Hassan[3]

[1] National Cancer Research Center (NCRC), University of Baghdad, Iraq

[2] Department of Basic Sciences. College of Dentistry, University of Baghdad, Iraq

[3] Department of Medical Microbiology-College of Medicine-University of AL_Qadysha-Iraq

ABSTRACT

Background: Colorectal Cancer (CRC) is one of the most serious health problems and Herpes viridae may hasten the progression of colon cancer.

Aim: The purpose of conducting this research is to investigate the existence of Herpes Simplex Virus (HSV1) infection in samples of Colorectal Cancer (CRC) compared with normal tissue.

Material and Methods: 40 samples of tissues (30 patients) with CRC, and (10 samples) of normal tissue (without cancer) were obtained, for immunohistochemically analysis of Herpes Simplex Virus (HSV1) expression

Results: The results showed no significant data to justify the link between both Herpes Simplex Virus (HSV1) and human colorectal cancer. Despite of presence of Herpes Simplex Virus (HSV1) found in six samples (20 %) by using Immunohistochemistry staining. There is a low relationship between the presence of HSV1 and CRC. The results supported a histopathological diagnostic element; it could possibly be seen in the diagnosis and treatment of CRC.

Key words: Colorectal Cancer (CRC), Herpes Simplex Virus (HSV1) Immunohistochemical (IHC).

Address for correspondence:
Basim Mohammed Khashman,
National Cancer Research Center (NCRC), University of Baghdad, Iraq
E-mail: basim@bccru.uobaghdad.edu.iq

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INTRODUCTION

Colorectal Cancer (CRC) is currently one of the most concerning health issues in the world. In 2012, 1.4 million additional cases of CRC had been diagnosed, as according to documents, and this form of tumor claimed the lives of over 700,000 people [1]. Colorectal Cancer (CRC) effects are typically absent till a mass rises to a large size. Colorectal Cancer (CRC) is prevalent in Australia, America, Canada, Singapore, North Western Europe, Japan, and China with a low incidence observed in Asian countries and Africa [2]. According to the National Colorectal Cancer Panel discussion in 2015, there is an exponential increase in CRC occurrence which could achieve up to 80%. [3]. Such causes include a high-fat diet, being overweight, family background, Eating red meat, cigarettes, alcohol drinking, k- RAS mutagenesis, tumor suppressor gene inhibition, MLH1 and MSH2 mutants, DNA methylation interruption, microsatellite instability, and viral infections [4- 6]. It is now thought that a strong link exists between viral infectious conditions and various types of tumours [7]. Furthermore, Herpes viridae may hasten the progression of colon cancer [8]. Herpes viridae viruses are categorized as double-stranded DNA family viruses that can evade the immune system through various mechanisms [9]. Herpes Simplex Virus (HSV1) is one of the most prevalent viruses causing chronic infectious diseases in humans [10]. During the initial infection, HSV1 replicates in mucoepithelial cells of the throat and oral cavity. As a neurotropic virus, it infects sensory neurons and causes a long-term viral infection, most commonly in the trigeminal ganglia. [11]. Possible causes, in addition to genetic risk factors, may play a role in CRC pathogenicity [12]. High-fat diet, fatness, family background, red consumption of meat, and cigarettes, consumption of alcohol, k-RAS mutation, contagious disease, and tumor suppressor gene inhibition are examples of environmental exposures [13,14]. There seems to be a strong link for both contagious risk factors and various cancers [15]. Herpes viridae may hasten the

progression of colon cancer [16]. The Herpes viridian group contains a variety of proteins, including EBNA-1, which might disrupt cell growth control [17]. The aim of this research study the prevalence of HSV1 in Iraqi CRC biopsies

MATERIALS AND METHODS

Immunohistochemistry assay of HSV1 expression

Thirty of formalin-fixed paraffin embedded samples of archival tissues from CRC patients (18 female and 12 male) were collected from the Gastrointestinal and liver teaching hospital in Baghdad City between the months of September 2020 and March 2021. To determine the grade of CRC, a pathologist examined the CRC samples. Every block had been 4 mm thick once cut and it was adhered to positive charge slides. Haematoxylin and eosin staining were required. The first tissue section was located on a standard slide. Other positive charge slides had been immunohistochemically stained with anti-HSV-1 antibodies from (ABCAM company/UK) according to the protocol described. Immunostaining on CRC tissue is negative (colourless), whereas cells with a brown cytoplasmic colour change are positive. A light microscope was used, as well as a scoring system which considers all antibody force and the intensity of positive cells [18]. The Least Significant Variation-LSD test (ANOVA) was done using the Statistical Analysis Software in analysis parameters to create a significant comparison among means. In this study, percentages were analysed using the Chi-square test (0.05 and 0.01 probability) [19].

RESULTS AND DISCUSSION

30 test results (12 female and 18 male) were obtained from patients with CRC Figure 1. grade G2, ages generally range from (22 years-79 years), to a mean age of 55.5 years. They were all matched by Tumor Adjacent Normal (TAN) samples.

Immunohistochemistry has been used to establish the expression of HSV1. In this study, Powerful brown discoloration was shown in most cells with positive (20%) expression was observed in 6 samples of CRC Table 1 and Figure 2. Were there no positive results in the control group.

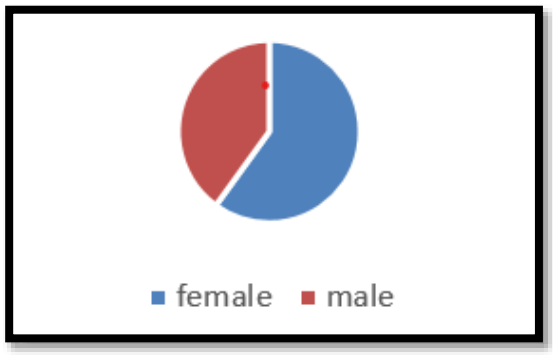

Fig. 1. Distribution of CRC patients according to sex

Tab. 1. Distribution of sample study according to HSV1 expression

	HSV1 No. (%)	Control
Positive	6 (20 %)	0
Negative	24 (80%)	30
Total	30	30
Chi-Square (χ^2)	(2.13) NS	NS

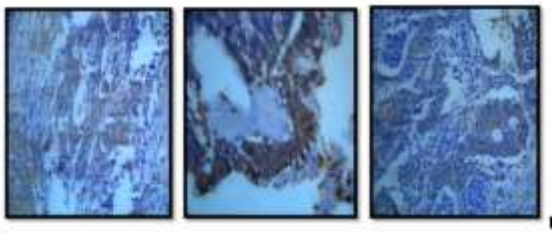

Fig. 2. Immunohistochemically results in Colorectal Carcinoma tissues. (40x): Positive expression of HSV1 in Colorectal carcinoma

Colorectal cancer is considered one of the world's most serious medical conditions through aspects of health complications, and it is able to take responsibility for the world's short life expectancy. Gross' new finding of a viral cause of mouse model leukaemia sparked a surge in the investigation for oncogenesis virus infections in human tumours. According to current knowledge, oncogenic viruses are responsible for approximately 15.0% of total world cancer incidence [20]. Oncogenic viruses could promote human carcinogenesis by causing genetic instability and chromosomal abnormalities [21]. So several risk factors,

particularly viral ones, have been linked to the progression of CRC. Distinct oncovirus-specific proteins were always thought to apprehend few other biological processes in cells, of consequences ranging from cell growth regulation to key role in the early stages of a broad variety of human forms of cancer [7]. The purpose of this study is to look into the role of HSV1 in CRC sufferers as well as the role of CRC progression. We found that the percentage of the presence of this virus is low, and this is due to the lack of samples taken. In addition Collagen and mucin substances in better and healthier colon tissues can inhibit HSV-1 viral infection, but their reduction of expression in malignant tissues outcomes in HSV-1 induction [22]. Previous research has also shown that herpes viridae could still cause certain different cancers [23]. These findings agree with one that looked at the detection of CMV, EBV, HSV-1, and VZV antibodies [24]. HSV DNA was found through both cancerous and compared normal tissue of five CRC patients (33.3 percent) [25]. Another study showed no statistically significant difference in the existence of human herpesvirus among both CRC case and control groups [26]. Also in Iran, there is a study that has proven that there are no herpes viruses in Iranian patients infected with CRC [27]. But currently, most of the studies that have been discussed at the present time are to investigate this virus for a therapeutic purpose, as they found that involvement of this virus (HSV1) in colorectal cancer treatment [28]. The combined effect of (IL-18) and HSV Thymidine Kinase (HSV-TK) could boost Human Telomerase Reverse transcriptase (hTERT) promoter activity in mice, eventually eradicating colorectal cancer. [29]. Few statistically significant correlations between infection with viruses and CRC were observed in investigations on human herpesviruses (including CMV, EBV, HSV-1, and VZV). However, there were significant discrepancies in the laboratory analytical methodologies used among research, and almost all of the included studies had relatively small sample sizes (CRC case counts ≤ 60). While there were significant variances across the primers used, most research using the nested-PCR approach found higher CMV infection rates than studies using southern blot or Immuno Histochemistry (IHC). These findings highlight the potential confusing impact of laboratory procedures on the comparison of research findings. Further consensus on the criteria for detecting human herpesvirus DNA will be crucial for future studies. Furthermore, given the viral hit-and-run oncogenesis idea, negative results must be read cautiously [30]. Another theory holds that viruses can cause cancer by integrating their viral genomes into human genomes; the former may vanish and be undetectable at the time during the cancer diagnosis. Human herpesvirus infections may play a role in the development of colorectal cancer, even if epidemiological research does not conclusively link them to CRC [31].

CONCLUSION

We conclude from the study that there is a low relationship between the presence of HSV1 and CRC, but the result is not significant between HSV1 and CRC.

AUTHOR CONTRIBUTIONS

Basim M. Kashman made a design for this study and made Immunohistochemistry staining of the tissue sections as well. Heba F. Hassan wrote, processed the data, reviewed the original copy and all the researchers supervised the study and financed this research. All authors have read and agreed to the published version of the manuscript.

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