**How to Cite**:
Alqirbi, H. I. A., Hassan, H. F., & Khashman, B. M. (2022). The possible role of high risk HPV infection in Iraqi patients with colorectal cancer. *International Journal of Health Sciences*, *6*(S6), 3437–3443. https://doi.org/10.53730/ijhs.v6nS6.11458

# The possible role of high risk HPV infection in Iraqi patients with colorectal cancer

**Hujaz Ismail Abdulrazzaq Alqirbi**
Department of Microbiology, Al-kindy College of Medicine, Baghdad University, Iraq

**Heba F. Hassan**
Department of Basic Sciences. College of Dentistry. University of Baghdad, Iraq

**Basim Mohammed Khashman**
National cancer research center (NCRC), University of Baghdad, Iraq
*Corresponding author email: basim@bccru.uobaghdad.edu.iq

***Abstract*---**Aims: the aim of this study is to study the existence of a relationship between CRC and HPV in samples of Iraqi patients. Material and methods: 30 samples of formalin-fixed, paraffin- embedded archival tissues from CRC patients were obtained, together with 10 samples of normal tissue (free cancer), for immunohistochemical analysis and HPV expression.Results: Immunohistochemical (IHC) staining revealed only four cases with HPV infections while. At ≤ P 0. 05, there is no significant difference.Conclusion: The results of this study we discovered statistically no relation with both HPV infection and CRC although, the presence of oncovirus may play a role tumorigenic progression.

***Keywords*---**HPV, CRC, oncovirus, IHC, oncogenesis.

## Introduction

The third most prevalent form of tumor is colorectal cancer (CRC) diagnosed in (6.1%) and the second leading cause of death (9.2 %). It is predicted that by 2035, the total number of deaths from CRC will increase from (60% -71.5%)[1]. It is widely recognized that disease is a sign of a

country's socio-economic status development [2]. Lifestyle, body obesity, and food trends all have a role in the rise in morbidity[3]. Physical activity appears to have a protective impact, according to the data. As the frequency of red color and its treatment rises, so does the danger of acquiring the condition, meat and alcoholic beverages are two of the most popular foods in the world [2,4]. According to the most recent WHO data from 2018, the predicted mortality rate from CRC cancer in Iraq was 6.30 percent. Despite the fact that the death rate for colorectal cancer has increased in various Arab nations (5.64 %Oman, 7.14 %Saudi Arabia 13.92% Jordan, 14.88 %Syria, 8.14% Qatar and 4.23% Egypt) [5]. CRC is a multi-step process that frequently takes more than ten years to develop, This implies that opportunities for early detection and prevention exist [6]. Infections with (HPV) human papillomavirus are the most prevalent sexual transmission viruses. and epidemiological data between HPV with CRC is controversial and CRC's pathogenesis is still unknown, despite the fact that number of studies have mentioned HPV may have a consequence on the progression of CRC [7]. In a review article published in 2011, HPV occurrence in CRC tissues was confirmed at 41.7 %, compared to 32.0 percent in neighboring normal tissues [8]. While HPV DNA was not found in CRC tissues in several studies [9,10]. Therefore, the aim of this study investigate the virus infection in CRC patients and to study the existence of a relationship between CRC and HPV in samples of Iraqi patients.

## Materials and Methods

### Immunohistochemistry assay of RPD3 and HPV expression

Thirty samples of formalin-fixed, paraffin-embedded archival tissues from CRC patients (12 female &18 male) were obtained from the Liver and Digestive System Technical Hospital in Baghdad city between the months of February 2020 and September 2021. A pathologist examined the CRC samples to determine the grade of CRC. When cut, each block was 4 mm thick and was applied to positively charged slides. To be stained with hematoxylin and eosin. The first tissue section was put on a regular slide. Other sections were immunohistochemically stainig using anti- HPV16 antibody from (ABCAM company/ United Kingdom) according to manufacturer's protocol [11].

### Determine of Immunohistochemistry

Absence of immunostaining on CRC tissue indicates a negative reading, whereas cells with brown nuclear and cytoplasmic coloration reveal a positive reading. Using a light microscope and a scoring system that considered both antibody strength and the frequency of positive cells [11].

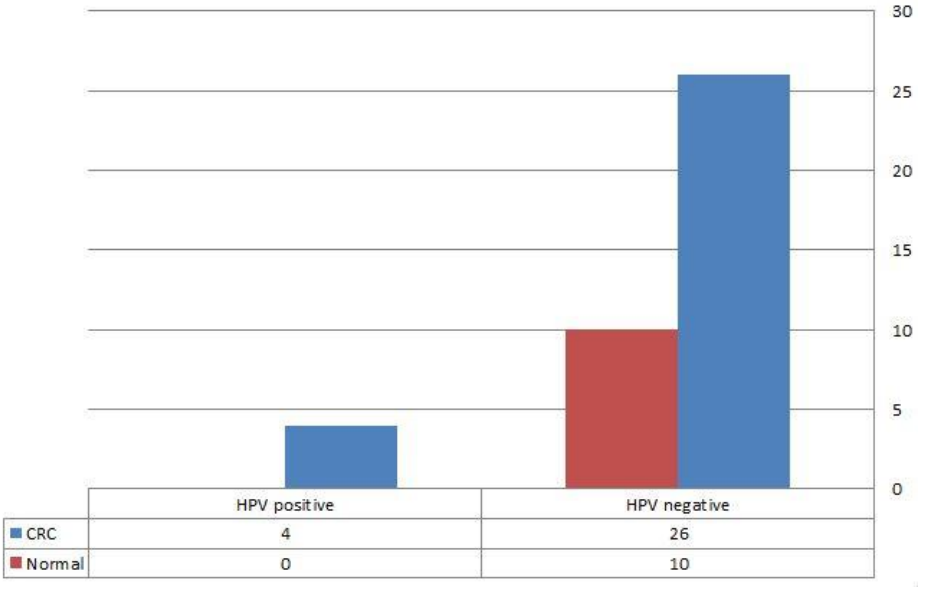
**Statistical Analysis**

To determine the impact of various components. Excel and the Fisher exact test was used to analyze percentages in this study at(0.05 Significance Level) [12].

**Results and Discussions**

thirty specimens (12 females &18 males) were collected from patients with CRC with ages ranged from (22 to 79) year, with an average of 55.5 year. They all had tumor adjacent normal (TAN) samples that matched. A method was used for detection is Immunohistochemistry . The expression ratio of HPV appeared in only four samples (15%) of CRC .There is no significant difference at $P < 0.05$ (Figure 1).

Table 1: Immunohistochemistry expression of HPV expression



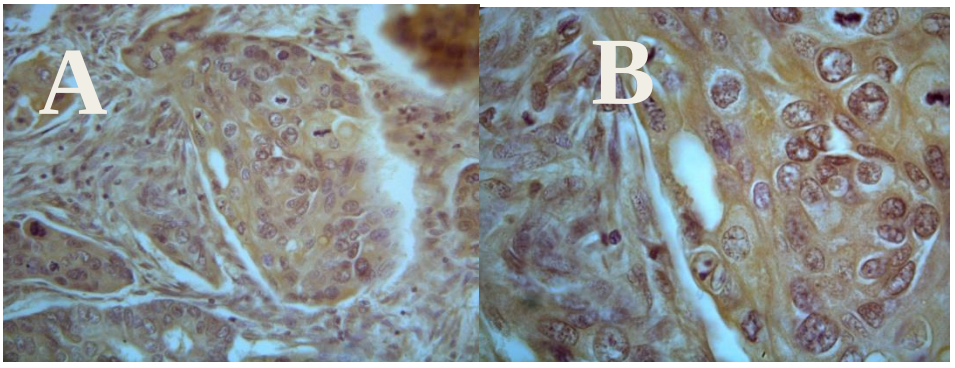



Figure 1. Immunohistochemical results in Colorectal Carcinoma tissues. A (40x), B (100X): Positive expression of HPV in Colerectal carcinoma.

**Discussion**

Colorectal cancer (CRC) was still the 3rd most frequent tumor in people all over the world. CRC is among the most prevalent generates of tumors, and the patients' prediction with CRC particularly dictated by their diagnosis step. As a result, early identification is critical for extending life expectancy. [13]. In this study HPVs had been identified as causal organism of invasive cervical tumor , with high-risk HPVs being found in (96 %) of these malignancies [14]. HPV pathogen can cause a change in the infected cell's biochemistry which is intriguing given that high-sugar diets, as well as metabolic problems that cause overweight as a whole, had been linked to an elevated risk of CRC [15,16]. Numerous researchers, one of which was conducted by our group, have found that elevated HPVs, notably types 16, 18, 31, 33& 35 were viewable in patients CRCs [17,18]. It's interesting to note that high-risk HPV infection was insufficient to cause malignant transformation changes in person with normal epithelial tissues. Multiple genetic alterations must also occur in infected cells or/and be infected by some other oncovirus to complete their conversion and as a result form tumors. Based on this theory a study was conducted utilizing human normal epithelial (HNE) cells to investigate the influence of collaboration of the high HPVs and other of the high-danger HPVs and other human oncogenes, carcinogenesis was found that high- danger type 16 E6/E7 oncoproteins collaborate with receptor of ErbB-2 to cause cellular conversion in HNE cells .This had been aided by the delocalization of -catenin from either the plasma membrane towards the nucleus, and it was later discovered that the E6,E7&ErbB-2 collaboration targets cyclin D1 via the transformation of -catenin's activity from a cell-cell adhesion molecule to a transcriptional regulator by -catenin delocalization from the plasma membrane to the nucleus [19]. And also found that in human HNE and mouse normal embryonic fibroblast (NEF) cells, D-type cyclins

D1, D2& D3 were required for cell changes triggered such as E6,E7&ErbB-2 collaboration [19,20]. Finally, reveal that in human normal epithelium and tumor cells, the cooperative influence of E6 and E7 through ErbB-2 is induce by -catenin tyrosine phosphorylation and activation of pp60 (c-Src) kinase [21]. Thus, collaboration with both E6&E7 E6&E7 oncoproteins from high-risk HPVs and other oncogenes may aid in the development of colorectal cancer [22].

## Conclusion

This study's findings reveals no obvious relation with both HPV infection and CRC as oncovirus for initiation the tumor although, the infection may increase the disease burden.

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