Acta Scientific MEDICAL SCIENCES (ISSN: 2582-0931)

Volume 9 Issue 5 May 2025

Research Article

Prevalence of Human Cytomegalovirus in Breast Cancer Patients: A Cross-Sectional Study

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DOI: 10.31080/ASMS.2025.09.2070

Received: March 17, 2025

Published: April 10, 2025

Abstract

Background: Human Cytomegalovirus (HCMV) is a widespread herpesvirus that remains latent in the body of healthy individuals and reactivates during the weakness of the immune system. This virus has been implicated in many malignancies and has been found to cause graft rejections and several other complications. This study aimed to determine the prevalence of HCMV-DNA viremia among breast cancer, and associate it the type and grade of the cancer.

Methods: 88-female patients with confirmed breast cancer have been included in the study. Blood samples (5 ml) were collected from patients at armed forces hospitals from January 2023 to March 2024. Detection of CMV-DNA is achieved through molecular methods, specifically using quantitative PCR (qPCR) with the COBAS 5800 system. Statistical analysis was performed by Chi-square test of independence with P value significant < 0.05.

Results: HCMV-DNA detected in 11.3% (10:88) of the cases. Among these, 9 cases were ductal carcinoma, and single was medullary carcinoma. HCMV prevalence was highest in grade I tumour (6 cases), then by grade II (2 cases), and grade III (2 cases). Most cases exhibited low viral load (8:10), while only two cases has medium viral load.

Conclusion: Our Results suggests a low prevalence of HCMV-DNA viremia among our study participants, most cases detected in ductal carcinoma, and early-stage tumour. Further research is essential and required to classify HCMV role in breast cancer progression and prognosis.

Keywords: CMV; HCMV-DNA Viremia; Immune System; Breast Cancer

Introduction

Breast cancer is initiated by various genetic and environmental factors. Studies shows that genetics plays a role in increasing the risk of breast cancer [1]. Environmental factors, such as exposure to pollutants, can also contribute to its development [2].

Human cytomegalovirus (HCMV) is a ubiquitous member of the Herpesviridae family, with high prevalence rate around the world, several studies have determined that HCMV can lead to health complications in immunocompromised patients [3,4]. This virus is asymptomatic on healthy hosts, and when the immune system is compromised and weakened, the virus reactivates and causes severe complications [3]. In addition, HCMV in cancer patients raises questions about its potential role in the progression of the disease and associated with poor prognosis in breast cancer [5].

While this virus is typically known to be asymptomatic, HCMV is established to be lifelong latent infections, and correlated with many diseases [7,8,13]. Work in the medical field and research have been analyzing the role of this virus with many diseases and found out to have a major impact on patients especially when the immune system is weakened, these roles have been studied in transplantation and malignancies [3,7,10,13]. A study published before has analyzed the prevalence of HCMV in breast cancer patients, and revealed that 2 samples from their 27 samples were positive for HCMV genes UL122 and UL83 [15]. HCMV also were reported to target many cells in the body even the tissue of the breast, this can potentially lead to poor prognosis and complications among breast cancer patients [5,9].

In this study, the aim is to detect the prevalence of HCMV among breast cancer patients according to type and grade.

Materials and Methods

Study group

A total of 88 participants, all from Taif city were enrolled in the study with confirmed breast cancer. The Inclusion criteria was that the patient must be from Taif city, diagnosed with breast cancer, otherwise for any patient with different type of caner or not a resident in Taif city were excluded.

Sample collection and preparation

This cross-sectional study started from January 2024 to the end of March 2024, a 5 ml blood drawn into EDTA tube. And tested for HCMV DNA by quantitative PCR (qPCR).

Detection of viral nucleic acid

The COBAS 5800 system uses fluorescent probes to detect amplified viral DNA in real-time. The results provided by the system are binary, with the output being either "Detected" or "Not Detected," depending on the viral load and threshold cycles reached during amplification. This system meet the international validation requirement, and shows high clinical sensitivity/specificity, clinical sensitivity for HCMV is 1.000 and the clinical specificity is 0.995. With full automation system for sample and data analysis that reduces the error and maximizes consistency.

Statistical analysis

To evaluate the findings of our study, the chi-square test of independence was applied. P value when less than 0.05 was considered a significant finding.

Ethical approval

This study has obtained ethical approval from the research and ethics committee of Ministry of Health and Taif University. Informed consent was provided to the participant and their approval is necessary prior of sample collection or using any of their data.

Results

The study has studied 88 samples of breast cancer patients for HCMV-DNA viraemia. In table 1, the detected cases were compared to the undetected cases of breast cancer, then, distributed by the type and grade of the cancer. Only 10 cases have shown detectable HCMV load which is 11.3%. To explain more, HCMV Low viral load: 100–1,000 IU/ml, moderate viral load: 1,000–10,000 IU/, high viral load: >10,000 IU/ml. This study only detected HCMV among medullary with a single case, and ductal with 9 cases. Moreover, 6 cases on grade I, 2 cases grade II, and 2 cases from grade III. To identify HCMV viral load in each of the detected cases, in this study the cases were distributed according to the viral load in table 2. Clearly, most of the cases have low HCMV load, with total of 8 cases explained as follows: 7 with ductal, 1 with medullary. And regarding the grade, 6 cases with grade I, and a single case with grade II, a single case of grade III. Also, medium HCMV viral load were detected as follows: 2 cases in the ductal only. And one from grade I and the other from grade II. No high CMV viral load was detected by this study.

Discussion

We have investigated in this study HCMV-DNA viraemia among breast cancer patients, which showed 11.3% and a total of 10 detected cases of HCMV. Our findings assist more in the literature that focuses on the potential role of HCMV on breast cancer patients. Majority of the detected cases were among ductal carcinomas with 9 out of the 10 detected cases. And only a single

		Not detected	Detected	Total (88)
Age (mean, SD)		51± 5	60 ± 8	53 ± 15
Type	Tubular	10	0	10
	Lobular	19	0	19
	Medullary	22	1	23
	Ductal	27	9	36
P value		0.021		-
Grade	I	44	6	50
	II	16	2	18
	III	18	2	20
Metastasis	-	0	0	0
P value		0.025		-

Table 1: The status of the patients compared by age, type and grade of cancer.

			HCMV DNA load		
		Total (10)	Low	Medium	High
Type	Medullary	1	1	0	0
	Ductal	9	7	2	0
P value			0.07		
Grade	I	6	6	0	0
	II	2	1	1	0
	III	2	1	1	0
P value			0.41		

Table 2: Viraemia due to HCMV load were distributed according to breast cancer type and grade.

case in medullary carcinoma. This is consistent with a previous study that reported the higher prevalence of HCMV among ductal breast cancer patients [15]. Another study reported widespread HCMV around all types of breast cancer [4]. Regarding the tumors grade, this study detected 'predominantly 'among grade I tumor with 6 detected cases from the total 10. Then followed by grade II, and grade III with also 2 cases. Those findings are correlated with previous study [11]. Both our findings and the literature suggest a correlation between HCMV and poor prognosis among cancer patients. The HCMV viral load was at low levels with 8 cases having low HCMV-DNA viraemia, and two cases with medium HCMV-DNA viraemia. And no case was detected with higher HCMV-DNA viraemia. Our findings did not align with the previous study by Cobbs., *et al.* they reported higher HCMV load with more aggressive breast cancer [5]. A previous study has investigated the role of this virus in breast cancer patients, which evaluated the epidemiological and laboratory findings, which indicated that HCMV can cause poor prognosis among breast cancer patients [16]. Another consistent study studied the correlation between HCMV seropositivity and cytokines level in relation to breast cancer progression, and reported that HCMV can play a major role in the alteration of the immune system balance and can promote tumor growth, Also, modulate the tumor microenvironment [17].

Still our study has limitations, the small sample size, the lack of the study of cofounders factors, and inability to track the patients over time to assess if the viral infection can influence cancer recurrence or treatment response.

Conclusion

Our Results suggests a low prevalence of HCMV-DNA viremia among our study participants, most cases detected in ductal carcinoma, and early-stage tumour. Most cases exhibited low and medium viral load. Further research is essential and required to clarify HCMV role in breast cancer progression and prognosis.

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