



# Seroprevalence of Epstein-Barr Virus IgG among Breast Cancer Patients in Shendi City, Sudan

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## Abstract

**Introduction:** Breast cancer is the most common malignancy among women worldwide, yet conventional risk factors do not fully explain its etiology. Epstein-Barr virus (EBV) has been suggested as a possible cofactor. However, data on EBV seroprevalence among Sudanese breast cancer patients are lacking. This study aims to determine the seroprevalence of EBV (VCA) IgG antibodies among breast cancer patients in Shendi City, Sudan.

**Methods:** A descriptive cross-sectional study was conducted at the Tumor Therapy and Cancer Research Center, Shendi University, from July to November 2021. Seventy patients with histologically confirmed breast cancer were enrolled. Blood samples were tested for total EBV IgG antibodies using a commercial ELISA kit. Descriptive statistics and chi-square tests were applied.

**Results:** The mean age of participants was  $50.2 \pm 10.5$  years (range: 30–80 years). Most patients were female (98.6%), married (87.1%), and diagnosed at stage II (60%). EBV IgG seropositivity was detected in 61.4% of patients. No significant associations were found between EBV positivity and age, disease stage, hormone therapy, duration of illness, or number of children.

**Conclusion:** This study documents the seroprevalence of EBV (VCA) IgG among Sudanese breast cancer patients in Shendi. These findings provide baseline data and highlight the need for larger studies with molecular techniques and control groups to clarify the potential role of EBV in breast cancer.

**Keywords:** Seroprevalence; EBV; IgG; Breast cancer; Sudan

## Introduction

Breast cancer constitutes the most frequently diagnosed malignancy and a leading cause of cancer-related mortality among women globally, imposing a significant burden on healthcare systems in both developed and developing nations [1]. This burden is particularly acute in Sub-Saharan Africa, including Sudan, where patients often present at a younger age with more

advanced-stage disease and a more aggressive clinical course compared to Western populations, leading to disproportionately high mortality rates [2]. The etiology of breast cancer is multifactorial, and while established risk factors provide some explanation, they fail to fully account for the elevated incidence and unique presentation observed in regions like Sudan. This has

prompted investigation into alternative oncogenic drivers, including environmental and infectious agents.

Among these potential contributors, the Epstein–Barr virus (EBV), a ubiquitous human gammaherpesvirus infecting over 90% of the adult population worldwide, has been a subject of interest. EBV is a well-established oncogenic virus, implicated in the pathogenesis of several lymphoid malignancies such as Burkitt lymphoma and Hodgkin lymphoma, as well as epithelial cancers like nasopharyngeal carcinoma [4–10]. Its potential role in breast carcinogenesis, however, remains controversial and inconclusive. Numerous studies have investigated this link, yielding inconsistent results; some have detected the EBV genome or expressed proteins in breast tumor tissues, while others have found no such association [11–18]. These discrepant findings are likely attributable to methodological variations, including differences in detection techniques (serology versus molecular assays on tissue), sample types, and geographical or genetic heterogeneity among the studied populations. Critically, despite the high burden of breast cancer in Sudan and the ongoing debate regarding EBV's oncogenic potential, there is a pronounced lack of data on EBV exposure and its possible association with breast cancer in this specific demographic [11]. To address this significant knowledge gap, the present study was designed to determine the seroprevalence of EBV in breast cancer patients in Shendi City, Sudan. By employing serological assays to detect EBV-specific antibodies, this research aims to establish crucial baseline data on viral exposure and provide a foundation for future, more extensive investigations into the potential role of this ubiquitous virus in breast oncogenesis within this understudied population.

## Materials and Methods

### Study Design and Setting

A descriptive, hospital-based, cross-sectional study was conducted at the Tumor Therapy and Cancer Research Center, Shendi University, Sudan. The study aimed to determine the seroprevalence of Epstein-Barr virus (EBV) and recruit a consecutive sample of eligible patients. The data and sample collection period spanned from July to November 2024.

### Study Population and Eligibility Criteria

The study population comprised 70 adult female patients with a new or existing, histologically confirmed diagnosis of breast cancer. A consecutive sampling method was employed to recruit participants who presented at the center during the study period. Patients without a confirmed histopathological diagnosis of breast cancer were excluded from the study to ensure the specificity of the study population. Sample Collection and Processing

### Sample Collection and Processing

From each enrolled participant, approximately 5 mL of venous blood was aseptically drawn via venipuncture and collected into commercially available EDTA-coated vacuum tubes (BD Vacutainer®, USA) to prevent coagulation. The blood samples were immediately processed by centrifugation at  $3000 \times g$  for 5 minutes at room temperature to separate the plasma fraction. The resulting plasma was carefully aliquoted into sterile, pre-labeled cryovials and stored at  $-20 \text{ }^{\circ}\text{C}$  in a dedicated freezer until subsequent serological analysis, with all samples processed within 4 hours of collection to preserve analyte integrity

### Serological Testing for EBV

The detection of total immunoglobulin G (IgG) antibodies against the Epstein-Barr virus viral capsid antigen (EBV VCA) was performed using a commercial, qualitative Enzyme-Linked Immunosorbent Assay (ELISA) kit (Foresight, Acon Laboratories, Inc., San Diego, USA), according to the manufacturer's prescribed protocol. This assay was selected based on its high reported diagnostic performance, with a sensitivity of 98.0% and a specificity of 98.3%. All samples, along with the provided calibrators and controls, were tested in duplicate to ensure result reliability, and optical density was measured using an ELISA plate reader.

### Data Analysis

Data were analyzed using SPSS version 28. Descriptive statistics were used to summarize demographic and clinical variables. Associations between EBV positivity and selected variables were explored using the chi-square test, with a significance level of  $P < 0.05$ . Given the small sample size, further regression analysis was considered exploratory only.

## Results

A total of 70 patients diagnosed with breast cancer were enrolled in this study, comprising 69 females (98.6%) and one male (1.4%). The mean age of participants was  $50.2 \pm 10.5$  years, with the majority falling within the 41–60-year age range (61.4%). Most patients were married (87.1%) and resided in rural areas (60.0%). Regarding educational status, 31.4% had primary education, 27.2% university education, 25.7% secondary education, and 15.7% were illiterate. Clinically, most participants were diagnosed at Stage II (60.0%), followed by Stage III (21.4%) and Stage I (18.6%). Approximately 42.9% reported receiving hormonal therapy, while 57.1% did not (Table 1). Serological testing revealed that EBV (VCA) IgG antibodies were present in 43 (61.4%) of the participants, indicating previous exposure to EBV infection, whereas 27 (38.6%) tested negative (Table 1). Analysis of associations between EBV seropositivity and various demographic and clinical factors revealed no significant relationships with age group ( $P = 0.808$ ), cancer stage

( $P = 0.544$ ), use of hormonal supplements ( $P = 0.085$ ), duration of disease ( $P = 0.181$ ), or number of children ( $P = 0.181$ ). However, a statistically significant association was observed between EBV IgG seropositivity and marital status ( $P = 0.004$ ), where married women exhibited a higher seroprevalence of EBV antibodies compared to unmarried women (Table 2). These findings suggest a widespread exposure to EBV among breast cancer patients in Shendi City, Sudan, and provide an important foundation for further molecular investigations into its potential role in breast carcinogenesis.

**Table 1: Sociodemographic and Clinical Characteristics of Breast Cancer Patients.**

Variable	Category	Frequency (n)	Percentage (%)
Sex	Female	69	98.6%
	Male	1	1.4%
Age (Years)	30–40	16	22.9%
	41–50	21	30.0%
	51–60	22	31.4%
	61–70	9	12.9%
	71–80	2	2.9%
Marital Status	Married	61	87.1%
	Single	9	12.9%
Education Level	Illiterate	11	15.7%
	Primary	22	31.4%
	Secondary	18	25.7%
	University	19	27.2%
Residence	Rural	42	60.0%
	Urban	28	40.0%
Cancer Stage	Stage I	13	18.6%
	Stage II	42	60.0%
	Stage III	15	21.4%
Hormonal Supplements	Yes	30	42.9%
	No	40	57.1%
EBV (VCA) IgG Result	Positive	43	61.4%
	Negative	27	38.6%

**Table 2: Association between EBV IgG Seropositivity and Patient Factors.**

Variable	P-value
Marital Status	0.004
Age Group	0.808
Cancer Stage	0.544
Hormonal Supplement	0.085

Duration of Disease	0.181
Number of Children	0.181

## Discussion

Breast cancer continues to represent a major global health challenge, with its incidence steadily increasing in both developed and developing nations [1,2]. In Sub-Saharan Africa, including Sudan, the disease tends to affect women at younger ages and often follows a more aggressive clinical course [2]. Given the multifactorial nature of breast cancer, attention has increasingly turned to potential infectious cofactors, including oncogenic viruses such as Epstein–Barr virus (EBV) [3]. In this cross-sectional study conducted at the Tumor Therapy and Cancer Research Center – Shendi University, we determined the seroprevalence of EBV among breast cancer patients and examined its relationship with key demographic and clinical factors. The predominance of female patients (98.6%) and the mean age of 50.2 years observed in this cohort are consistent with global and regional epidemiological trends, reinforcing the fact that breast cancer predominantly affects middle-aged women. The detection of EBV IgG antibodies in 61.4% of participants indicates a high prevalence of prior EBV exposure, aligning with the virus’s known global ubiquity [4–10]. This seroprevalence is comparable to reports from neighboring countries, such as Egypt (58–63%) [18] and Eritrea (55%) [19], suggesting that EBV exposure among breast cancer patients is common across the region. However, seropositivity alone cannot distinguish latent infection from active viral replication or directly implicate EBV in tumor development.

The statistically significant association between EBV seropositivity and marital status ( $P = 0.004$ ) may reflect differences in social interaction patterns, household crowding, or lifestyle factors influencing viral transmission. EBV is primarily transmitted via saliva, and exposure risk may correlate with interpersonal contact and family structure, both of which could differ by marital status. However, this finding should be interpreted cautiously, as it does not necessarily imply a biological link between marital status and cancer risk. No significant associations were observed between EBV serostatus and clinical parameters such as age, cancer stage, hormonal therapy, disease duration, or parity. These findings are in agreement with several previous studies that also failed to establish a consistent relationship between EBV infection and clinicopathological features of breast cancer [12–18]. The lack of association may be attributed to the serological nature of the test, which reflects past infection rather than direct viral involvement in tumor tissue. Although this study provides valuable baseline seroepidemiological data, it is limited by its cross-sectional design, modest sample size, and reliance on serological detection,

which cannot confirm active EBV presence in malignant tissue. Future research should employ more sensitive molecular techniques, such as polymerase chain reaction (PCR) targeting EBNA-1 or LMP-1 genes, in situ hybridization, or immunohistochemistry, to detect viral DNA or protein within tumor cells [20]. Including a well-matched control group would further clarify whether EBV infection prevalence is higher among breast cancer patients than in the general population.

## Conclusion

This study demonstrates a high seroprevalence of EBV among breast cancer patients in Shendi City, Sudan, consistent with trends observed in neighboring countries. While no clear associations with clinical parameters were established, these results emphasize the importance of expanding investigations using molecular diagnostic approaches. Such studies are essential to elucidate whether EBV acts as an incidental passenger or a potential cofactor in the pathogenesis of breast cancer, thereby contributing to a better understanding of cancer etiology in Sudan and the wider Sub-Saharan region.

## Limitation

While this study offers important insights, certain aspects of its design present opportunities for further investigation. The reliance on serological data provides a robust measure of past viral exposure but does not directly inform on the presence of the virus within tumor tissue. Additionally, the focus on a patient cohort from a single center, while providing a clear initial profile, highlights the value of future multi-center studies that could include matched control groups for a broader comparative perspective.

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Not applicable.

## Author contributions

H.A.E.A. conceptualized the study, designed the methodology, and supervised the research process. S.M.A contributed to data collection, analysis, and interpretation of results. G.M.M was responsible for laboratory experiments and technical validation. W.I.Y.A contributed to data analysis. M.S.I.A contributed to data analysis. B.M.T.G assisted in manuscript drafting, literature review, and data visualization. All authors critically reviewed, revised, and approved the final version of the manuscript for submission.

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## Data availability

No datasets were generated or analysed during the current study.

## Declarations Ethics approval

Ethical approval was obtained from the relevant authorities before commencing the study. Blood samples were collected after receiving consent from the laboratory administration, patients, and their co-patients. The study adhered to the Ethical Principles for Medical Research Involving Human Subjects, as outlined in the Declaration of Helsinki (1975, revised in 2000).

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