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**Original Research Article**

# Sero-Detection of Human Cytomegalovirus (CMV) Infections among Cervical Carcinoma Patients in Gezira State, Sudan

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## Abstract

***Background:*** Cytomegalovirus (CMV), a member of the herpesviridae family, is believed to play a role in the development of cervical carcinoma in women. About 50–85% of people worldwide are infected with CMV by early adulthood. ***Objective:*** The purpose of this study was to ascertain the prevalence of CMV in Medani, Gezira State, among women who had cervical cancer. ***Materials and Methods:*** The study involved 50 women in total. Participants' blood samples (5 mL each) were drawn and transferred into sterile, plain blood containers. An enzyme-linked immunosorbent assay (ELISA) was used to analyze the serum for CMV IgG and IgM antibodies after it was collected by centrifugation at 3000 g for five minutes (Snibe Maglumi X3). ***Results:*** According to the findings, 32 (64%) of the 50 women tested positive for CMV antibodies, while 18 (36%) tested negative. Two (6%) of the 32 positive patients had IgM antibodies, which indicated a recent infection, whereas 30 (94%) had IgG antibodies, which indicated a previous or latent infection. According to the distribution of CMV frequency by age group, older women had a greater frequency: 3% of women aged 20–30, 22% of women aged 31–40, and 75% of women aged 40 and above. Furthermore, women with a managed menstrual cycle had a higher frequency (26%) than those with an uncontrolled cycle (20%). In addition, women who married young were more likely to do so (38%) than those who married later (26%). ***Conclusions:*** According to the study's findings, women in Gezira State with cervical cancer had a notably high frequency of CMV, especially those who were older. To confirm these results and investigate the part CMV plays in cervical carcinogenesis, more studies with larger sample numbers and more sophisticated diagnostic methods are advised.

**Keywords**: CMV, women, IgG, IgM, cervical carcinogenesis, Gezira.



## 1. INTRODUCTION

Human Cytomegalovirus (CMV) is a common beta herpes virus that has infected people all over the world. It can easily harm people with weakened immune systems [1]. One of the most frequent causes of congenital viral infections is the human cytomegalovirus (HCMV), also known as HHV-5, which is a member of the beta herpes family. Permanent hearing loss, visual loss, and neurological disability are linked to congenital HCMV infection [2]. A CMV infection mostly affects the kidneys, salivary glands, and other organs and is typically asymptomatic. Nonetheless, immune-compromised patients may experience viral replication, which could exacerbate organ damage and dysfunction [3]. The virological and immunological features of a basic CMV infection have been the subject of numerous investigations. Additionally, CMV can result in latent infection, with seroprevalences among high-risk groups ranging from over 80% in low-income nations to about 50% in the overall adult population in high-income countries [3]. By producing oncogenic proteins or interfering with cell replication, two crucial processes in the development of cancer, human herpesviruses (HHVs) can cause cell transformation. One of the HHVs that was long believed to play a part in the formation of cervical lesions was CMV. By early adulthood, between 50 and 85 percent of people worldwide are infected with CMV. It can spread through parenteral, sexual, and oral means. Even though CMV is not linked to human cancer, some research indicates that it might be especially linked to a few types of cancer [5, 6]. Intravenous ganciclovir is the preferred medication for treating CMV disease; however, valganciclovir may be used in certain cases to treat severe CMV and is also the preferred medication for solid-organ transplant patients to avoid the disease [7]. In the world, cervical cancer ranks third among

cancers that affect women. Cervical cancer remains a significant health issue in affluent nations despite improvements in identification and treatment. The most common disease among women between the ages of 15 and 44 is cervical cancer, particularly in underdeveloped nations [8]. Several additional co-factors were found, including poverty, long-term pregnancies, smoking, infection with various STIs (Human Immunodeficiency Virus, Chlamydia trachomatis, Cytomegalovirus, etc.), and young age at full-term pregnancy [9]. In addition, the Epstein-Barr virus (EBV), Cytomegalovirus (CMV), and Herpes simplex virus (HSV) are among the members of the herpes viral family that have been linked to an increased risk of cervical neoplasia and have been known to induce lifelong latency in their hosts [10]. Because Indigenous women follow unique customs, they are more likely to contract STIs, which increases their risk of developing cervical cancer [11].

## 2. MATERIALS AND METHODS

This observational, descriptive, cross-sectional study was conducted at the National Cancer Institute in Medani, Gezira State, Sudan, from November 2022 to March 2023. The study population consisted of 50 females diagnosed with cervical carcinoma, regardless of age.

### 2.1 Sample size

A total of fifty (n=50) cervical cancer-diagnosed women were collected from November 2022 to March 2023.

### 2.2 Collection of blood specimens

A volume of 5 ml of blood was collected from each patient through the venipuncture technique and then displaced into the plain container.

### 2.3 Sample processing

Each blood specimen was centrifuged at 3000 rpm for 5 minutes to obtain the serum The latter was gently collected into a plain container and stored at -20 °C until the serological analysis.

### 2.4 Analysis of specimens

The specimens were analyzed for the qualitative detection of CMV IgG and IgM antibodies by commercially available enzyme-linked immunosorbent assay 'CMV IgG and IgM ELISA' kits. The assays were performed following the instructions of the manufacturer. According to the information included in the kit's insert, the immunoassay used SNIBE MAGLUMI X3, has 98.0% sensitivity and 98.3% specificity.

### 2.5 Principle of the test

Indirect immunofluorescence techniques, Mouse anti-human IgG or IgM labeled antibody is used, and purified CMV antigen to coat nanomagnetic microbeads. Sample, Calibrator or Control with Buffer Goat Anti-Human IgM or goat Anti-Human IgG ） and magnetic microbeads coated with CMV antigen are mixed thoroughly and incubated at 37, forming a sandwich; After sediment in a magnetic field, decant the supernatant, then cycle washing for 1 time. Then add mouse labeled antibody, incubation and washing for the 2nd time. Subsequently, the starter reagents are added, and a flash chemiluminescent reaction is initiated. The light signal is measured by a photomultiplier as RLU within 3 seconds and is proportional to the concentration of CMV IgG or IgM present in samples [12].

### 2.6 Data analysis

To process the data, appropriate statistical treatments and equations were used through the statistical software. After completing the study data collection, it was sorted, coded, and then analyzed, and the researcher entered the data of this sample into a computer using Statistical Packaged for Social Science (SPSS) (version 23), the researcher used of several tests and statistical methods "descriptive statistics (Frequency and Percentage) to describe the sample data', chi-square test, And run to summarize continuous and categorical variables of the socio demographic and clinical factors; the predictors were identified and considered significant at a P-value less than 0.05.

## 3. RESULTS

**Table 1: Frequency of CMV antibodies among the study group**

| Variables | Frequency | Percentage |
|---|---|---|
| Positive | 32 | 64% |
| Negative | 18 | 36% |

**Table 2: Frequency of CMV IgG and IgM among the study group**

| Variables | Frequency | Percentage |
|---|---|---|
| IgG | 30 | 94% |
| IgM | 2 | 6% |
| **Total** | **32** | **100%** |

**Table 3: Association between CMV antibodies with controlled menstrual cycle**

| Variables | Positive | Negative | P- value |
|---|---|---|---|
| Yes | 13 | 6 | 0.00 |
| No | 10 | 21 | |

**Table 4: Association between CMV antibodies in women who married at young age.**

| Variables | Positive | Negative | P- value |
|---|---|---|---|
| Yes | 19 | 3 | 0.03 |
| No | 13 | 15 | |

**Table 5: Association between CMV antibodies in women who had a previous malignancy**

| Variables | Positive | Negative | *P- value* |
|---|---|---|---|
| Yes | 1 | 0 | 0.52 |
| No | 31 | 18 | |

**Table 6: Association between CMV antibodies and with who had a family history of malignancy**

| Variables | Positive | Negative | *P- value* |
|---|---|---|---|
| Yes | 5 | 1 | 0.42 |
| No | 41 | 3 | |

## 4. DISCUSSION

According to the study's findings, women with cervical cancer have a significant prevalence of cytomegalovirus (CMV) seropositivity. Sixty-four percent of the 50 women in the study had CMV, and most of them had IgG positivity, which suggests a latent or previous infection. This finding is consistent with earlier research by Jenny Stykova and colleagues that found a high prevalence of CMV in women with cervical carcinoma; of the 52 cervical samples, 54% were CMV-positive, with the majority of them having IgG [13]. This is probably because the virus can alter immune responses and may play a role in the development of cervical cancer. There was a significant correlation (P = 0.02) between the age groups' CMV seropositivity distributions. Women over 40 had a higher frequency (75%), compared to 22% of women between 31 and 40 and only 3% of women between 20 and 30. This pattern is consistent with findings from other studies, such as one that found an age-dependent increase in CMV frequency, with 69% of women aged 45 and older reporting a frequency that was roughly 2.5 times higher than 31% of younger women. The greater frequency in older age groups could be the result of immunological senescence-induced increased sensitivity or cumulative exposure over time [14]. Menstrual cycle control and CMV seropositivity were shown to be significantly correlated in this study (P = 0.00). CMV positive was higher in women with controlled "regular" menstrual cycles (26%) than in women with uncontrolled "irregular" periods (20%). Although the exact mechanism relating to menstrual cycle regulation and CMV seropositivity is unknown, it may have something to do with how immune responses are influenced by hormonal changes. Nevertheless, there is a dearth of research on this topic, indicating that more study is necessary. Early marriage frequently correlates with earlier sexual activity and increased exposure to sexually transmitted infections, including CMV. These findings are supported by studies like one conducted in Africa that found that women who married young had a higher frequency of CMV positivity (38%) compared to those who did not (26%) (P = 0.03). Another study found that women who married young had a higher frequency of CMV when they had earlier sexual activity (66% compared to 34%; p value = 0.01) [15]. There was no discernible correlation between CMV seropositivity and either a familial history of cancer or a history of malignancy (p values of 0.52 and 0.42, respectively). This is consistent with earlier research, such as a study that found behavioral or environmental factors, rather than genetic predisposition, are more likely to be connected to CMV [16]. Geographical and socioeconomic factors have a significant impact on the global variation in CMV frequency. High-frequency rates of 40–100% were observed globally [17] in a meta-analysis by Cannon, with greater rates in low- and middle-income nations. Like the current study, Puranik's findings supported the possibility that CMV IgG plays a co-factor in oncogenesis by highlighting its prevalence in women with gynecological malignancies [18].

The study's noteworthy correlations between age, menstrual cycle management, age at marriage, and CMV seropositivity offer fresh perspectives, although more research is needed to prove causation.

## 6. CONCLUSION

According to this study, women with cervical cancer have a high prevalence of CMV seropositivity (64%), and most of them have IgG antibodies, which are a sign of a latent or previous infection. The results point to possible relationships between CMV seropositivity and a number of behavioral and demographic characteristics. Older women (>40 years) and those who married at an early age exhibited considerably higher

frequency, whereas menstrual cycle regulation was also connected with CMV positivity. These findings are consistent with earlier studies that suggested CMV might modulate the immune system to contribute to cervical carcinogenesis. However, there was no discernible link between CMV seropositivity and a family history of cancer or a history of malignancy. The findings highlight how crucial it is to take into account CMV as a possible cause of cervical cancer, especially in high-risk groups.

## 7. RECOMMENDATION

1. Improved screening initiatives, especially for women in high-risk groups.
2. Knowledge of CMV and its possible link to cervical cancer in the public health domain.
3. Safe sexual practices and reproductive health education should be the focus of public health initiatives, especially for women living in low-resource environments.
4. Preventive measures include creating and assessing vaccines and antiviral treatments to stop CMV infection, particularly in groups that are more susceptible to cervical cancer.
5. To confirm these results and investigate the part CMV plays in cervical carcinogenesis, more studies with bigger sample numbers and more sophisticated diagnostic methods are advised.

**Consent:** The patient's written consent has been collected.

**Ethical Approval:**

The study was approved by the Department of Medical Microbiology in Medical Laboratory Sciences at Shendi University, the study was matched to the ethical review committee board. Sample collection was done after signing a written agreement with the participants. Permission for this study was obtained from the local authorities in the study area. This study's aims and benefits were explained with the assurance of confidentiality. All protocols in this study were done according to the Declaration of Helsinki (1964).

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