RESEARCH ARTICLE

Seroprevalence of human cytomegalovirus among pregnant women who had undergone abortion(s) attending El-Damazin Hospital for Obstetrics and Gynecology, Sudan: A cross-sectional study [version 1; peer review: 2 not approved]

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Abstract

Background: Human cytomegalovirus (HCMV) is a major cause of congenital infections. It is more widespread in developing countries and communities with low socioeconomic status. The infection can cause pregnancy loss or spontaneous abortion. Tests are available for the detection of HCMV IgG and IgM antibodies. Many pregnant women in Blue Nile State, Sudan, have suffered from recurrent pregnancy loss, and currently there is no available data concerning the prevalence of HCMV in Blue Nile state. This study aimed to determine HCMV antibodies (IgG and IgM) among pregnant women, who had undergone abortion(s), attending El-Damazin Hospital for Obstetrics and Gynecology.

Methods: This was a descriptive, cross-sectional hospital-based study. 270 pregnant women, who had undergone abortion(s) and who attended El-Damazin Hospital for Obstetrics and Gynecology, were included in the study from September to December 2018. Personal and clinical data were collected directly from each participant into a predesigned questionnaire. Serum samples were separated and stored at -20°C until used. Samples were analyzed for HCMV IgG and IgM using enzyme-linked immune-sorbent assay (ELISA).

Results: Participants were categorized into three age groups: 15-25 years (33.7%; 91/270); 26-40 years (62.2%; 168/270); and >41 years (4.1%; 11/270). The majority of the participants had IgG antibodies to HCMV (74.8%; 202/270), while only 13.3% (36/270) had IgM antibodies

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Approval Status

	1	2
version 1		
10 Oct 2019	view	view

1. Luiz Fernando Almeida Machado , Federal University of Pará, Belém, Brazil
2. Irena Tabain , Croatian Institute of Public Health, Zagreb, Croatia

Any reports and responses or comments on the article can be found at the end of the article.

to HCMV. Most abortion cases were documented in the first trimester (85.6%; 231/270) and this had a significant relationship with IgG level ($P=0.003$). Low socioeconomic status was recorded in 84.8% (229/270) of participants and showed significant correlation with IgG level ($P=0.025$), whereas illiteracy was reported in 41.9% (113/270) of participants and did not have a significant relationship.

Conclusions: Seroprevalence of HCMV in this study population was 74.8% for IgG antibodies. There was an association between HCMV IgG level and first trimester abortion and low socioeconomic status among the studied women.

Keywords

HCMV, Abortion, IgG, First trimester, Socioeconomic, El-Damazin, Sudan.

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Author roles: **Elbushra S:** Data Curation, Funding Acquisition, Investigation, Software, Writing – Original Draft Preparation; **Ahmed MS:** Methodology, Resources, Validation; **Talha AA:** Supervision, Visualization; **Gamar TA:** Formal Analysis, Visualization, Writing – Review & Editing; **Ahmed EA:** Conceptualization, Investigation, Project Administration, Writing – Review & Editing

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Introduction

Cytomegalovirus (CMV) is the most ubiquitous member of the herpes virus family. Human cytomegalovirus (HCMV) is the most common cause of congenital malformation resulting from viral intrauterine infection in developed countries¹. CMV infects a high percentage of individuals during their life and after recovery of disease it hides in leukocytes. Although this virus is not considered as hazardous to health, in pregnant women it is a major factor that threatens the health of neonates². Primary CMV infection occurs in 0.15%–2.00% of all pregnancies and may be transmitted to the fetus in 40% of cases³.

Seroprevalence of HCMV in adults ranges from 55% in developed countries to as high as over 90% in developing countries like China⁴. In Sudan, age is significantly associated with CMV IgM detection, and history of miscarriage was associated with CMV IgG positive women⁵. Additionally in Sudan, a study conducted in 2013 by Elamin and Omer at Khartoum Teaching Hospital reported the seroprevalence rate among pregnant women with recurrent abortion as 55.3% and 3.2% for HCMV IgG and IgM antibodies, respectively⁶. Another recent study in Sudan conducted at Omdurman Maternity Hospital reported a sero-frequency rate of HCMV among pregnant women as 74.4% for CMV IgG and 14.4% for HCMV IgM⁷.

HCMV can produce maternal infection and exhibits a high tropism for cervical mucosa and is considered as the most implicated virus in recurrent spontaneous abortion (RSA)⁸. Many pregnant women in Blue Nile State, Sudan, have suffered from recurrent pregnancy loss, and currently there is no available data concerning the prevalence of HCMV in Blue Nile state; therefore, this study aimed to determine HCMV antibodies (IgG and IgM) among pregnant women, who had undergone abortion(s) in this state.

Methods

Study design

This was a descriptive cross-sectional hospital-based study aimed to detect the seroprevalence of CMV among pregnant women, who had undergone RSA, attending El-Damazin Hospital for Obstetrics and Gynecology in Blue Nile State, Sudan, between March 2017 and February 2019.

Permission to carry out the study was obtained from the College of Graduate Studies, Faculty of Medical Laboratory Sciences, University of Gezira and Ministry of Health, Blue Nile State, Sudan. All women examined were informed about the purpose of the study before collection of the specimens and written consent for participation was taken.

Participants and variables

A total of 270 blood samples, taken for the purpose of this study, were collected under aseptic conditions from the participants and sera were separated in sterile containers and stored at -20°C until tested. The inclusion criterion were all pregnant women attending El-Damazin Hospital for Obstetrics and Gynecology, Sudan to undergo an abortion.

Sample size was calculated using the following formula⁹:

$$N = \frac{(1.96)^2 P(1-p)}{d^2}$$

Demographic and clinical data were collected directly from each woman into a predesigned questionnaire (*Extended data*), including personal information (age, education (no education = illiterate), occupation, socioeconomic status (determined using household income: low, <US\$57 per month; moderate, US\$57–200 per month; high, >US\$200 per month), nationality, number of abortions, duration of pregnancy) and laboratory data.

The laboratory work was carried out in the Regional Public Health Laboratory and Sudanese Chinese Friendship Hospital in El-Damazin using Stat Fax microplate reader (Model: 3200) and Stat Fax washer (Model: 2600) and commercially available ELISA kits (BIOS Microwell Diagnostic System, Chemux Bioscience, Inc., USA for CMV IgM, Lot No: 18-D-055; Fortress Diagnostics Ltd, UK for CMV IgG Lot No: CG-1807-1). Positive and negative results for IgG and IgM were recorded according to calculated cut-off values. For CMV IgG, the cut-off value was obtained by subtracting the blank absorbance from the mean absorbance of calibrator 2.

For CMV IgM the cut-off value was obtained by multiplying the optical density (OD) of the calibrator by factor (F) printed on label of calibrator. CMV IgM index for each sample obtained by dividing OD of sample over the cut-off.

Data analysis

Data analysis was done using Statistical Package for Social Sciences (SPSS version 24; IBM SPSS). Pearson Chi-squared test was used to test for statistical significance (P value), which was taken as significant when $p < 0.05$.

Results

A total of 270 women were enrolled in the study. The majority of the women were aged between 26 and 40 years. Low socioeconomic status was recorded in 84.8% (229/270) of participants, and illiteracy and women obtaining primary education was observed in 80% of participants. Most women were observed to be in the first trimester of pregnancy (85.5%; 231/270) (*Table 1*). In total, 27.8% (75/270) of the women had a history for 1–7 abortions, while 72.2% (195/270) had no history.

The seroprevalence of HCMV IgG and IgM among the 270 women was 74.8% (202/270) and 13.3% (36/270), respectively (*Figure 1*).

HCMV IgG detection was significantly correlated to socioeconomic status and gestation stage, but was not correlated to age group and education level (*Table 2*).

Discussion

CMV is globally distributed, with 40–100% of the global population positive for CMV antibodies^{10,11}, particularly among low economic individuals¹². In Sudan, there are only a few published data (Western and Central Sudan, and Khartoum) concerning epidemiology of HCMV among pregnant women.

Table 1. Demographic data of pregnant women who had spontaneous abortion in Sudan between September and December 2018.

		N	%
Age groups	15– 25 years	91	33.7
	26 – 40 years	168	62.2
	>41 years	11	4.1
Socioeconomic status	Low income	229	84.8
	Moderate income	41	15.2
Gestation	1st trimester	231	85.5
	2nd trimester	38	14.1
	3rd trimester	1	0.4
Education	Illiterate	113	41.9
	Basic	98	36.2
	Primary	5	1.9
	Secondary	31	11.5
	University	23	8.5
	Total	270	100

In our study area, which it located in the South of Sudan, there are no findings about the seroprevalence of HCMV in pregnant women who have had abortions.

The relationship between seroprevalence of HCMV and socioeconomic and education level among the present study population is significant, which may explain poor health status and susceptibility to certain diseases. Numerous studies have evaluated socioeconomic and education level for seroprevalence of HCMV, and most of these studies confirm the strong association between the socioeconomic disparities and high seropositivity^{13–17}.

HCMV IgG level in this study was significantly correlated to abortion in the 1st trimester gestation, which has also been shown by other studies^{1,18}. HCMV infection is considered a significant public health problem because it can cause disease in those with weakened immune systems, which has been confirmed by a study in Sudan in which a high frequency (98.3%) of seroprevalence of HCMV among pregnant women was reported¹⁹.

In the present study, the sero-prevalence of HCMV among the participants was 74.8% for IgG and 13.3% for IgM; these findings are in total agreement with another study in Sudan among

Figure 1. Sero-prevalence of HCMV IgG and IgM among 270 aborted pregnant women.

Table 2. Correlation of positive HCMV IgG status with socioeconomic status, gestation, age group and education level in Sudanese women who had undergone spontaneous abortion in the time period September–December 2018 (n=202).

	N (%)					Chi squared	P value
Socioeconomic status	Low	Moderate					
	82.2 (166)	17.8 (36)				4.329	0.025
Gestation	1st trimester	2nd trimester	3rd trimester				
	89.6 (181)	9.9 (20)	0.5 (1)			11.797	0.003
Age group	15– 25 years	26 – 40 years	>41 years				
	34.6 (20)	60.9 (123)	4.5 (9)			0.729	0.694
Education level	Illiterate	Basic	Primary	Secondary	University		
	43.1 (87)	35.1 (71)	2.5 (5)	11.4 (23)	7.9 (16)	2.601	0.627

pregnant women⁷, but is in contrast to other study in Iran in which the frequency for HCMV IgG and IgM was 14.28% and 28.25%, respectively²⁰. Larger and smaller frequencies of HCMV IgG level have also been reported in Egypt²¹ and Iran²², respectively. The IgM level found in this study is similar to findings reported in Poland (13%) by Fowler and Boppana²³, and similar results were obtained by other authors in Iraq²⁴ and India²⁵. Higher results have been reported in Egypt (32.6%) for HCMV IgM¹⁸, and lower results have been reported in Turkey²⁶ and Korea²⁷ (1% and 1.7%, respectively). Many factors may contribute to HCMV transmission and prevalence, such as socioeconomic and lifestyle factors, and it should be noted that most immunocompetent carriers of HCMV remain asymptomatic²⁸.

In this study, 11.9% of the study population revealed primary infection with HCMV, i.e. positive results for both IgG and IgM. This frequency is larger than that recorded previously in a hospital in Khartoum²⁹.

Conclusions

Seroprevalence of HCMV in Blue Nile State, Sudan, among pregnant women who had undergone abortion(s) was 74.8% for IgG and 13.3% for IgM. HCMV prevalence in pregnant

women -was most prevalent for women in the first trimester-with low economic status.

Data availability

Underlying data

Figshare: HCMV seroprevalence, Blue Nile State, Sudan, <https://doi.org/10.6084/m9.figshare.9895715.v1>³⁰

This project contains the following underlying data:

- ELISA antibody titre data
- Demographic and clinical data for participants

Extended data

Figshare: HCMV seroprevalence, Blue Nile State, Sudan, <https://doi.org/10.6084/m9.figshare.9895715.v1>³⁰

This project contains the following extended data:

- Questionnaire in English.

Data are available under the terms of the [Creative Commons Zero “No rights reserved” data waiver](#) (CC0 1.0 Public domain dedication).

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Version 1

Reviewer Report 27 September 2021

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Irena Tabain

Department of Virology, Croatian Institute of Public Health, Zagreb, Croatia

Thank you for the opportunity to review the manuscript.

Cytomegalovirus is the most common congenital infection, which mostly follows maternal primary infection¹.

- Firstly, only one abbreviation for cytomegalovirus should be used.
- The study has several limitations:
 - It would be important to know the CMV seroprevalence in women with healthy and alive babies.
 - The control group is missing.
 - Unfortunately, the authors presented only the correlation between IgG and parameters and IgM correlation is missing. Since PCR detection is not used, correlation of presented parameters with IgM is important.
 - Discussion and conclusions should be supported with results.
 - And finally, it should be noted that other causes of obstetric complications are excluded (e.g. toxoplasmosis, rubella).
- Conclusions are not adequate, but this information is important, and therefore, the study protocol needs an annex, and the annex study carried out and then updated data could be presented.

Best regards!

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Is the work clearly and accurately presented and does it cite the current literature?

No

Is the study design appropriate and is the work technically sound?

No

Are sufficient details of methods and analysis provided to allow replication by others?

No

If applicable, is the statistical analysis and its interpretation appropriate?

Partly

Are all the source data underlying the results available to ensure full reproducibility?

Partly

Are the conclusions drawn adequately supported by the results?

No

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Microbiology, Virology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Reviewer Report 22 September 2021

<https://doi.org/10.5256/f1000research.21696.r92377>

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Luiz Fernando Almeida Machado

Biology of Infectious and Parasitic Agents Post-Graduate Program, Federal University of Pará, Belém, Brazil

The aim of the manuscript is to determine the seroprevalence of IgG and IgM antibodies to HCMV in women who have suffered a miscarriage in a hospital in Sudan.

- The study has a series of limitations that do not allow estimating the prevalence of HCMV, as it only detected antibodies and not HCMV DNA. In addition, the main focus was on IgG,

which could indicate previous contact with the virus, and not IgM, which could indicate a recent virus infection.

- Another important point is that only a qualitative serological test was performed. To get an idea of the prevalence of HCMV infection, it would be interesting to quantify IgG, as well as the IgG avidity test, in addition to HCMV DNA research (the latter being an option only, as it requires a more refined infrastructure).
- What is the relationship between abortion and IgM? The authors do not comment on the presence of IgM in the results and conclusion.
- Another interesting point would be to verify the prevalence of anti-HCMV antibodies in a control group of women who had live children during the study period, to see if there is a difference in the prevalence between the two groups. Did women who had live children also not have a high prevalence of IgG? Probably yes.
- The authors could make a table making the correlation between abortion and the presence of IgM as well.
- Why does Table 2 only correlate with IgG and not IgM? Although the prevalence of IgM is lower than IgG, the rate is very high when compared to studies^{1,2,3}.
- What are the limitations of the study? Did the women in the study receive prenatal care?
- Authors should establish some exclusion criteria in the study, such as a history of toxoplasmosis, syphilis, and rubella, which are also important causes of abortion in the first trimester of pregnancy.

All this information is important so that it is not prematurely concluded that the presence of IgG in women of low economic status is a risk factor for abortion in the first trimester of pregnancy. Therefore, my opinion is that the study should be further developed in order to be indexed.

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Is the work clearly and accurately presented and does it cite the current literature?

No

Is the study design appropriate and is the work technically sound?

No

Are sufficient details of methods and analysis provided to allow replication by others?

No

If applicable, is the statistical analysis and its interpretation appropriate?

Partly

Are all the source data underlying the results available to ensure full reproducibility?

No

Are the conclusions drawn adequately supported by the results?

No

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Microbiology, General Virology, Molecular Epidemiology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

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