BMJ Open

Seroprevalence and associated factors of maternal cytomegalovirus in Southern Ethiopia: a cross-sectional study

Mengistu Hailemariam Zenebe ,[1,2,3] Zeleke Mekonnen,[3] Eskindir Loha ,[4,5] Elizaveta Padalko[6]

To cite: Zenebe MH, Mekonnen Z, Loha E, *et al*. Seroprevalence and associated factors of maternal cytomegalovirus in Southern Ethiopia: a cross-sectional study. *BMJ Open* 2021;**11**:e051390. doi:10.1136/bmjopen-2021-051390

► Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2021-051390).

Received 18 March 2021
Accepted 24 September 2021

[1]Medical Laboratory Sciences, Hawassa University College of Medicine and Health Sciences, Hawassa, South Ethiopia, Ethiopia
[2]Department of Diagnostic Sciences, Ghent University Faculty of Medicine and Health Sciences, Gent, Belgium
[3]Medical Laboratory Sciences, Jimma University Institute of Health, Jimma, Ethiopia
[4]Department of Global Public Health and Primary Care, University of Bergen, Bergen, Norway
[5]Chr Michelson Institute, Bergen, Norway
[6]Department of Diagnostic Sciences, Ghent University Hospital, Ghent, Belgium

Correspondence to
Mengistu Hailemariam Zenebe; mengamariam@yahoo.com

ABSTRACT

Objectives The aim of this study was to assess the seroprevalence and associated factors of cytomegalovirus (CMV) among pregnant women in Southern Ethiopia.

Design Cross-sectional study.

Setting The study was conducted in Hawassa University comprehensive and specialised hospital. Hawassa, Southern Ethiopia.

Participants A total of 600 consecutive pregnant women attending the delivery ward were recruited for the study from August to October 2020.

Outcome measures The study assessed the rate of maternal anti-CMV IgG and IgM antibodies. The association of obstetric history, sociodemographic and behavioural characteristics with seropositivity of CMV was also evaluated based on the collected data using structured questioners.

Results Seropositivity for CMV IgM antibodies was 8.2% (49/600) (95% CI 6% to 10.5%), whereas the CMV IgG was 88.7% (532/600), (95% CI 89.5% to 94.0%). Seroprevalence of CMV IgM was higher in women of older age, currently unmarried, having nursery schooled children and with any of the detected curable sexually transmitted infections, while seroprevalence of CMV IgG was significantly associated only with women having nursery schooled children. Seroprevalence was not significantly associated with previous adverse pregnancy outcome, gravidity, being a child daycare occupant mother and newborn birth weight.

Conclusion In the present study, we identified a high rate of CMV IgM and CMV IgG seroprevalence among pregnant women in Southern Ethiopia. Given that there is no existing CMV diagnosis, special attention should be designed to pregnant women in parallel to the existing antenatal care facility. Besides, training healthcare professionals will support awareness conception among pregnant women concerning the sequels of CMV infection during pregnancy.

Strengths and limitations of this study

- This study is the first to present the seroprevalence of maternal cytomegalovirus from the Southern region in Ethiopia and that provides the first awareness in medical, governmental and societal stakeholders.
- The study assessed both anti-cytomegalovirus (CMV) IgG and anti-CMV IgM seropositivity that can predict the possible threat of congenital CMV infection to the developing fetus.
- In this study, the factors associate with the level of seropositivity were explored among pregnant women.
- We were unable to distinguish primary from secondary (reinfection or reactivation) CMV infection as there was no baseline data to decide about seroconversion at the beginning of pregnancy.
- Being a hospital-based study, our finding will not be representative of all pregnant mothers in the locality since a significant portion of mothers may not deliver in the hospital.

INTRODUCTION

Cytomegalovirus (CMV) is the most common infection during pregnancy that poses the risk of congenital CMV infections (cCMV) worldwide.[1] In immunocompetent hosts, primary CMV infection may be asymptomatic or may cause mild self-limiting disease with fever, headaches and myalgia and, after primary infection, the virus remains latent. Latency following a primary infection may relapse by periodic reactivations that give rise to recurrent infections later in life when the body immunity is suppressed.[2]

During pregnancy CMV infection or reactivation is mostly asymptomatic; however, it might lead to fetal infection and cCMV syndromes.[3] cCMV infection of the fetus of mothers having pre-existing anti-CMV antibodies is also possible due to the risk of reactivation or reinfection with a different strain of CMV during pregnancy.[4] Therefore, unlike previous perception, the high maternal CMV seroprevalence in developing countries like Ethiopia does not eliminate the threat of cCMV infection of the newborn. Worldwide, cCMV following non-primary maternal infections is more common in individuals of lower socioeconomic backgrounds.[5] In addition, due to a high seroprevalence of CMV in the community of the developing countries, there would be a rare possibility of recurrent CMV infection as a result of reinfection.[6] As to the

report from Portugal, maternal recurrent infections can have a significant impact on cCMV infections.[7]

So far, previous studies have shown that maternal CMV seroprevalence rates were ranging from low (50% to 70%) in developed countries to high (>70%) in developing countries.[1] Presently, data on the prevalence of maternal CMV and associated risk factors are scanty in Ethiopia. The only available study conducted in Ethiopia had reported the seroprevalence of 15.5% for CMV IgM and 88.6% for CMV IgG.[8]

In Africa, the highest prevalence of CMV IgG was estimated to range from 72% to 97.5%[9 10] and of CMV IgM antibodies to range from 0% to 15.5%.[11] However, for several reasons, CMV infections among pregnant women in Africa have been overlooked.[12] One of the main reasons for inattention is the perception that being infected in early childhood endures immunity for subsequent infection, so maternal reactivation or reinfection during pregnancy is unlikely to cause severe congenital infection.[13] However, in pregnant women, the immune system is somehow suppressed. So ignoring maternal CMV and the subsequent effect of cCMV infection in Africa is shortsighted; furthermore, the possible confounding effects of HIV infection, malnutrition, tuberculosis and a general higher disease burden of the continent must be taken into account.[14]

The objective of the study was to assess the seroprevalence of CMV IgM and IgG among pregnant women and determine associated factors in Southern Ethiopia. Information regarding the maternal prevalence of CMV and associated risk factors is almost absent in Ethiopia. Being the first study in the Southern region of Ethiopia, the finding will deliver the first awareness in medical, governmental and societal stakeholders in the region. Moreover, the study will attract healthcare professionals' attention and improve antenatal care (ANC) in this domain. Indeed, it will generate awareness in the community, mainly pregnant women, regarding the consequence of CMV during pregnancy in Ethiopia.

METHODOLOGY

Study design and setting

From August to October 2020, a cross-sectional study was conducted among pregnant women who came for delivery in the obstetrics ward at Hawassa University Comprehensive and Specialized Hospital (HU-CSH), Ethiopia. The HU-CSH is one of the teaching hospitals serving as a referral centre for both public and private hospitals for more than 5 million inhabitants in the Southern Region and the neighbouring region of Ethiopia. The hospital has around 500 beds, accommodating more than 2500 pregnant women for ANC visits and conducting about 5400 deliveries annually.

Participants

All pregnant women were recruited regardless of gestational age; however, a mother with any critical illness (such as airway obstruction, current history of seizures or unconsciousness) that would deter them from participation in the study were excluded. Interrelated with the first phase of this project,[15] where the initial 350 pregnant women had been tested for curable sexually transmitted infection (STI) (*Chlamydia trachomatis*, *Neisseria gonorrhoeae* and *Trichomonas vaginalis*) using GeneXpert (Xpert CT/NG and Xpert TV assays, Cepheid, Sunnyvale, California). In this second phase of the study, by including those initially enrolled 350 pregnant women, a total of 600 consecutively enrolled pregnant women were participated. A midwife at the obstetric ward provided general information about the study to all pregnant women before recruitment.

Sample size and sampling

The sample size was calculated based on the single population proportion formula by considering 15.5% prevalence of maternal anti-CMV IgM from a previous study conducted in central Ethiopia,[8] a 3% margin of error and a 95% confidence level. Thus, the minimum sample size was 560. However, a total of 600 women were consecutively enrolled to signify the findings of seroprevalence of CMV among pregnant women in the study settings. Sampling was based on convenience and continued until a total of 600 participants were reached. If there is non-response during data collection, the study will be solved by taking subsequent participants until the intended sample size is achieved.

Data collection

Sociodemographic, obstetric and behavioural data

Trained midwives at the obstetric ward provided general information about the study to pregnant women who came for delivery. Pregnant women agreeing to join in the study were interviewed using a structured questionnaire translated in Amharic, the language spoken by most people in the study area. The translated questionnaire was pretested on random mothers at the antenatal clinic to ensure the validity and feasibility of the questions as conducted in similar studies, and the principal investigator carefully checked the process of each data collection everyday. Information related to sociodemographic characteristics (eg, age, marital status and educational level), obstetric history and behavioural data was collected.

Sample collection and storage

The midwife-nurse aseptically collected a 3 mL of blood sample from each subject. The collected samples were transported to the HU-CMHS microbiology laboratory within 12 hours of collection, and the processed serums were kept at −20°C until transported. Then frozen samples at −20°C were transported on dry ice packs to the testing laboratory.

Laboratory methods

Testing was performed in Belgium, Ghent University hospital, department of laboratory medicine, using a commercially available enzyme immunoassay (ELISA)

kit (EUROIMMUN Medizinische Labordiagnostika AG, Lübeck, Germany) for anti-CMV IgG and IgM according to the manufacturer's instructions. The sensitivity amounted to 99.2%, with a specificity of 100%. Results were evaluated semiquantitatively by calculating a ratio of the extinction value of the patient sample over the extinction value of the calibrator optical density at 450 nm. Seropositivity was defined according to the guidelines given by the manufacturer, CMV negative when the ratio cut-off value was <0.8, the borderline between 0.8 and 1.1, and positive if >1.1 for both IgG and IgM.

Ethical considerations

The study was conducted in accordance with the Declaration of Helsinki, the significance of the study was clarified to each study participant and parents of a few minorities before obtaining informed consent. Permission attained from the minor (under the age of 18 years) participants' parent or legal guardian according to the Ethiopian national research Ethics review guideline. Eventually, consent was granted from each participant including those who were under the age of 18 years with a participant confirmatory agreement to participate in the study. Confidentiality of the participant's information was ensured by anonymous typing.

Data analysis

Descriptive statistics were used to characterise the sociodemographic and obstetric and medical characteristics of the participants. We evaluated the seroprevalence of CMV and associated factors using a logistic regression model. Bivariate comparisons using χ^2 or Fisher's exact test where suitable were used to examine the relationships between participant characteristics and CMV test result. Finally, multivariable logistic regression was used to identify characteristics independently associated with serostatus of CMV and adjusting for other factors. Variables with a significant level of ≤0.2 were included in the final model. P value <0.05 is considered statistically significant. SPSS software V.20.0 (SPSS Chicago, Illinois) was used for all analyses.

Patient and public involvement

No patients or the public were directly involved in the design, conduct, reporting or dissemination plans of this research.

RESULTS

Participants

Six hundred pregnant women were assessed for seroprevalence of CMV and all women met the inclusion criteria and enrolled in the study, generating a 100% response rate. The mean of maternal age was 27.0 ± (SD) 5.2, with a ranging between 17 and 41. More than one-third of the study participants were under the age of 25. About one-fourth of the women were primigravida. Out of the 600 participants, 84 (14%) were currently unmarried, 475 (79.2%) were residing in urban setting, 377 (62%) were above or at secondary level of education. Forty-eight (8%) of the newborns were underweighted (<2.5 Kg), and 64 (10%) of the births were preterm. Regarding STI test result, 51 (14.6%) pregnant women were tested positive for any of curable STIs (table 1).

In this study, 95.8% of mothers had no knowledge of congenitally transmitted infection or the associated risks in pregnancy and 8.6% of them had previous adverse pregnancy outcome. The χ^2 analysis showed that seropositivity for CMV IgM significantly associated (p<0.05) with marital status, gestational age, having nursery school baby in the household, sharing a cup with children and having any of detected curable STIs. However, there was no significant association with birth weight, gravidity and having previous adverse pregnancy outcome, that is, preterm birth, stillbirths and early neonatal death (table 1).

Seroprevalence

Seropositivity of CMV IgM antibodies was 8.2% (49/600) (95% CI 6% to 10.5%), whereas seroprevalence of CMV IgG was 88.7% (532/600), (95% CI 89.5% to 94.0%). Of 532 CMV IgG positive women, 483 (80.4%) were negative for IgM. Among all pregnant women, 68 (11.4%) were tested negative for both anti-CMV IgG and IgM, and none showed anti-CMV IgG negativity but IgM positivity (table 2).

CMV seropositivity and associated factors

In bivariable analysis, seropositivity of CMV IgM was more common in elder women (>35) compared with the youngest age group (<25), in women who were currently unmarried, giving preterm birth, sharing a feeding cup with children or having nursery schooled children. Moreover women were positive for any of curable STIs also had a higher seroprevalence of CMV compared with those negative for STIs (table 3).

Furthermore, in multivariable logistic regression, being over the age of 30 years had higher odds for CMV IgM seropositivity compared with being under 25 (adjusted OR (AOR)=4.9, 95% CI 1.0 to 23.4), currently unmarried women (AOR=3.8, 95% CI 1.7 to 7.9), preterm birth (AOR=3.9, 95% CI 1.5 to 10.3) and having nursery schooled children (AOR=2.7, 95% CI 1.1 to 6.4). Mothers with STIs had an association with seroprevalence (AOR=4.1, 95% CI 1.6 to 10.6) compared with mothers who were diagnosed negative for STIs.

Maternal seroprevalence was not significantly associated with residence, education level, occupation, being employed in a child daycare centre or being a healthcare worker (table 3).

Regarding CMV IgG seropositivity, women within the age group of 30–35 have shown a significantly higher risk of CMV IgG positivity compared with women of <25 years in bivariable analysis. However, the detected significant risk in the bivariable analysis in this study is not sustained in the multivariable analysis. The discrepancy possibly due to the fact that most of the exposure to CMV infection

Table 1 Maternal characteristics and associated factor with CMV IgM seropositivity in Southern Ethiopia

Characteristics	Total (N=600) n (%)	IgM positive (n=49) n (%)	IgM negative (n=551) n (%)	P value*
Age of mothers (years)				
<25	233 (38.8)	14 (28.6)	219 (39.7)	0.148
25–29	162 (27.0)	14 (28.6)	148 (26.9)	
30–35	170 (28.3)	15 (30.6)	155 (28.1)	
>35	35 (5.8)	6 (12.2)	29 (5.3)	
Marital status				
Married	516 (86.0)	37 (75.5)	479 (86.9)	
Currently unmarried	84 (14.0)	12 (24.5)	72 (13.1)	0.027
Residence				
Urban	475 (79.2)	44 (89.8)	431 (78.2)	0.056
Rural	125 (20.8)	5 (10.2)	120 (21.8)	
ANC follow-up during pregnancy				
Yes	576 (96.0)	48 (98.0)	528 (95.8)	
no	24 (4.0)	1 (2.0)	23 (4.2)	0.712
Employed as daycare worker				
Yes	40 (6.7)	6 (12.2)	34 (6.2)	0.126
No	560 (93.3)	43 (87.8)	517 (93.8)	
Employed as healthcare				
Yes	32 (5.3)	6 (12.2)	26 (4.7)	0.055
no	568 (94.7)	43 (87.8)	525 (95.3)	
Education				
Primary and below	223 (37.2)	13 (26.5)	210 (38.1)	0.108
Secondary and above	377 (62.8)	36 (73.5)	341 (61.9)	
Gestational age				
Term	536 (89.3)	36 (73.5)	500 (90.7)	
Preterm	64 (10.7)	13 (26.5)	51 (9.3)	<0.001
Birth weight				
<2.5 Kg	48 (8.0)	3 (6.1)	45 (8.2)	0.789
>2.5 Kg	552 (92.0)	46 (93.9)	506 (91.8)	
Gravidity				
Primigravida	147 (24.5)	14 (28.6)	133 (24.1)	0.489
Multigravida	453 (75.5)	35 (71.4)	418 (75.9)	
Previous adverse pregnancy outcome †				
Yes	39 (8.6)	2 (5.7)	37 (8.9)	0.756
No	414 (91.4)	33 (94.3)	381 (91.1)	
Knowledge on congenitally transmitted infections				
Yes	25 (4.2)	1 (2.0)	24 (4.4)	
No	575 (95.8)	48 (98.0)	527 (95.6)	0.712
Under-five children in the household				
Yes	396 (66.0)	31 (63.3)	365 (66.2)	0.673
no	204 (43.0)	18 (36.7)	186 (33.8)	
Daycare or nursery school baby in the household				
Yes	259 (43.2)	31 (63.3)	228 (41.4)	0.003

Continued

Table 1 Continued

Characteristics	Total (N=600) n (%)	IgM positive (n=49) n (%)	IgM negative (n=551) n (%)	P value*
no	341 (56.8)	18 (36.7)	323 (58.6)	
Sharing feeding cup with children				
Yes	107 (17.8)	14 (28.6)	93 (16.9)	0.040
no	493 (82.2)	35 (71.4)	458 (83.1)	
Sharing eating utensil with children				
Yes	88 (14.7)	8 (16.3)	80 (14.5)	0.732
No	512 (85.3)	41 (83.7)	471 (85.5)	
Sharing teeth brush with children				
Yes	42 (7.0)	3 (6.1)	39 (7.1)	0.999
No	558 (93.0)	46 (93.9)	512 (92.9)	
***N.gonorrhoeae* detected (n=350)**				
Yes	15 (4.3)	3 (10.0)	12 (3.8)	0.128
No	333 (95.7)	27 (90.0)	306 (96.2)	
C.***C. trachomatis* detected (n=350)**				
Yes	29 (8.3)	5 (16.7)	24 (7.5)	0.089
No	319 (91.7)	25 (83.3)	294 (92.5)	
T.***T. vaginalis* detected (n=350)**				
Yes	11 (3.1)	2 (6.9)	9 (2.8)	0.241
No	335 (96.8)	27 (93.1)	308 (97.2)	
Any of curable STI detected (n=350)				
Yes	51 (14.6)	10 (33.3)	41 (12.8)	0.005
No	299 (85.4)	20 (66.7)	279 (87.2)	

*Chi-square.
†Previous adverse pregnancy includes; early neonatal death, stillbirth and preterm birth.
STI, sexually transmitted infections.

were in early childhood in developing countries like Ethiopia, so that CMV IgG seroprevalence seems comparable in all age categories . In addition, participants might have a similar type of behaviour at different ages. Furthermore, women having primary or lower educational levels are associated with a higher risk of CMV IgG seropositivity than having secondary or above educational levels in bivariable analysis (OR 1.7). But not associated in adjusted analysis, this might be due to the common exposure and awareness level of the study participants.

In this study, women having nursery schooled children shown association both in bivariable and multivariable analysis (AOR=1.8, 95% CI 1.0 to 3.0). However, the other maternal characteristics were not associated with CMV IgG seropositivity (table 4).

Table 2 Cytomegalovirus IgM and IgG test result of pregnant women

Anti CMV IgM antibody	Anti-CMV IgG antibody n (%)		
	Positive	Negative	Total n (%)
Positive	49 (8.2)	0 (0)	49 (8.2)
Negative	483 (80.4)	68 (11.4)	551 (91.8)
Total	532 (88.7)	68 (11.4)	600

CMV, cytomegalovirus.

DISCUSSION

In this study, an overall seroprevalence of 8.2% for CMV IgM and 88.7% for CMV IgG was detected among pregnant women in Southern Ethiopia. Factors associated with CMV IgM seropositivity were age, marital status, the presence of curable STIs and sharing a cup with children. A statistically significant association was also observed between CMV seropositivity and preterm delivery.

The reported seropositivity of CMV IgG (88.7%) in this study was comparable to a result found in previous study of pregnant women in central Ethiopia (88.5%); however,

Table 3 Unadjusted and adjusted associated factors of maternal CMV IgM seropositivity in Southern Ethiopia

Characteristics	Unadjusted *		Adjusted *	
	OR 95% CI)	P value	OR (95% CI)	P value
Age of mothers (years)				
<25	1		1	
25–29	1.5 (0.7 to 3.2)	0.318	1.2 (0.4 to 4.0)	0.739
30–35	1.5 (0.7 to 3.2)	0.283	3.0 (1.0 to 9.0)	0.048
>35	3.2 (1.2 to 9.1)	0.026	4.9 (1.0 to 23.4)	0.047
Marital status				
Married	1		1	
Currently unmarried	2.2 (1.1 to 4.3)	0.030	3.8 (1.3 to 11.2)	0.015
Residence				
Urban	2.5 (1.0 to 6.3)	0.064	2.3 (0.7 to 7.9)	0.171
Rural	1		1	
Daycare worker				
Yes	2.1 (0.8 to 5.3)	0.110	1.1 (0.2 to 5.4)	0.857
No	1		1	
Healthcare worker				
Yes	2.8 (1.1 to 7.2)	0.031	1.2 (0.2 to 7.4)	0.841
no	1		1	
Education				
Primary and below	0.6 (0.3 to 1.1)	0.111	0.7 (0.3 to 1.8)	0.475
Secondary and above	1		1	
Gestational age				
Term	1		1	
Preterm	3.5 (1.8 to 7.1)	<0.001	3.9 (1.5 to 10.3)	<0.006
Daycare or nursery school baby				
Yes	2.4 (1.3 to 4.5)	0.004	2.7 (1.1 to 6.4)	0.027
no	1		1	
Sharing a cup with children				
Yes	2.0 (1.1 to 3.8)	0.044	2.2 (0.9 to 5.4)	0.074
no	1			
Any of curable STIs (n=350)				
Yes	3.4 (1.5 to 7.8)	0.004	4.1 (1.6 to 10.6)	0.003
No	1			

*Logistic regression.
STI, sexually transmitted infection.

a substantially higher rate of CMV IgM (15.5%) was documented compared with our finding.[8] Furthermore, seropositivity of CMV IgG in our study was in line with a review done in Africa, with ranges from 60% to 100%.[11] Seropositivity rates of 77.3% for IgG and 8.1% for IgM in Kenya,[9] 93% for IgG and 11.1% for IgM in Nigeria,[16] 94% for IgG and 8.5% for IgM in Tanzania[17] were also comparable to our finding.

In our study, seroprevalence of CMV IgM is in concordance with several African studies.[9 16–18] However, our rate was considerably higher when compared with 0.4% in Tanzania,[19] 2.5% in Sudan[20] and 7% in Egypt.[21] In the absence of maternal screening, this high rate is alarming for policymakers. By far in most of the developed countries, pregnant women are screened for CMV due to the panic effect and consequence to the developing fetus and newborn.[22 23] However, in most developing countries, including Ethiopia, maternal CMV still lacks awareness, is overlooked and not diagnosed at least for pregnant women.[24] The high rate of CMV IgM may not only reflect primary infection but might also be attributed to reinfection or reactivation of CMV during pregnancy. So the reported high seropositivity in this study points to the existing negligence and the need to start screening to

Table 4 Unadjusted and adjusted associated factors of maternal CMV IgG seropositivity in Southern Ethiopia

Characteristics	Unadjusted *		Adjusted *	
	OR 95% CI)	P value	OR (95% CI)	P value
Age of mothers (years)				
<25	1			
25–29	1.2 (0.7 to 2.3)	0.482	1.0 (0.5 to 1.9)	0.991
30–35	2.2 (1.1 to 4.3)	0.028	1.8 (0.9 to 3.8)	0.095
>35	1.3 (0.4 to 3.9)	0.663	0.9 (0.3 to 1.0)	0.877
Marital status				
Married	1			
Currently unmarried	0.8 (0.37 to 1.7)	0.573		
Residence				
Urban	0.8 (0.4 to 1.5)	0.493		
Rural	1			
Daycare worker				
Yes	0.9 (0.3 to 2.3)	0.810		
No	1			
Healthcare worker				
Yes	0.9 (0.3 to 2.6)	0.831		
no	1			
Education				
Primary and below	1.7 (1.0 to 2.8)	0.041	0.6 (0.4 to 1.0)	0.037
Secondary and above	1			
Gestational age				
Term	1			
Preterm	0.9 (0.4 to 1.9)	0.756		
Daycare or nursery school baby				
Yes	1.9 (1.1 to 3.1)	0.017	1.8 (1.0 to 3.0)	0.045
no	1			
Sharing a cup with children				
Yes	1.1 (0.6 to 2,3)	0.705		
no	1			
Any of curable STIs (n=350)				
Yes	0.8 (0.3 to 1,9)	0.578		
No	1			

*Logistic regression.
STI, sexually transmitted infection.

detect pregnant women at risk for congenital transmission of CMV.

Earlier studies have shown that there was considerable debate regarding the relationship between maternal age and CMV seroprevalence. In this study, elder age had significant association with CMV IgM seroprevalence but no association observed in CMV IgG. The same finding was reported in Kenya,[25] Nigeria[26] and Tanzania.[19] However, a study in Ethiopia,[8] Egypt,[21] Sudan,[20] China[27] and in Nigeria[28] has reported that age had no association with maternal CMV infection. Unlike our finding, studies in Iraq a high rate of CMV IgM in young women was reported,[29] whereas, in USA CMV IgM seroprevalence varied by age with the highest among younger and lower among those elder age was reported.[30] The increment of association of CMV IgM seroprevalence with age in this study may indicate the more lifetime episodes exposure of elders than youngsters or might be the existence of previous infection, which can probably reactivated in the current pregnancy. In fact, the observed difference in CMV IgM seroprevalence by age may be useful to realise the risk of cCMV transmission and are useful for ascertaining target populations for intervention to reduce cCMV transmission.[30]

On the other hand, mother who have nursery schooled children among households has shown a significant association with seroprevalence of both CMV IgM and IgG. For pregnant women, the predictable source of CMV infection is young children mainly exposure to nursery schooled children.[31] Children easily get infected in school and frequently shed CMV in their saliva or urine for many years continuously that could spread readily even in a preschool setting.[32] This places seronegative pregnant women who have a young child in the home or in day care at increased risk of seroconversion.[33 34] Susceptibility to the acquisition of CMV infection is high possibly through the direct contact with contagious secretions from their children essentially in a situation of poor hygienic practice like in Ethiopia.[35]

Among candidate predictors for maternal CMV seropositivity, occupations like being healthcare worker or child day-care worker; being multigravida, lower educational level and having other children at home did not show any association. However, there was significant association for those with preterm delivery. Although, maternal CMV infection may result in preterm delivery, its isolated impact could not be assessed since we did not study other potential confounding factors.[36]

Likewise, CMV IgM seropositivity was found to be significantly associated with STIs detected at delivery and currently being unmarried. Mothers who were positive for any of curable STIs had a four-time CMV IgM seropositivity. It is also reported that STIs including CMV to be more common in unmarried pregnant women.[31 35 37] Although CMV is a virus that is transmitted through many body fluids, sexual transmission from a seropositive male partner is an additional established route by which women may be infected with CMV.[38] Indeed, it is somehow expected that sexual transmission is also responsible for the reinfection of seropositive mothers with different virus strains in high-seroprevalence populations.[39]

Although, CMV IgG avidity testing is a valuable laboratory tool for distinguishing primary from non-primary CMV infection, an avidity test was not performed in this study. Hence, this study lacks differentiation of CMV IgM positivity of either primary or non-primary (reinfection or reactivation) as we collected samples at the end of the pregnancy period that avidity test will not be suitable. Moreover, it was a hospital-based study and not representative of all pregnant mothers in the locality since a significant portion of mothers may not deliver in the hospital. We lack also appropriate risk factors assessment tool due to the cross-sectional nature of the study; hence, a more representative large-scale survey is needed to identify possible risk factors prospectively. Furthermore, this is the first study from the Southern region in Ethiopia and that makes the first awareness in medical, governmental and societal stakeholders. Thus, more studies may need to be accomplished before the introduction of appropriate measures.

CONCLUSION

In this study, we identified a high rate of both CMV IgM and CMV IgG seropositivity among pregnant women in Southern Ethiopia. The presence of curable STIs, elder age and unmarried women showed a significant association with CMV IgM seropositivity. Furthermore, having nursery schooled children showed a significant association with CMV IgM and IgG seropositivity. Given that there is no existing CMV diagnostic facility, special attention should be designed to pregnant women in parallel to the existing ANC service. Besides, training healthcare professionals will support awareness conception for pregnant women concerning the sequels of CMV infection during pregnancy.

Acknowledgements We thank the HU-CSH microbiology laboratory staffs for the provision of all laboratory accommodations during sample processing and storage. We would like to recognise the study participants and a special thanks to midwife nurses at the obstetrics ward of the HU-CSH. Lastly, we want to express our thanks to VLIR-UOS for providing a PhD scholarship.

Contributors MHZ and EP led the conceptualisation and of the study. MHZ carried out the laboratory work of this research protocol and was the primary author for this manuscript. MHZ, EL, ZM and EP wrote the first draft of this manuscript and performed the statistical analysis and interpretation. EL, ZM and EP provided critical review and contributed to the write-up and approved the final version of the manuscript. All authors read and approved the final manuscript.

Funding This study was a PhD work and a PhD Scholarship is supported by the research from the Belgian Development Cooperation through the VLIR-UOS Network Programme (University Collaboration for Better Health in Ethiopia (UCBHE).

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Consent obtained directly from patient(s)

Ethics approval Ethical approval from all of the appropriate institutional review boards was obtained. The ethics review committee of Hawassa University (CMHS/283/2012), Jimma University (IHRPGD/458/2020), National Health Research Ethics Review Committee (SRA/14.1/1 44 483/2020) Ethiopia and Ghent University (PA2019-038/BC-08458) Belgium, approved the study. The study was conducted in accordance with the Declaration of Helsinki.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. Data for this study were available upon request to principal authors.

ORCID iDs
Mengistu Hailemariam Zenebe http://orcid.org/0000-0002-7048-0594
Eskindir Loha http://orcid.org/0000-0003-0003-2734

REFERENCES

1 Manicklal S, Emery VC, Lazzarotto T, *et al*. The "silent" global burden of congenital cytomegalovirus. *Clin Microbiol Rev* 2013;26:86–102.
2 Nolan N, Halai U-A, Regunath H, *et al*. Primary cytomegalovirus infection in immunocompetent adults in the United States - A case series. *IDCases* 2017;10:123–6.
3 Lazzarotto T, Blázquez-Gamero D, Delforge M-L, *et al*. Congenital cytomegalovirus infection: a narrative review of the issues in screening and management from a panel of European experts. *Front Pediatr* 2020;8:13.

4 Britt WJ. Maternal immunity and the natural history of congenital human cytomegalovirus infection. *Viruses* 2018;10:405.
5 Mussi-Pinhata MM, Yamamoto AY. Natural history of congenital cytomegalovirus infection in highly seropositive populations. *J Infect Dis* 2020;221:S15–22.
6 Henrich W, Meckies J, Dudenhausen JW, *et al*. Recurrent cytomegalovirus infection during pregnancy: ultrasonographic diagnosis and fetal outcome. *Ultrasound Obstet Gynecol* 2002;19:608–11.
7 Paixão P, Brito MJ, Virella D, *et al*. Recurrent maternal CMV infection associated with symptomatic congenital infection: results from a questionnaire study in Portugal. *BMJ Paediatr Open* 2019;3:e000455.
8 Yeshwondm M, Balkachew N, Delayehu B, *et al*. Seroepidemiology study of cytomegalovirus and rubella among pregnant women at St. Paul's Hospital millennium medical College, Addis Ababa, Ethiopia. *Ethiop J Health Sci* 2016;26:427.
9 Maingi Z, Nyamache A. Seroprevalence of Cytomegalo virus (CMV) among pregnant women in Thika, Kenya. *BMC Res Notes* 2014;7:794.
10 Khairi S, Intisar K, Enan K. Seroprevalence of cytomegalovirus infection among pregnant women at Omdurman maternity Hospital, Sudan. *J Med Lab Diagn* 2013;4:45–9.
11 Mhandire D, Rowland-Jones S, Mhandire K, *et al*. Epidemiology of cytomegalovirus among pregnant women in Africa. *J Infect Dev Ctries* 2019;13:865–76.
12 Bates M, Brantsaeter AB. Human cytomegalovirus (CMV) in Africa: a neglected but important pathogen. *Journal of Virus Eradication* 2016;2:136–42.
13 Ross SA, Fowler KB, Ashrith G, *et al*. Hearing loss in children with congenital cytomegalovirus infection born to mothers with preexisting immunity. *J Pediatr* 2006;148:332–6.
14 Bates M, Brantsaeter AB. Human cytomegalovirus (CMV) in Africa: a neglected but important pathogen. *J Virus Erad* 2016;2:136–42.
15 Zenebe MH, Mekonnen Z, Loha E, *et al*. Prevalence, risk factors and association with delivery outcome of curable sexually transmitted infections among pregnant women in southern Ethiopia. *PLoS One* 2021;16:e0248958.
16 Fowotade A, Okonko IO, Agbede OO, *et al*. High seropositivity of IgG and IgM antibodies against cytomegalovirus (CMV) among HIV-1 seropositive patients in Ilorin, Nigeria. *Afr Health Sci* 2015;15:1–9.
17 Ray K, Mahajan M. Seroprevalence of cytomegalovirus antibodies in patients attending STD and antenatal clinics. *J Commun Dis* 1997;29:85–90.
18 Mhandire D, Duri K, Kaba M, *et al*. Seroprevalence of cytomegalovirus infection among HIV-infected and HIV-uninfected pregnant women attending antenatal clinic in Harare, Zimbabwe. *Viral Immunol* 2019;32:289–95.
19 Chibwe E, Mirambo MM, Kihunrwa A, *et al*. Magnitude of the cytomegalovirus infection among pregnant women attending antenatal clinics in the city of Mwanza, Tanzania. *BMC Res Notes* 2017;10:489.
20 Hamdan HZ, Abdelbagi IE, Nasser NM, *et al*. Seroprevalence of cytomegalovirus and rubella among pregnant women in Western Sudan. *Virol J* 2011;8:217.
21 Kamel N, Metwally L, Gomaa N, *et al*. Primary cytomegalovirus infection in pregnant Egyptian women confirmed by cytomegalovirus IgG avidity testing. *Med Princ Pract* 2014;23:29–33.
22 Gyselaers W, Jonckheer P, Ahmadzai N. *What are the recommended clinical assessment and screening tests during pregnancy? good clinical practice (GCP)*. 248. Brussels: Belgian Health Care Knowledge Centre (KCE), 2017.
23 Vaudry W, Rosychuk RJ, Lee BE, *et al*. Congenital cytomegalovirus infection in high-risk Canadian infants: report of a pilot screening study. *Can J Infect Dis Med Microbiol* 2010;21:e12–19.
24 Revello MG, Gerna G. Diagnosis and management of human cytomegalovirus infection in the mother, fetus, and newborn infant. *Clin Microbiol Rev* 2002;15:680–715.
25 Maingi Z, Nyamache AK. Seroprevalence of Cytomegalo virus (CMV) among pregnant women in Thika, Kenya. *BMC Res Notes* 2014;7:794..
26 Kolo RL, Umoh VJ, Jatau ED, *et al*. Seroprevalence of cytomegalovirus among antenatal patients attending primary health centres in some parts of Kaduna state, Nigeria. *SAJEB* 2013;3:43–8.
27 Jin Qing'e, Su J, Wu S. Cytomegalovirus infection among pregnant women in Beijing: seroepidemiological survey and intrauterine transmissions. *J Microbiol Biotechnol* 2017;27:1005–9.
28 Yeroh M, Aminu M, Musa BOP. Seroprevalence of cytomegalovirus infection amongst pregnant women in Kaduna state, Nigeria. *Af J Clin Exp Micro* 2015;16:37–44.
29 Aljumaili ZKM, Alsamarai AM, Najem WS. Cytomegalovirus seroprevalence in women with bad obstetric history in Kirkuk, Iraq. *J Infect Public Health* 2014;7:277–88.
30 Wang C, Dollard SC, Amin MM, *et al*. Cytomegalovirus IgM seroprevalence among women of reproductive age in the United States. *PLoS One* 2016;11:e0151996.
31 Fowler KB, Pass RF. Risk factors for congenital cytomegalovirus infection in the offspring of young women: exposure to young children and recent onset of sexual activity. *Pediatrics* 2006;118:e286–92.
32 Cannon MJ, Hyde TB, Schmid DS. Review of cytomegalovirus shedding in bodily fluids and relevance to congenital cytomegalovirus infection. *Rev Med Virol* 2011;21:240–55.
33 Pass RF, Hutto C, Ricks R, *et al*. Increased rate of cytomegalovirus infection among parents of children attending day-care centers. *N Engl J Med* 1986;314:1414–8.
34 Hyde TB, Schmid DS, Cannon MJ. Cytomegalovirus seroconversion rates and risk factors: implications for congenital CMV. *Rev Med Virol* 2010;20:311–26.
35 Tookey PA, Ades AE, Peckham CS. Cytomegalovirus prevalence in pregnant women: the influence of parity. *Arch Dis Child* 1992;67:779–83.
36 Pitlick MM, Orr K, Momany AM, *et al*. Determining the prevalence of cytomegalovirus infection in a cohort of preterm infants. *J Neonatal Perinatal Med* 2015;8:137–41.
37 Shakya S, Thingulstad S, Syversen U, *et al*. Prevalence of sexually transmitted infections among married women in rural Nepal. *Infect Dis Obstet Gynecol* 2018;2018:1–9.
38 Staras SAS, Flanders WD, Dollard SC, *et al*. Influence of sexual activity on cytomegalovirus seroprevalence in the United States, 1988-1994. *Sex Transm Dis* 2008;35:472–9.
39 Adachi K, Xu J, Yeganeh N, *et al*. Combined evaluation of sexually transmitted infections in HIV-infected pregnant women and infant HIV transmission. *PLoS One* 2018;13:e0189851.