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Prevalence of Human Cytomegalovirus (CMV) among Pregnant Libyan Women

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Abstract— The CMV is a member of the order Herpesvirales, family Herpesviridae, and genus Beta-herpesvirinae, it is one of eight herpes viruses known to infect humans and is one of the most common congenital infections that complicate pregnancies and the well-being of newborns. The present study is a cross sectional study conducted in Benghazi / Libya over a period of (January-December) 2022 to estimate the prevalence of CMV-IgG and CMV-IgM in 150 pregnant Libyan women, with age range between 18-46 years old (mean ag 28.73) at any gestational period attending Benghazi medical center and Al-kish polyclinic, demographic and historical data like age, gestational period, parity, number of abortions, past surgery and gravidity, were collected by well structured data collection sheet. The sera were obtained from the blood samples, IgG, IgM antibodies were quantified by Elecsys according to the manufacturer instructions. Obtained results were analyzed using the appropriate statistical analysis. The results of CMV seroprevalence revealed that, 42 % of study subjects had exposed to CMV infection at some point of their life, and may also had be latent infection, 34% of study subjects were susceptible to infection with CMV, 24% had acute or recent infection. A significant association between CMV, age and education levels, 55.56 % of pregnant women with high education level showed recent or reactive state, 41.18% were susceptible to infection, while 33.33% showed previous or latent infection. There was a highly significant association between CMV seroprevalence and residence, pregnant women living in urban areas, had more recent or reactive infection and higher susceptibility to infection in the future than those living in rural regions. Parity was a significantly associated with CMV seroprevalence, multi-parity women showed more reactive or recent CMV infection, no significant association of CMV seroprevalence and gestational age of pregnant women was found, no significant association of these characters and CMV seroprevalence.

Keywords- Cytomegalovirus (CMV), Pregnant Women.

I. INTRODUCTION

Human cytomegalovirus (CMV; also known as human herpesvirus 5) is is a double-stranded DNA virus, it is the prototype member of the *Betaherpesvirinae*. Like all herpesviruses, it establishes latency and persists for the life of the individual. Infection with CMV is common throughout the globe (Zuhair *et al.*, 2019). The proportion of adults with specific IgG antibodies approximates to 60% in developed countries and more than 90% in many developing countries (Zuhair *et al.*, 2019). Infection is more common in those from lower socio-economic groups and from non-Caucasian backgrounds (Pembrey *et al.*, 2013). Children born in the UK to women who have moved from high-risk countries have the lowered risk of their adopted country (Pembrey *et al.*, 2017). The saliva and urine of young children are major sources of virus, especially for those with child caring responsibilities (Staras *et al.*, 2008). CMV is not highly contagious, with a basic reproductive number of ~1.7–2.4 (Mayer *et al.*, 2017). It can also be spread sexually, by transfusion of whole blood or by organ transplantation (Atabani *et al.*, 2012). It is important to note that there are usually no symptoms associated with CMV infection, except for occasional cases of infectious mononucleosis. This is because a robust immune response to CMV normally prevents the high viral loads required to cause the end organ disease (EOD) seen in immunocompromised individuals. However, despite the absence of overt symptoms, there is evidence that infected individuals may have long-term adverse outcomes related to induction of a chronic inflammatory cell-mediated immune response to this apparently innocuous virus (indirect effects) (Griffiths, 2020).
The natural history of CMV infection is complex, with three different subtypes of infection (Atabani *et al.*, 2012). Primary infection occurs when an individual with no immunity against this virus becomes infected for the first time. Afterwards, the virus establishes latency from which it may reactivate (second type of infection). The third type of infection is called reinfection when contact with an infectious individual results in superinfection of someone who has already been infected, despite their possession of natural immunity (Atabani *et al.*, 2012). Any of these three subtypes of infection can complicate pregnancy, making CMV the commonest cause of congenital infection (Cannon & Davis, 2005). It is also the most common and the most serious opportunistic infection after solid organ transplantation (SOT) or haematopoietic stem cell

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transplantation (SCT) and remains an important opportunistic infection in individuals with HIV (Atabani *et al.*, 2012). However, early diagnosis and proper management are crucial in immunosuppressed patients during pregnancy and in the postnatal period (Bennett, *et al.*, 2015). If primary CMV infection occurs periconceptionally or in the first trimester of pregnancy, it can impact fetal development and result in severe abnormalities, known as a congenital CMV infection (Pass & Arav-Boger, 2018). The diagnosis of both maternal and fetal infections is often a challenge and can be established directly or indirectly. The serum testing of the mother is highly important and can predict fetal infection (Saldan, *et al.*, 2017). The direct detection of CMV from the amniotic fluid of fetal blood may put the fetus at risk, while imaging findings are not pathognomonic for CMV fetal infection. Most frequent anomalies are cranial, but extracranial findings may also relate to viral infection. Cranial anomalies, especially microcephaly and ventriculomegaly, are associated with a poor postnatal prognosis (Boucoiran *et al.*, 2021). Congenital CMV infection is considered the most common non-genetic cause of fetal sensorineural hearing loss (Liu *et al.*, 2021). Both the level of fetal transmission and severity of the disease can be lowered with proper intrapartum and postpartum therapies, such as immunoglobulins and antiviral administration to the mother and fetus during pregnancy and in the postpartum period (Kagan & Hamprecht, 2017). This review aimed to shed light on the state-of-the-art methods for the prevention, prenatal diagnosis, and management of congenital CMV infection.

A. Aims of work:

1. To evaluate the seroprevalence of Cytomegalovirus among pregnant women.
2. To evaluate the relation between CMV seroprevalence, age, education level, residence, parity and gestational period.
3. To evaluate the relation between CMV seroprevalence and obstetrical parameters.

II. METHODS AND MATERIALS

A. Study location and design:

The present study is a cross sectional study conducted in Benghazi / Libya over a period of (January-December) 2022 to estimate the prevalence of CMV-IgG and CMV-IgM in 150 pregnant Libyan women, with age range between 18-46 years old (mean age= 28.8) at any gestational period attending Benghazi medical center and Al-kish polyclinic, demographic and historical data like age, gestational period, parity, number of abortions, past surgery, receiving blood transfusion and gravidity, were collected by well-structured data collection sheet.

B. Ethical Approval:

The data collection sheet was signed by patients who previously informed about the research purpose. Approvals also obtained from the medical affairs of both BMC and Al-kish center before beginning of the study.

C. Sample collection and processing:

Three milliliters of direct veinus blood was collected under aseptic technique into K3EDTA vacuum blood collection tubes, carefully labeled and allowed to clot at room temperature, then transferred to the laboratory in a cold chain. The blood was centrifuged at 3000rpm for 5 minutes. The supernatant sera obtained after centrifugation were carefully collected into labeled tubes using pasture pipette and refrigerated until IgG, IgM antibodies were quantified by Elecsys in Al saleem laboratory.

Fig. (I): *Sample collection and processing.*

D. Detection of anti-CMV IgG and IgM antibodies:

Serologic tests that detect CMV antibodies (IgM and IgG antibody to CMV) are widely available from commercial laboratories. A positive test for CMV IgG indicates that a person was infected with CMV at some time during their life, but does not indicate when a person was infected. This applies

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for persons ≥12 months of age when maternal antibodies are no longer present. Measurement of CMV IgG in paired samples taken one to three months apart can be used to diagnose primary infection; seroconversion (1st sample IgG negative, 2nd sample IgG positive) is clear evidence for recent primary infection. The presence of CMV IgM cannot be used by itself to diagnose primary CMV infection because IgM can also be present during secondary CMV infection, which includes reinfection with a different strain or reactivation of latent CMV acquired in the past. IgM positive results in combination with low IgG avidity results are considered reliable evidence for primary infection. An algorithm for immuodiagnosis of CMV infection during pregnancy is shown in the figure (3-1) according to the following publications: (Guerra *et al.,* 2007; Duff, 2007; Saldan *et al.*, 2017).

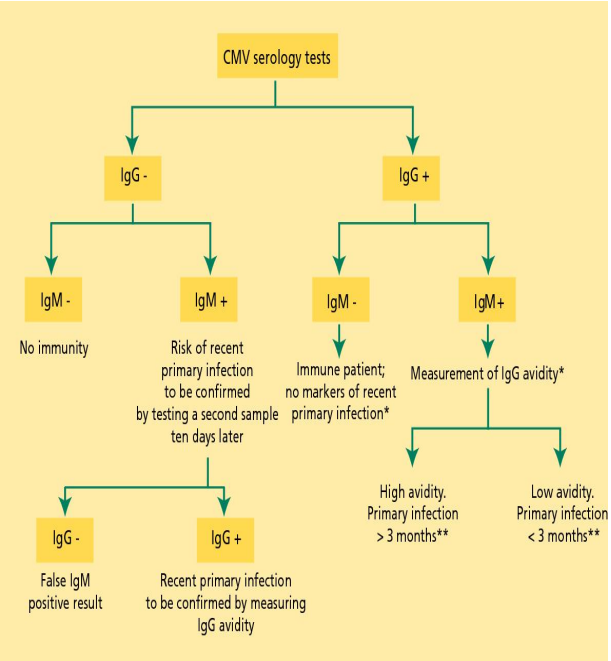

Fig. (II): *Proposed diagnostic algorithm for CMV serology screening in pregnant women (Saldan et al., 2017).*

E. Detection of anti-CMV IgG and IgM by Elecsys:

Elecsys devices is a full automated devices based on the electro chemiluminescence immunoassay "ECLIA" technique intended for use on the cobas e 801 immunoassay analyzer. Roche Diagnostics, Inc. Immunoassay for the in vitro qualitative detection of IgM and IgG antibodies to CMV in human serum, lithium- heparin plasma, K2- EDTA plasma, and K3- EDTA plasma. The test is intended as an aid in the diagnosis of recent or current CMV infection in individuals for which a CMV IgM and IgG tests was ordered, including pregnant women.

F. Detection of CMV IgG :

Principle:

Detection of CMV IgG by Elecsys depend on sandwich ELISA principle. The total duration of assay: 18 minutes.1st incubation: 12 µL of sample, biotinylated recombinant CMV- specific antigens, and CMV- specific recombinant antigens labeled with a ruthenium complexa) form a sandwich complex. 2nd incubation: After addition of streptavidin-coated microparticles, the complex becomes bound to the solid phase via interaction of biotin and streptavidin. The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell II M. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier. Results are determined via a calibration curve which is instrument specifically generated by 2- point calibration and a master curve provided via the cobas link.

Reagents provided:

1. The cobas pack (M, R1, R2).
   a. M -Streptavidin-coated microparticles
   b. R1- CMV- Ag~biotin.
   c. R2 -CMV- Ag~Ru(bpy)32+ .
2. CMVIGG Cal-1 Negative calibrator 1
3. CMVIGG Cal-2 Positive calibrator 2

Assay procedure:

1. During the first incubation, 6 µL of sample were automatically prediluted 1:20 with diluent (Diluent Universal). Biotinylated monoclonal anti-human IgG specific antibodies were also added.
2. During the second incubation, CMV-specific recombinant antigen labeled with a ruthenium complex and streptavidin-coated microparticles were added. Anti-CMV IgG antibodies present in the sample reacted with the ruthenium-labeled CMV-specific recombinant antigen. The complex became bounded to the solid phase via interaction of biotin with streptavidin.
3. The reaction mixture was aspirated into the measuring cell where the microparticles were magnetically captured onto the surface of the electrode. Unbounded substances were then removed with ProCell II M. Application of a voltage to the electrode then induces chemiluminescent emission which was measured by a photomultiplier.
4. The analyzer automatically calculated the cutoff based on the measurement of Calibrator 1 and Calibrator 2.

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Results interpretation:

The result of the samples was given either as reactive, borderline, or non-reactive as well as in the form of a cutoff index (signal of sample/cutoff)(COI) as shown in table (I).

Fig. (III): *Elecsys CMV IgG kit.*

Table (I) *Results interpretation of CMV IgG test.*

Numeric result	Result message	Interpretation/further steps
< 0.5 U/ml	Non-reactive	Not infected with CMV and therefore susceptible to primary infection.
≥ 0.5 to < 1.0 U/ml	Borderline	Samples should be retested. In case the result is still borderline, a second sample should be collected (e.g. within 2 weeks) and testing should be repeated.
≥ 1.0 U/ml	Reactive	Positive for CMV IgG-specific antibodies indicating either acute or past infection. Such individuals are potentially at risk of transmitting the virus (e.g. mother to fetus) but are at current not necessarily contagious.

G. Detection of CMV IgM:

Test principle:

The Elecsys CMV IgM immunoassay is based on the m-Capture test format. During the first incubation step, biotinylated monoclonal anti-h-IgM-specific antibodies binds specifically to IgM the diluted test specimen. CMV-specific recombinant antigen labeled with a ruthenium complex and streptavidin-coated microparticles are then added for the second incubation. Anti-CMV IgM antibodies present in the sample react with the ruthenium-labeled CMV-specific recombinant antigen. The complex becomes bound to the solid phase via interaction of biotin with streptavidin. The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Unbound substances are then removed with ProCell II M. Application of a voltage to the electrode then induces chemiluminescent emission which is measured by a photomultiplier.

Reagents provided

The following reagents are provided in the Elecsys CMV IgM assay kit:

1. THE REAGENT RACK PACK (COBAS E PACK) CONSISTS OF REAGENTS (M, R1, AND R2)
2. M: STREPTAVIDIN-COATED MICROPARTICLES.
3. R1: ANTI-H-IGM-AB~BIOTIN,
4. R2: CMV-AG~RU(BPY).
5. CMVIGM CAL1: NEGATIVE CALIBRATOR 1.
6. CMVIGM CAL2: POSITIVE CALIBRATOR 2.

Assay steps:

1. During the first incubation, 6 µL of sample were automatically prediluted 1:20 with diluent (Diluent Universal). Biotinylated monoclonal anti-human IgM specific antibodies was also added.
2. During the second incubation, CMV-specific recombinant antigen labeled with a ruthenium complex and streptavidin-coated microparticles were added. Anti-CMV IgM antibodies present in the sample react with the ruthenium-labeled CMV-specific recombinant antigen. The complex became bounded to the solid phase via interaction of biotin with streptavidin.
3. The reaction mixture was aspirated into the measuring cell where the microp articles were magnetically captured onto the surface of the electrode. Unbound substances were then removed with ProCell II M. Application of a voltage to the electrode then induced chemiluminescent emission which is measured by a photomultiplier.

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4. The analyzer automatically calculated the cutoff based on the measurement of Calibrator 1 and Calibrator 2.

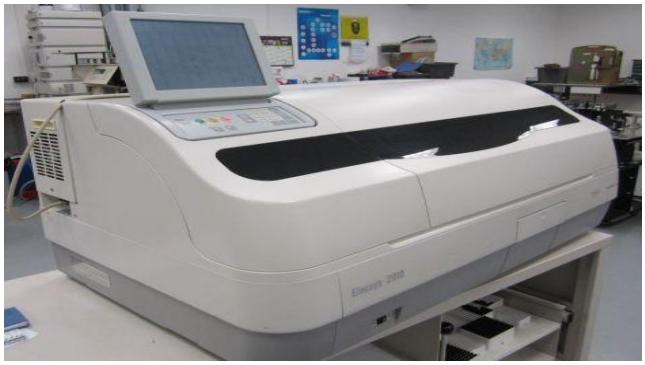
Interpretation of Results:

The result of the samples is given either as reactive, borderline, or non-reactive as well as in the form of a cutoff index (signal of sample/cutoff)(COI) as shown in Table (II).

Fig. (IV) *Elecsys CMV IgM package*

Table (II) *Results interpretation of CMV IgM test*

Numeric Result	Result Message	Interpretation/Further Steps
COI < 0.7	Non-reactive	CMV IgM-specific antibodies not detected.
0.7 > COI > 1.0	Borderline	Re-test the sample. If the result is indeterminate (borderline), collect and test a second sample within the following 2 weeks.
COI > 1.0	Reactive	CMV IgM-specific antibodies detected.



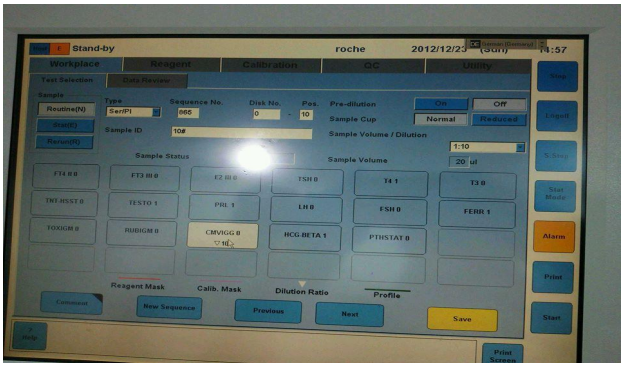


Fig (V) *Elecsys analyzer (Roche Diagnostics)*

H. Statistical analysis:

Data collected by questionnaire, results of the laboratory analysis were summarized in an excel sheet and after entering all data the collected information were validated by comparison and manual checking with the original paper form data were exported to SPSS for statistical analysis to explore the seroprevalence of IgG and IgM and its association with other factors. Data were analyzed using SPSS software (social package statistic software, version 22), cross-tabulation and spearman correlation tests, were applied to explore the prevalence of CMV and its association with other factors significance was accepted at P-values below 0.05 the confidence interval was set at 95%.

III.RESULTS AND DISCUSSION

A. Evaluation of descriptive data of pregnant women:

Data collected through interviewer administered questionnaires during the study, were derived the demographic data of respondents shown in the table (III) below showed that from the 150 pregnant women sampled in the study had a mean age of (28.73 ±7.476) years. On the level of education about 41.3 (62) reached tertiary education, 40%

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(60) had secondary level education, and about 18.7 % (28) had primary education level. Concerning parity status about 20% (30) had not given birth prior to the study, 20% (30) had conceived once, 23.33% (35) had conceived twice, 36.67% (55) had conceived three or more than three times. Concerning number of abortions about 68% (102) women had no abortions, 24% (36%) experienced one abortion, and 8% (12) had two or more abortions. Concerning the living environment, about 86% (129) were living in urban places while about 14% (21) were living in rural places, table (4-1) summarizes the results of the demographic and clinical findings of 150 pregnant women.

Table (III): *Summery of demographic and clinical findings of 150 pregnant women.*

Indicators	Frequency	Percent
Age		
< 20	20	13.33%
20-29	70	46.67%
30-39	48	32%
> 40	12	8%
Education level		
Primary	28	18.7%
Secondary	60	40%
High School	62	41.3%
Residence		
Urban	129	86%
Rural	21	14%
Parity interval		
No birth	30	20%
Once	30	20%
Twice	35	23.33%
Multi-parity	55	36.67%
Gestational age		
First trimester	23	15.3%
Second trimester	63	42%
Third trimester	64	42.7%

B.Seroprevalence of HCV in pregnant women:

Laboratory results of the blood samples which were collected from the 150 pregnant women in the study were tested for the presence of anti-CMV IgG showed about 34% (51 subjects) had undetectable IgG, about 22.67% (34 subjects) showed borderline results, while 43.33% (65 subjects), showed detectable IgG. Regarding the results of anti-HCV IgM antibodies of 150 pregnant women showed 76% (114 of the subjects) had undetectable IgM, while about 20 % (30 subjects) showed borderline results, only 4% (6 subjects) were positive to IgM antibodies, as shown in table (IV) and figure (VI).
The net results of CMV seroprevalence revealed that, 42 % of study subjects had exposed to CMV infection at some point of their life, and may also had be latent infection, 34% of study subjects were susceptible to infection with CMV, 24% had acute or recent infection, the distribution of study subjects according to CMV infection categories are described in table (V) and figure (VII).

Table (IV): *Distribution of study subjects according to CMV seroprevalence*

Categories	N	Percent
IgG		
Positive	65	43.33%
Borderline	34	22.67%
Negative	51	34%
Total	150	100%
IgM		
Positive	6	4%
Borderline	30	20%
Negative	114	76%
Total	150	100%

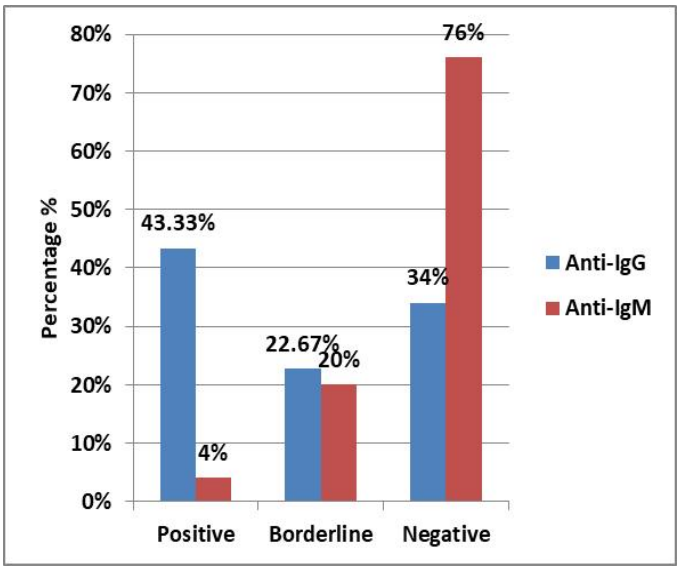

Fig. (VI): *Distribution of study subjects according to CMV seroprevalence*

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Table (V): *Distribution of study subjects according to CMV infection categories.*

Categories	Seroprevalence	N.	Percent
Previous/ Latent	Negative IgM and positive IgG	63	42%
Susceptible	Negative or borderline IgM and negative IgG	51	34%
Reactive/ Recent	Positive or borderline IgM and positive IgG	36	24%

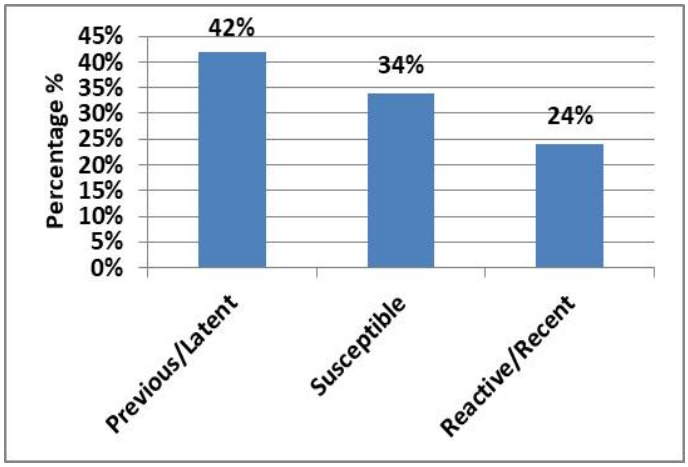

Fig. (VII): *Distribution of study subjects according to CMV infection categories*

CMV Seroprevalence and age:

A significant association between CMV and age (p-value 0.034), age group 30-39 showed higher seroprevalence, age group above 40 years showed less seroprevalence, while women of age 20-29 were at risk of primary infection.

Table (VI): *The CMV seroprevalence according to age groups.*

Age groups					
Category	**< 20**	**20-29**	**30-39**	**> 40**	**Total**
Previous / Latent	5 (7.9%)%	32 (50.8%)	24 (38.1%)	2 (3.2	63 (100%)
Susceptible	5 (9.8%)	30 (58.82%)	12 (23.53%	4 (7.84	51 (100%)
Reactive/ Recent	10 (27.78%)	8 (22.22%)	12 (33.33%	6 (16.6	36 (100%)
Total	20 (100%)	70 (100%)	48 (100%)	12 (100	150 (100%)

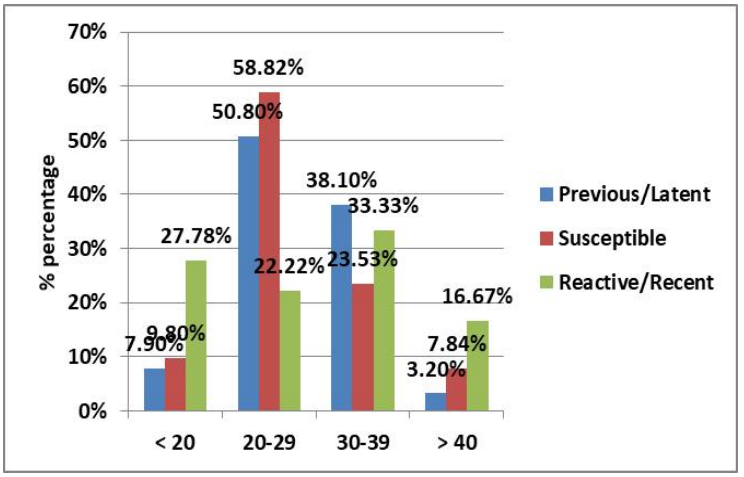

Fig.(VIII): *The CMV seroprevalence according to age groups.*

CMV Seroprevalence and education level:

Regarding the education level of the study subjects, a significant association between the CMV seroprevalence and education levels (p-value 0.049), 55.56 % of pregnant women with high education level showed recent or reactive state, 41.18% were susceptible to infection. While 33.33% showed previous or latent infection.

Table (VII): *The CMV seroprevalence according to education level*

Category	Education level			
	Elementary	**Secondary**	**High**	**Total**
Previous/Latent	8 (12.7%)	34 (53.97%)	21 (33.33%)	63 (100%)
Susceptible	10 (19.61%)	20 (39.22%)	21 (41.18%)	51 (100%)
Reactive/Recent	10 (27.78%)	6 (16.67%)	20 (55.56%)	36 (100%)
p-value=0.049		**r=0.54**		

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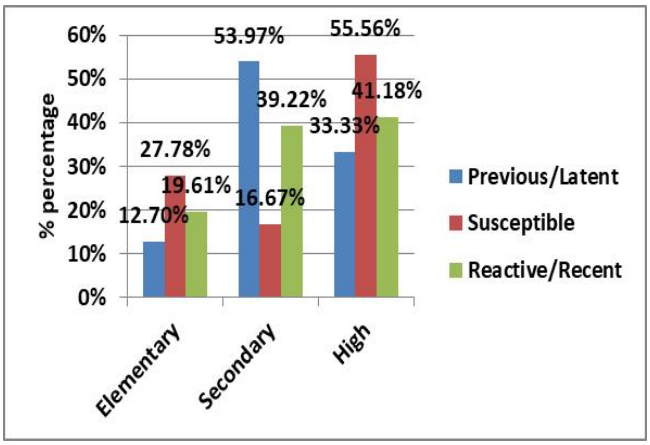

Fig. (IX): *The CMV seroprevalence according to education level*

CMV Seroprevalence and Residence:

There was a highly significant association between CMV seroprevalence and residence (p-value 0.02), pregnant women living in urban areas, had more recent or reactive infection and higher susceptibility to infection in the future than those living in rural regions.

Table (VIII): *CMV Seroprevalence according to residence.*

Category	Residence		
	Urban	Rural	Total
Previous/Latent	53 (84.13%)	10 (15.87%)	63 (100%)
Susceptible	45 (88.24%)	6 (11.76%)	51 (100%)
Reactive/Recent	31 (86.11%)	5 (13.89%)	36 (100%)
p-value 0.002		**r=0.87**	

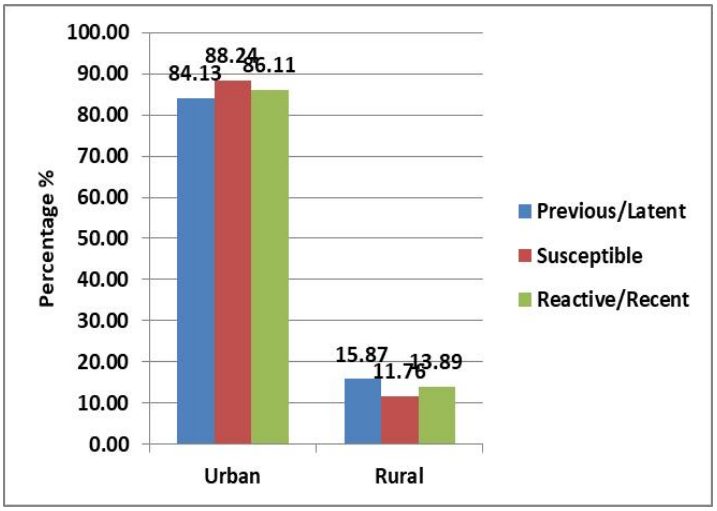

Fig. (X): *CMV Seroprevalence according to residence.*

CMV Seroprevalence and parity:

As shown in the table (IX), Parity was a significantly associated with CMV seroprevalence, p-value 0.03, multi-parity women showed more reactive or recent CMV infection .

Table (IX): *CMV Seroprevalence according to parity.*

Category	Parity				
	No birth	Once	Twice	Multi-parity	Total
Previous/ Latent	9 (14.29%)	15 (23.81%)	17 (26.98	22 (34.92%)	63 (100%)
Susceptible	18 (35.29%)	9 (17.65%)	16 (31.37	8 (15.69%)	51 (100%)
Reactive/ Recent	3 (8.33%)	6 (16.67%)	2 (5.56	25 (69.44%)	36 (100%)
r= 0.72			**p-value 0.03**		

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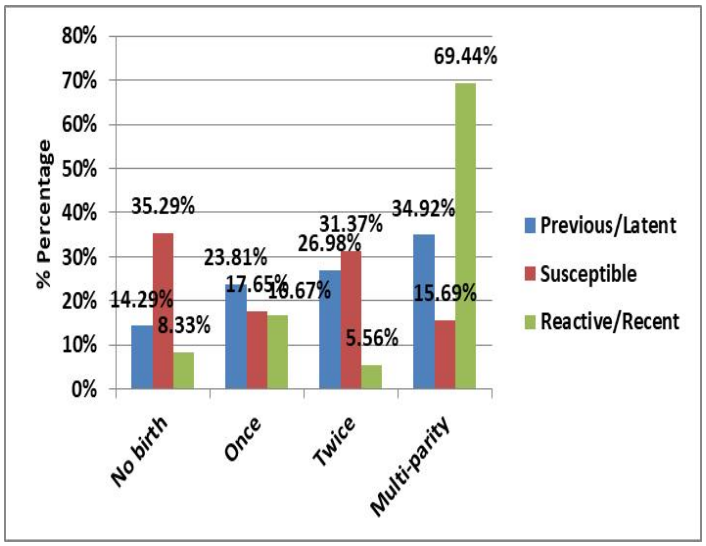

FIG (X): *CMV Seroprevalence according to parity.*

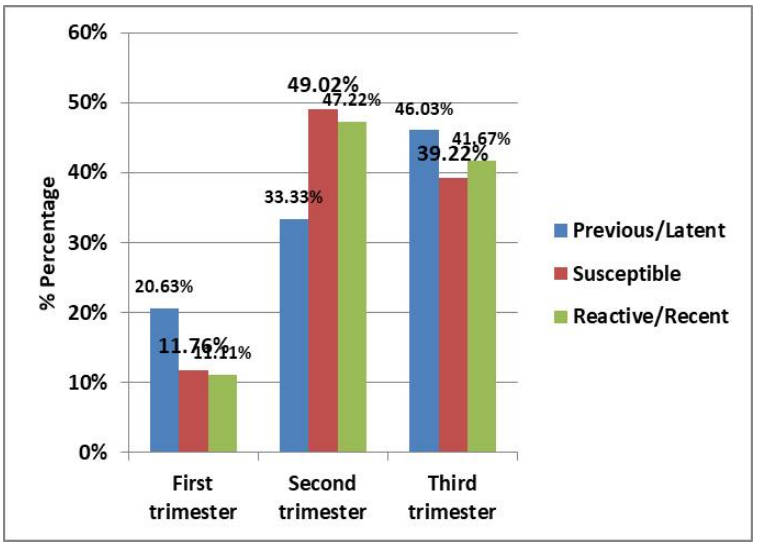

Fig. (XI): *Seroprevalence according to gestational age.*

CMV Seroprevalence and gestational age:

By evaluating CMV seroprevalnce according to gestational age, no significant association of CMV seroprevalence and gestational age of pregnant women was found p- value (0.067).

Table (X): *Seroprevalence according to gestational age.*

Category	Gestational age			
	First trimester	Second trimester	Third trimester	Total
Previous/ Latent	13 (20.63%)	21 (33.33%)	29 (46.03%)	63 (100%)
Susceptible	6 (11.76%)	25 (49.02%)	20 (39.22%)	51 (100%)
Reactive/ Recent	4 (11.11%)	17 (47.22%)	15 (41.67%)	36 (100%)
r= 0.054		p-value 0.067		

CMV Seroprevalence and number of abortions:

Regarding the obstetrical characteristic of the pregnant women, no significant association of these characters and CMV seroprevalence p-value > 0.05.

Table (XI): *CMV Seroprevalence according to number of abortions*

Obstetrical characteristics			
Category	Yes	No	Total
Preterm Deliveries			
Previous/Latent	1	62	63
Susceptible	5	46	51
Reactive/Recent	3	33	36
r= 0.044		p-value 0.3	
Abortion (Miscarriage)			
Previous/Latent	3	60	63
Susceptible	3	48	51 (100%)
Reactive/Recent	2	34	36 (100%)
r= 0.032		p-value 0.2	
Stillbirths			
Previous/Latent	1	62	63 (100%)
Susceptible	1	50	51 (100%)
Reactive/Recent	1	35	36 (100%)
r= 0.079		p-value 0.097	
Malformed Children			
Previous/Latent	0	63	63 (100%)
Susceptible	0	51	51 (100%)
Reactive/Recent	1	35	36 (100%)
r= 0.09		p-value 0.08	

Primary human cytomegalovirus (CMV) infection during pregnancy is a major cause of congenital malformation, and can result in significant perinatal morbidity and health care expense complicates approximately 1% of all live births. Primary maternal CMV infection carries a 30% to 40% risk of

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vertical transmission to the fetus. Although existing data suggest a benefit to HIG prophylaxis, additional clinical trials are needed to confirm these observations. Until then, the use of HIG and other antiviral agents for treatment remains experimental. In the absence of proven therapies for congenital CMV infection, prevention is critical. Most importantly, patients, especially those exposed to young children, should be counseled about the importance of careful hand hygiene practices, an intervention that has been proven to decrease the risk of primary CMV infection and subsequent fetal transmission (Carlson *et al.,* 2010). The risk of CMV infection is increased in children of mothers with confirmed seroconversion of anti-CMV IgM/IgG antibodies during pregnancy; however, the serological status of the contraceptive period is sporadically known**.** The present study was performed to investigate the seroprevalence and correlates of CMV infection in pregnant women in Benghazi/Libya. The results of the study demonstrated low seroprevalence of IgG. the overall prevalence of Anti- CMV IgG antibodies in pregnant women was only (43.3%) who were infected some time in their life and recovered from the primary infection, other past literature showed higher prevalence, studies conducted in Egypt (Kamel *et al*., 2014), Bahrain (AlKhawaja *et al*., 2011), Iraq (AL–Jurani, 2014) and Turkey (Parlak *et al*., 2015) showed 100%, Palestine (99.6%) (Neirukh *et al*., 2013); Sudan (97.5%), (Khairi *et al*., 2013); Tunisia (96.3%) (Hannachi *et al*., 2011); Yemen (98.7%)(Alghalibi *et al*., 2016) and Iran (98.8%) (Josheghani *et al*., 2015). The results of IgG seroprevalence were comparable to reports conducted in England (49%) (Pembrey *et al*., 2013), France (43.7%) (N'Diaye *et al*., 2014) and Belgium (30.2%) (Leuridan *et al*., 2012). The prevalence of CMV infection observed in this study was different to that reported in other developing communities but comparable to that reported in developed communities. This may be attributed to the inclusion of CMV screening among the antenatal profile tests and better hygienic standards (Guerra *et al*., 2007). About 22.67% had borderline results these cases needed more investigations, while 34.33%who were never infected with CMV during their lives and they are susceptible for CMV primary infection during the pregnancy and must undergo routine screening for CMV antibodies during pregnancy**.** Following an initial CMV infection, the host begins to produce IgG antibodies to the virus within 1–2 weeks, and the production of CMV-specific IgG antibodies continues lifelong (Schultz & Chandler, 1991). The most straightforward confirmation of primary CMV infection is determined based on findings of CMV-IgG seroconversion (i.e., conversion from negative to positive CMV-IgG antibody test findings).

In a pregnant woman, the detection of CMV-IgG seroconversion is possible with paired of serum samples that can be used to identify infections based on pinpoint blood samples that are collected preconceptionally and during pregnancy (Rajasekariah *et al*., 2013). However, such matched tests are rarely available during pregnancy. Moreover, in many countries, preconception serological screening for CMV is not recommended due to practical health-economics-related reasons or the uncertainty of serological testing (Rawlinson *et al*., 2017). Furthermore, seronegative women require periodic serological testing to detect seroconversion. A reassessment of CMV-IgG findings is usually performed early in the second trimester in order to detect cases of seroconversion. Reassessments are performed at least once during the third trimester (at 35–37 weeks of gestation) to identify neonates who are at risk of congenital CMV infection in cases of late seroconversion. Laboratory results of the blood samples which were collected from the 150 pregnant women in the study were tested for the presence of antibodies (CMV IgM) showed 76% of the cases had undetectable IgM and about 20 % showed borderline results and about 4% were seropositive to CMV IgM. The presence of CMV IgM cannot be used by itself to diagnose primary CMV infection because IgM can also be present during secondary CMV infection, which includes reinfection with a different strain or reactivation of latent CMV acquired in the past, borderline results needed more investigation our results were much different from previous literature, CMV IgM seropevalence recorded by Bagheri *et al.,* (2012) was (2.5%), Umeh *et al.,* (2015) (3.5%), De Paschale *et al.,* (2009) (0.8 %) Kamel *et al.,* (2014). In other literature Bagheri *et al*., (2012) the majority of pregnant women (72.1%) were positive for CMV IgG and 2.5% were positive for CMV IgM. In Palestine Al-Hindi *et al*., (2010) the anti-CMV IgM was 6% among pregnant females, whereas in Turkey Uyar *et al*., (2008), the positivity for anti-CMV IgG antibody was 97.3%, while 1% were positive for anti-CMV IgM. CMV total IgG antibodies were found in 92.1% in Saudi Arabia (Ghazi *et al*., 2002). CMV-IgM antibodies are generated following a primary CMV infection. More specifically, when examining CMV-IgM kinetics following a primary infection, peak levels are seen within the first 1–3 months, after which IgM titers decrease sharply within 2–3 months after the onset of infection and fall below the threshold of detection within 12 months (Revello & Gerna, 2002). Therefore, a diagnosis of primary CMV infection in pregnant women is most often based on a positive CMV-IgM antibody test, and the transient presence of specific IgM antibodies has long been used as a diagnostic marker for primary CMV infection. Sonoyama *et al.* reported that the probability of congenital CMV infection was appropriately 60% when pregnant women had positive CMV-IgM findings and fetal abnormalities on ultrasound (Sonoyama et l., 2012). However, the presence of CMV-IgM antibodies is not unique to primary CMV infections since assays for IgM antibodies lack specificity for primary infections. The CMV-IgM antibody has a high false-positive rate with regard to primary infections; <30% of pregnant women with positive IgM antibodies are determined to have a primary CMV infection (Lazzarotto *et al*., 2008). Although the frequency is less than 10%, CMV-specific IgM production occurs during non-primary infections (Revello & Gerna, 2002). Moreover, CMV-IgM antibodies

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may be produced during reactivation or reinfection and may persist for more than a year following an acute primary infection (Lazzarotto *et al.*, 2011). Association of IgG seropositivity with different obstetrical and medical parameters also evaluated by correlation test. A significant association of age with CMV IgG was found, a higher seroprevalence was demonstrated in elder pregnant women of 30- 39 years old, women above 40 years showed less seroprevalence, while women of age 20-29 were at risk of primary infection. This could be because as women age, their interactions and encounters with risk factors increase (Kolo *et al.*, 2013), many other investigators observed that, elder women were at higher risk of CMV infection Tookey *et al.*, (1992), Bate *et al.*, (2010), Hoshiba *et al.*, (1998) Other investigators Hamdan *et al.*, (2011), Kamel *et al.,(*2014), De Paschale *et al.*, (2009) demonstrated no significant differences in CMV IgG seroprevalence in different age groups. Illiteracy and low education levels were previously observed as risk factors for increased susceptibility to CMV infection, perhaps through direct contact with contagious secretions from their own children and poor hygiene practiced by these women (Walmus *et al.*, 1988; Bate *et al.*, 2004; Kramer *et al.*, 2006; Dowd *et al.*, 2008). In this study, CMV seroprevalence were significantly associated with high education level among pregnant women compared t low and intermediate education levels, this finding was inconsistent with that reported for other studies (Kombich *et al.*, 2012; Kolo *et al.*, 2013; Aljumaili *et al.*, 2014; Alghalibi, *et al.*, 2016).

In the current findings CMV infection was more predominant in urban women which agree with (Aljumaili *et al.*, 2014) and this finding was not consistent with previously reported studies (GratacapCavallier *et al.*, 1998; Forbes, 1998; Kolo *et al.*, 2013; Alghalibi, *et al.*, 2016). Likewise, low socioeconomic status is a strong risk factor for CMV infection (Bate *et al.*, 2010). Moreover, there was a significant association between CMV prevalence and parity, this was in concordance with other literatures, Hamdan *et al.*, (2011), Hoshiba *et al.*, (1998) demonstrated that women with high parity were at higher risk for CMV infection , Tookey *et al.*, (1992) demonstrated no significant association of parity interval and CMV IgG seroprevalence Higher CMV seroprevalence was independently associated with increasing number of live births (Hamdan *et al.*, 2011; Lanzieri *et al.*, 2016). Gestational age and other obstetrical parameters were independent from CMV seroprevalence which also reported in a study conducted by (Alghalibi, *et al.*, 2016).

However, a study carried out in Iraq found a significant association between CMV seropositivity and bad obstetric history (Aljumaili & Alsamarai, 2013). A significantly higher seroprevalence of CMV was reported in women with miscarriage history in Yemen (Edrees, 2010), in Saudi Arabia (Refaat *et al.*, 2014) and in Sudan (Khairi *et al.*, 2013).

IV.CONCLUSION

The seroprevalence of anti-HCV IgG was relatively low 43.33% compared to previous findings, 34% showed undetectable negative results, 22.67% were borderline and need repeated screening to establish the results. The seroprevalence of anti-HCV IgM was 4%, about 20% showed borderline results, 65% showed undetectable results. The net results of CMV seroprevalence revealed that, 42 % of study subjects had exposed to CMV infection at some point of their life, and may also had be latent infection, 34% of study subjects were susceptible to infection with CMV, 24% had acute or recent infection. A significant association between CMV and age, age group 30-39 showed higher seroprevalence, age group above 40 years showed less seroprevalence, while women of age 20-29 were at risk of primary infection. CMV seroprevalence was significantly associated with higher education level, urban living and parity interval. No significant association between CMV seroprevalence and obstetrical findings.

REFERENCES

[1] Acosta, E., Bowlin, T., Brooks, J., Chiang, L., Hussein, I., Kimberlin, D., Kauvar, L. M., Leavitt, R., Prichard, M., & Whitley, R. (2020). Advances in the Development of Therapeutics for Cytomegalovirus Infections. J Infect dis., 221(Suppl 1), S32–S44.

[2] Adler, B., & Sinzger, C. (2009). Endothelial cells in human cytomegalovirus infection: one host cell out of many or a crucial target for virus spread?. Thromb Haemost., 102(6): 1057–1063.

[3] Adler, S.P.& Reddehase, M.J. (2019). Pediatric roots of cytomegalovirus recurrence and memory inflation in the elderly. Med Microbiol Immunol., 208:323–328

[4] Alghalibi, SMS, Abdullah, QYM, Al-Arnoot, S. & Al-Thobhani A. (2016). Seroprevalence of Cytomegalovirus among Pregnant Women in Hodeidah city, Yemen. J Human Virol. Retrovirol., 3(5): 00106.

[5] Aljumaili, ZKM.& Alsamarai, AM., Risk factors for bad obstetric history in Kirkuk women, Iraq. International Journal of Infection Microbiology. 2013;2(3):70–77.

[6] AL–Jurani, AHH. (2014). Seroprevalence of Anti–Cytomegalovirus IgM, IgG antibodies among pregnant women in Diyala province. Diyala Journal for Pure Sciences, 10(2):83–87.

[7] AlKhawaja, S., Ismaeel, A., Botta, G., et al. (2011). The prevalence of congenital and perinatal cytomegalovirus infections among newborns of seropositive mothers. J Infect Dev Ctries. 6(5):410–415.

[8] Andrews, DM., Scalzo, AA., Yokoyama, WM., Smyth, MJ., & Degli-Esposti, MA. (2003). Functional interactions between dendritic cells and NK cells during viral infection. Nature immunol., 4(2), 175–181.

[9] Andronaco, DW. (2020). Congenital Cytomegalovirus and Hearing Loss. JOGNN, 49(3), 293–304.

[10] Arnouts L., Van Mechelen K., Laroche S., Meuwissen M., Boudewyns A., Martens M. & Mahieu L. (2022). Non-primary CMV infection not always innocent. A case-report and literature review. Acta Clin. Belg. 77:96–100.

[11] Atabani, SF., Smith, C., Atkinson, C., Aldridge, RW., Rodriguez-Perálvarez, M., Rolando, N., Harber, M., Jones, G., O'Riordan, A., Burroughs, A. K., Thorburn, D., O'Beirne, J., Milne, RS., Emery, VC., & Griffiths, PD. (2012). Cytomegalovirus replication kinetics in solid

organ transplant recipients managed by preemptive therapy. Am J Transplant., 12(9), 2457–2464.

[12] Auriti, C., De Rose, D. U., Santisi, A., Martini, L., Piersigilli, F., Bersani, I., Ronchetti, MP., & Caforio, L. (2021). Pregnancy and viral infections: Mechanisms of fetal damage, diagnosis and prevention of neonatal adverse outcomes from cytomegalovirus to SARS-CoV-2 and Zika virus. Molecular basis of disease, 1867(10), 166198.

[13] Bate, SL., Dollard, SC. & Cannon, MJ. (2010). Cytomegalovirus seroprevalence in the United States: the national health and nutrition examination surveys, 1988–2004. Clin Infect Dis., 50(11):1439-1447

[14] Bates, M., & Brantsaeter, AB. (2016). Human cytomegalovirus (CMV) in Africa: a neglected but important pathogen. J Virus Erad., 2(3):136–142.

[15] Beaudoin, ML., Renaud, C., Boucher, M., Kakkar, F. & Gantt, S. (2021). Boucoiran I. Perspectives of women on screening and prevention of CMV in pregnancy. Eur. J. Obstet. Gynecol. Reprod. Biol., 258:409–41.

[16] Bennett, J., Dolin, R. & Blaser, M. (2015). Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 9th ed.; Elsevier/Saunders: Philadelphia, PA, USA.

[17] Ben-Smith, A., Gorak-Stolinska, P., Floyd, S., Weir, RE., Lalor, MK., Mvula, H., Crampin, AC., Wallace, D., Beverley, PC., Fine, PE., & Dockrell, HM. (2008). Differences between naive and memory T cell phenotype in Malawian and UK adolescents: a role for Cytomegalovirus?. BMC Infect Dis., 8, 139.

[18] Blázquez-Gamero. D., Izquierdo, AG., del Rosal, T., Baquero-Artigao, F., Méndez, NI., Soriano-Ramos, M., Conejo, PR., González-Tomé, MI., García-Burguillo, A., Pérez, NP., et al. (2019). Prevention and treatment of fetal cytomegalovirus infection with cytomegalovirus hyperimmune globulin: A multicenter study in Madrid. J. Matern. Neonatal Med., 32:617–625.

[19] Boucoiran, I., Yudin, M., Poliquin, V., Caddy, S., Gantt, S. & Castillo, E. (2021). Guideline No. 420: Cytomegalovirus Infection in Pregnancy. J. Obstet. Gynaecol. Can., 43 (7):893–908.

[20] Bravender T. (2010). Epstein-Barr virus, cytomegalovirus, and infectious mononucleosis. Adolesc Med State Art Rev., 21(2), 251–ix.

[21] Britt W. (2008). Manifestations of human cytomegalovirus infection: proposed mechanisms of acute and chronic disease. Curr Top Microbiol Immunol., 325, 417–470.

[22] Burmeister, AR., Gordevicius, J., Paul, EN., Houck, C., George, S., Escobar Galvis, ML., Sha, Q., Brundin, P., Pospisilik, JA., Racicot, K., & Brundin, L. (2022). Maternal Herpesviridae infection during pregnancy alters midbrain dopaminergic signatures in adult offspring. Neurobiol disease., 169, 105720.

[23] Cadena-Mota S., Muñoz-Escalante J.C., Martínez-Rodríguez L.E., Bernal-Silva S., Tello-Martínez N., Torre-Rodríguez I., Hernández-Sánchez P.G., Castillo-Martínez F., Escalante-Padrón F., Lima-Rogel V., et al. (2022). Incidence of congenital and postnatal cytomegalovirus infection during the first year of life in Mexican preterm infants. Journal of Medical Virology., 94:3349–3358.

[24] Cannon, MJ., & Davis, KF. (2005). Washing our hands of the congenital cytomegalovirus disease epidemic. BMC public health, 5, 70.

[25] Cannon, MJ., Schmid, DS., & Hyde, TB. (2010). Review of cytomegalovirus seroprevalence and demographic characteristics associated with infection. Rev med virol., 20(4), 202–213.

[26] Caposio, P., Orloff, SL., & Streblow, DN. (2011). The role of cytomegalovirus in angiogenesis. Virus Res., 157(2): 204–211.

[27] Center of diseases and infection control (CDC), 2021. About Cytomegalovirus (CMV) [(accessed on 12 August 2022)]; Available online: https://www.cdc.gov/cmv/overview.html

[28] Chen, K., Cheng, MP., Hammond, SP., Einsele, H., & Marty, FM. (2018). Antiviral prophylaxis for cytomegalovirus infection in allogeneic hematopoietic cell transplantation. Blood advances, 2(16): 2159–2175.

[29] Chiopris, G., Veronese, P., Cusenza, F., Procaccianti, M., Perrone, S., Daccò, V., Colombo, C. & Esposito, S. (2020). Congenital Cytomegalo-virus Infection: Update on Diagnosis and Treatment. Microorganisms. 8:1516.

[30] Compton, T., & Feire, A. (2007). Early events in human cytomegalovirus infection. In A. Arvin (Eds.) et. al., Human Herpesviruses: Biology, Therapy, and Immunoprophylaxis. Cambridge University Press.

[31] Crough, T., & Khanna, R. (2009). Immunobiology of human cytomegalovirus: from bench to bedside. Clin Microbiol Rev., 22(1): 76–98.

[32] Cunningham, C., Gatherer, D., Hilfrich, B., Baluchova, K., Dargan, DJ., Thomson, M., Griffiths, PD., Wilkinson, G. W., Schulz, TF., & Davison, A. J. (2010). Sequences of complete human cytomegalovirus genomes from infected cell cultures and clinical specimens. J Gen Virol. , 91(Pt 3): 605–615.

[33] de Jong, MD., Galasso, GJ., Gazzard, B., Griffiths, PD., Jabs, DA., Kern, ER., & Spector, SA. (1998). Summary of the II International Symposium on Cytomegalovirus. Antiviral Res., 39(3): 141–162.

[34] Demmler-Harrison, GJ. & Miller, J.A. (2020). Houston Congenital Cytomegalovirus Longitudinal Study Group Maternal cytomegal-ovirus immune status and hearing loss outcomes in congenital cytomegalovirus-infected offspring. PLoS ONE. 15:e0240172.

[35] Dowd, JB., Haan, MN., Blythe, L., Moore, K. & Aiello, AE. (2008). Socioeconomic gradients in immune response to latent infection. Am J Epidemiol., 167 (1):112-120.

[36] Edrees, A. (2010). Prevalence Cytomegalovirus antibodies among pregnant women and newborns in the hospital president in Jebla, Ibb Yemen. M.Sc. Thesis, Department of Medical Microbiology, Faculty of Medicine and Health, Sana'a University, Yemen.

[37] Forbes, BA. (1998). Acquisition of cytomegalovirus infection: an update Clin Microbiol Rev, 2: 204-216.

[38] Fortunato, EA., & Spector, DH. (1999). Regulation of human cytomegalovirus gene expression. Adv Virus Res., 54, 61–128.

[39] Freeman, ML., Lederman, MM., & Gianella, S. (2016). Partners in Crime: The Role of CMV in Immune Dysregulation and Clinical Outcome During HIV Infection. Curr HIV/AIDS Rep., 13(1): 10–19

[40] Gardiner, BJ., Herrick, KW., Bailey, RC., Chow, JK., & Snydman, DR. (2019). Reactivation of Latent Cytomegalovirus Infection after Major Surgery: Risk Factors and Outcomes. Surgical infections, 20(5), 416–423.

[41] Gerna, G. & Lilleri, D. (2020). Human Cytomegalovirus Congenital (cCMV) Infection Following Primary and Nonprimary Maternal Infection: Perspectives of Prevention through Vaccine Development. Vaccines, 8:194.

[42] Ghazi, HO. (2002). Telmesani AM, Mahomed MF. TORCH agents in pregnant Saudi women. Med Princ Pract., 11(4):180–182.

[43] Gianella, S., & Letendre, S. (2016). Cytomegalovirus and HIV: A Dangerous Pas de Deux. J Infect dis., 214 Suppl 2(Suppl 2): S67–S74.

[44] Gianella, S., Massanella, M., Wertheim, JO., & Smith, DM. (2015). The Sordid Affair Between Human Herpesvirus and HIV. J Infect dis., 212(6): 845–852.

[45] Gibson, W. Structure and formation of the cytomegalovirus virion. Curr Top Microbiol Immunol. 2008;325:187-204.

[46] Grangeot - Keros, L., Vauloup-fellous, C., Leruez-Ville, M., & Ville, Y. (2010). Cytomegalovirus (CMV) and pregnancy.

[47] GratacapCavallier, B., Bosson, J., Morand, P., Dutertre, N., Chanzy, B., Seigneurin, J., et al. (1998). Cytomegalovirus seroprevalence in French pregnant women: parity and place of birth as major predictive factors Eur J Epidemiol, 14 (2):147-152.

[48] Griffiths P. (2020). The direct and indirect consequences of cytomegalovirus infection and potential benefits of vaccination. Antiviral res, 176, 104732.

[49] Griffiths, P., Baraniak, I., & Reeves, M. (2015). The pathogenesis of human cytomegalovirus. J Pathol., 235(2), 288–297.

[50] Griffiths, PD., & Baboonian, C. (1984). A prospective study of primary cytomegalovirus infection during pregnancy: final report. Br J Obstet Gynaecol, 91(4): 307–315.

[51] Guerra, B., Simonazzi, G., Banfi, A., Lazzarotto, T., Farina, A., Lanari, M., & Rizzo, N. (2007). Impact of diagnostic and confirmatory tests and prenatal counseling on the rate of pregnancy termination among women with positive cytomegalovirus immunoglobulin M antibody titers. Am J Obstet Gynecol., 196(3), 221.e1–221.e2216.

[52] Gupta, M. & Shorman, M. StatPearls. (2022). StatPearls Publishing; Treasure Island, FL, USA: 2022. [(accessed on 5 June 2022)]. Cytomegalovirus. Available online: https://www.ncbi.nlm.nih.gov/books/NBK459185/

[53] Hamdan, HZ., Abdelbagi, IE., Nasser, NM. & Adam, I. (2011). Seroprevalence of cytomegalovirus and rubella among pregnant women in Western Sudan. Virol J., 8: 217.

[54] Hannachi, N., Marzouk, M., Harrabi, I., et al. (2011). Seroprevalence of rubella virus, varicella zoster virus, cytomegalovirus and parvovirus B19 among pregnant women in the Sousse region, Tunisia. Bull Soc Pathol Exot.,104(1):62–67.

[55] Hughes, BL., Clifton, RG., Rouse, DJ., Saade, GR., Dinsmoor, MJ., Reddy, UM., Pass, R., Allard, D., Mallett, G., Fette, LM., et al. (2021). Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network. A Trial of Hyperimmune Globulin to Prevent Congenital Cytomegalovirus Infection. N. Engl. J. Med., 385:436–444.

[56] Jenks, CM., Hoff, S.R. & Mithal LB. (2021). Congenital Cytomegalovirus Infection: Epidemiology, Timely Diagnosis, and Management. Neoreviews.22:e606–e613.

[57] Josheghani, SB., Moniri, R., Taheri, FB., et al. (2015). The Prevalence of Serum antibodies in TORCH Infections during the First Trimester of Pregnancy in Kashan, Iran. IJN., 6:9

[58] Kagan, KO., & Hamprecht, K. (2017). Cytomegalovirus infection in pregnancy. Arch gynecol obstet., 296(1), 15–26.

[59] Kamel, N., Metwally, L., Gomaa, N., et al. (2013). Primary cytomegalovirus infection in pregnant Egyptian women confirmed by cytomegalovirus IgG avidity testing. Med Princ Pract. 2014;23(1):29–33. 19. Khairi S, Intisar K, Enan K, et al. Seroprevalence of cytomegalovirus infection among pregnant women at Omdurman Maternity Hospital, Sudan. J Med Lab Diagn., 4(4):45–49.

[60] Kamel, N., Metwally, L., Gomaa, N., Sayed Ahmed, W. A., Lotfi, M., & Younis, S. (2014). Primary cytomegalovirus infection in pregnant Egyptian women confirmed by cytomegalovirus IgG avidity testing. Medical principles and practice : international journal of the Kuwait University, Health Science Centre, 23(1), 29–33.

[61] Karageorgou, I., Kossyvakis, A., Jiménez, J., Garcia I. & Mentis, AA. (2022). Cytomegalovirus DNA detection in pregnant women with a high IgG avidity index: A valuable tool for diagnosing non-primary infections? J. Matern. Fetal Neonatal Med. 9:1–7.

[62] Khairi, S., Intisar, K., Enan, K., et al. (2013). Seroprevalence of cytomegalovirus infection among pregnant women at Omdurman Maternity Hospital, Sudan. J Med Lab Diagn., 4(4):45–49.

[63] Khalil, A., Sotiriadis, A., Chaoui, R., da Silva Costa, F., D'Antonio, F., Heath, P. T., Jones, C., Malinger, G., Odibo, A., Prefumo, F., Salomon, L. J., Wood, S., & Ville, Y. (2020). ISUOG Practice Guidelines: role of ultrasound in congenital infection. Tthe official journal of the International Society of Ultrasound in Obstetrics and Gynecology, 56(1):128–151.

[64] Kolo, RL., Umoh, J., Jatau, E. & Ella EE. (2013).Seroprevalence of cytomegalovirus among antenatal patients attending primary health centres in some parts of Kaduna State, Nigeria SAJEB, 3: 43-48.

[65] Kombich, JJ., Muchai, PC. & Borus, PK. (2012). Seroprevalence of natural rubella antibodies among antenatal attendees at Moi Teaching and Referral Hospital, Eldoret, Kenya. J Immunol Tech Infect Dis.,1:1.

[66] Kramer, A., Schwebke, I. & Kampf, G. (2006). How long do nosocomial pathogens persist on inanimate surfaces? A systematic review BMC Infectious Disease, 6: 130

[67] La Rosa, C., & Diamond, DJ. (2012). The immune response to human CMV. Future Virol., 7(3), 279–293.

[68] Lachmann, R., Loenenbach, A., Waterboer, T., Brenner, N., Pawlita, M., Michel, A., Thamm, M., Poethko-Müller, C., Wichmann, O., & Wiese-Posselt, M. (2018). Cytomegalovirus (CMV) seroprevalence in the adult population of Germany. PloS one, 13(7), e0200267.

[69] Lanzieri, TM., Kruszon-Moran, D., Gambhir, M. & Bialek, SR. (2016). Influence of parity and sexual history on cytomegalovirus seroprevalence among women aged 20-49 years in the USA. Int J Gynaecol Obstet. 2016;135(1):82-85.

[70] Lazzarotto, T., Guerra, B., Gabrielli, L., Lanari, M. & Landini, MP. (2011). Update on the prevention, diagnosis and management of cytomegalovirus infection during pregnancy. Clin. Microbiol. Infect., 17:1285–1293.

[71] Lazzarotto, T., Guerra, B., Lanari, M., Gabrielli, L., & Landini, MP. (2008). New advances in the diagnosis of congenital cytomegalovirus infection. J. Clin. Virol., 41:192–197.

[72] Leruez-Ville, M., Foulon, I., Pass, R. & Ville, Y. (2020). Cytomegalovirus infection during pregnancy: State of the science. Am. J. Obstet. Gynecol., 223:330–349.

[73] Leuridan, E., Ieven, M., Hens, N., & Van Damme, P. (2012). High susceptibility to cytomegalovirus infection of pregnant women in Flanders, Belgium. Facts, views & vision in ObGyn, 4(2):76–81.

[74] Liu, PH., Hao, JD., Li, WY., Tian, J., Zhao, J., Zeng, YM., & Dong, GQ. (2021). Congenital cytomegalovirus infection and the risk of hearing loss in childhood: A PRISMA-compliant meta-analysis. Medicine, 100(36): e27057.

[75] Ljungman, P., de la Camara, R., Robin, C., Crocchiolo, R., Einsele, H., Hill, JA., Hubacek, P., Navarro, D., Cordonnier, C. & Ward, KN. (2017). European Conference on Infections in Leukaemia group (2019). Guidelines for the management of cytomegalovirus infection in patients with haematological malignancies and after stem cell transplantation from the 2017 European Conference on Infections in Leukaemia (ECIL 7). The Lancet, Infect dis.,19(8): e260–e272.

[76] Lopo, S., Vinagre, E., Palminha, P., Paixao, MT., Nogueira, P., & Freitas, MG. (2011). Seroprevalence to cytomegalovirus in the Portuguese population, 2002-2003. Euro Surveill., 16(25): 19896.

[77] Maltezou, PG., Kourlaba, G., Kourkouni, E., Luck, S., Blázquez-Gamero, D., Ville, Y., Lilleri, D., Dimopoulou, D., Karalexi, M. & Papae-vangelou V. (2020). Maternal type of CMV infection and sequelae in infants with congenital CMV: Systematic review and me-ta-analysis. J. Clin. Virol., 129:104518.

[78] Manicklal, S., Emery, VC., Lazzarotto, T., Boppana, SB., & Gupta, RK. (2013). The "silent" global burden of congenital cytomegalovirus. Clin Microbiol Rev., 26(1): 86–102.

[79] Marsico, C. & Kimberlin, DW. (2017). Congenital Cytomegalovirus infection: Advances and challenges in diagnosis, prevention and treatment. Ital. J. Pediatr., 43:38.

[80] Mathias, CR. & Joung, SJS. (2019). Diagnostic challenges in congenital cytomegalovirus infection in pregnancy: A case report. Case Rep. Women's Health. 22:e00119.

[81] Mayer, BT., Krantz, EM., Swan, D., Ferrenberg, J., Simmons, K., Selke, S., Huang, ML., Casper, C., Corey, L., Wald, A., Schiffer, JT., & Gantt, S. (2017). Transient Oral Human Cytomegalovirus Infections Indicate Inefficient Viral Spread from Very Few Initially Infected Cells. J Viro.l, 91(12): e00380-17.

[82] Meesing, A. & Razonable, RR. (2018). New Developments in the Management of Cytomegalovirus Infection After Transplantation. Drugs, 78(11):1085–1103.

[83] Mettenleiter, TC., Klupp, BG. & Granzow, H. 2009. Herpesvirus assembly: an update. Virus Res 143:222–234.

[84] Mocanu, AG., Gorun, F., Ciohat, I., Navolan, D., Malita, D., Vilibic-Cavlek, T., Dahma, G., Neamtu, R., Popescu, D., Cioca, A., & Craina, M. (2021). Simultaneous Seroprevalence to Toxoplasma gondii,

Cytomegalovirus and Rubella Virus in Childbearing Women from Western Romania. Medicina (Kaunas, Lithuania), 57(9): 927.

[85] Mocarski ES., Shenk T. & Pass RF (2007) Cytomegaloviruses. In: Fields virology (Fields BN, Knipe DM, Howley PM, eds), pp 2702–2751. Philadelphia: Lippincott, Williams & Wilkins.

[86] Mocarski, ES., Jr., Shenk, T., Griffith, P. &Pass, RF. (2013). Cytomegaloviruses. In: Knipe DM, Howley PM, editors. Fields Virology. 6th Lippincott Williams & Wilkins; Philadelphia. 1960–2014.

[87] Moss, P., & Khan, N. (2004). CD8(+) T-cell immunity to cytomegalovirus. Hum Immunol., 65(5): 456–464.

[88] Mussi-Pinhata, MM. & Yamamoto, AY. (2020). Natural History of Congenital Cytomegalovirus Infection in Highly Seropositive Populations. J. Infect. Dis., 221(Suppl. 1):S15–S22.

[89] Navti, OB., Al-Belushi, M., Konje, JC., & FRCOG. (2021). Cytomegalovirus infection in pregnancy - An update. Eur J Obstet Gynecol Reprod Biol., 258: 216–222.

[90] N'Diaye, DS., Yazdanpanah, Y., Krivine, A., Andrieu, T., Rozenberg, F., Picone, O., Tsatsaris, V., Goffinet, F., & Launay, O. (2014). Predictive factors of cytomegalovirus seropositivity among pregnant women in Paris, France. PloS one, 9(2): e89857.

[91] Neirukh, T., Qaisi, A., Saleh, N., et al. (2013). Seroprevalence of Cytomegalovirus among pregnant women and hospitalized children in Palestine. BMC Infect Dis. 13:528.

[92] Nigro, G. (2017). Hyperimmune globulin in pregnancy for the prevention of congenital cytomegalovirus disease. Expert Rev Anti-Infect Ther.,15:977–986.

[93] Parlak, M., Çim, N., Erdin, BN., et al. (2015). Seroprevalence of Toxoplasma, Rubella, and Cytomegalovirus among pregnant women in Van. Obstet Gynecol. 2:79–82

[94] Pass, RF. &Arav-Boger, R. (2018). Maternal and fetal cytomegalovirus infection: Diagnosis, management, and prevention. F1000Research, 7, 255.

[95] Pembrey, L., Raynor, P., Griffiths, P., Chaytor, S., Wright, J., & Hall, AJ. (2013). Seroprevalence of cytomegalovirus, Epstein Barr virus and varicella zoster virus among pregnant women in Bradford: a cohort study. PloS one, 8(11), e81881.

[96] Pembrey, L., Waiblinger, D., Griffiths, P., Patel, M., Azad, R., & Wright, J. (2017). Cytomegalovirus, Epstein-Barr virus and varicella zoster virus infection in the first two years of life: a cohort study in Bradford, UK. BMC infectious diseases, 17(1), 220.

[97] Picarda, G., & Benedict, CA. (2018). Cytomegalovirus: Shape-Shifting the Immune System. J Immunol., (Baltimore, Md. : 1950), 200(12): 3881–3889.

[98] Podlech, J., Reddehase, M. J., Adler, B., & Lemmermann, N. A. (2015). Principles for studying in vivo attenuation of virus mutants: defining the role of the cytomegalovirus gH/gL/gO complex as a paradigm. Med Microbiol Immunol., 204(3), 295–305.

[99] Rajasekariah, H., Scott, G. & Robertson, PW. (2013). Rawlinson, W.D. Improving diagnosis of primary cytomegalovirus infection in pregnant women using immunoblots. J. Med. Virol. 85: 315–319.

[100] Ramchandar, N., Ding, Y., Farnaes, L., Dimmock, D., Hobbs, C., Kingsmore, SF., & Bainbridge, M. (2020). Diagnosis of cytomegalovirus infection from clinical whole genome sequencing. Scientific reports, 10(1), 11020.

[101] Rawlinson, WD., Boppana, SB., Fowler, KB., Kimberlin, DW., Lazzarotto, T., Alain, S., Daly, K., Doutré, S., Gibson, L., Giles, M.L., et al. (2017). Congenital cytomegalovirus infection in pregnancy and the neonate: Consensus recommendations for prevention, diagnosis, and therapy. Lancet Infect Dis., 17: e177–e188.

[102] Refaat, B., Ashshi. AM., Batwa, SA., et al. (2014). Seroprevalence of Chlamydia trachomatis, cytomegalovirus, herpes simplex virus 1 and 2 in Saudi women with normal and abnormal early pregnancy: A case control study. Afr J Microbiol Res., 8(40):3565–3569.

[103] Revello, MG. & Gerna, G. (2002). Diagnosis and management of human cytomegalovirus infection in the mother, fetus, and newborn infant. Clin Microbiol Rev.,15: 680–715.

[104] Ronchi, A., Zeray, F., Lee, LE., Owen, KE., Shoup, AG., Garcia, F., Vazquez, LN., Cantey, J. B., Varghese, S., Pugni, L., Mosca, F., & Sánchez, PJ. (2020). Evaluation of clinically asymptomatic high risk infants with congenital cytomegalovirus infection. J Perinatol., 40(1): 89–96.

[105] Ryckman, BJ., Jarvis, MA., Drummond, DD., Nelson, JA., & Johnson, DC. (2006). Human cytomegalovirus entry into epithelial and endothelial cells depends on genes UL128 to UL150 and occurs by endocytosis and low-pH fusion. J Virol., 80(2): 710–722.

[106] Saldan, A., Forner, G., Mengoli, C., Gussetti, N., Palù, G., & Abate, D. (2017). Testing for Cytomegalovirus in Pregnancy. Journal of clinical microbiology, 55(3):693–702.

[107] Sauer, A., Wang, JB., Hahn, G., & McVoy, MA. (2010). A human cytomegalovirus deleted of internal repeats replicates with near wild type efficiency but fails to undergo genome isomerization. Virology, 401(1): 90–95.

[108] Schultz, DA. & Chandler, S. (1991). Cytomegalovirus testing: Antibody determinations and virus cultures with recommendations for use. J. Clin. Lab. Anal., 5:69–73.

[109] Sonoyama, A., Ebina, Y, Morioka, I., Tanimura, K., Morizane, M., Tairaku, S., Minematsu, T., Inoue, N. & Yamada, H. (2012). Low IgG avidity and ultrasound fetal abnormality predict congenital cytomegalovirus infection. J. Med. Virol., 84:1928–1933.

[110] Stacey, MA., Marsden, M., Pham NTA., Clare, S., Dolton, G., Stack, G., Jones, E., Klenerman, P., Gallimore, AM. et al. (2014). Neutrophils recruited by IL-22 in peripheral tissues function as TRAIL-dependent antiviral effectors against MCMV. Cell Host Microbe.15(4):471-483.

[111] Staras, SA., Flanders, WD., Dollard, SC., Pass, RF., McGowan, JE., Jr, & Cannon, MJ. (2008). Cytomegalovirus seroprevalence and childhood sources of infection: A population-based study among pre-adolescents in the United States. J Clin Virol., 43(3):266–271.

[112] Struble E.B., Murata H., Komatsu T., Scott D. Immune Prophylaxis and Therapy for Human Cytomegalovirus Infection. Int. J. Mol. Sci. 2021;22:8728.

[113] Sufiawati, I., Herrera, R., Mayer, W., Cai, X., Borkakoti, J., Lin, V., Rosbe, K., & Tugizov, S. M. (2021). Human Immunodeficiency Virus (HIV) and Human Cytomegalovirus (HCMV) Coinfection of Infant Tonsil Epithelium May Synergistically Promote both HIV-1 and HCMV Spread and Infection. J Virol., 95(18): e0092121.

[114] Sylwester, AW., Mitchell, BL., Edgar, JB., Taormina, C., Pelte, C., Ruchti, F., Sleath, PR., Grabstein, KH., Hosken, NA., Kern, F., Nelson, JA., & Picker, LJ. (2005). Broadly targeted human cytomegalovirus-specific CD4+ and CD8+ T cells dominate the memory compartments of exposed subjects. The Journal of experimental medicine, 202(5): 673–685.

[115] Tanimura, K. & Yamada, H. (2018). Potential Biomarkers for Predicting Congenital Cytomegalovirus Infection. Int. J. Mol. Sci., 19:3760.

[116] Tanimura, K. & Yamada, H. (2019). Maternal and neonatal screening methods for congenital cytomegalovirus infection. J. Obstet. Gynaecol. Res., 45:514–521.

[117] Thigpen, J. (2020). Congenital Cytomegalovirus-History, Current Practice, and Future Opportunities. Neonatal Netw., 39:293–298.

[118] Tol, I., Heath, PT. & Khalil, A. (2021). Prevention strategies for congenital cytomegalovirus infection. Curr Opin Infect Dis., 34:546–551.

[119] Vanarsdall, AL., & Johnson, DC. (2012). Human cytomegalovirus entry into cells. Curr Opin Virol., 2(1): 37–42.

[120] Walmus, BF., Yow, MD., Lester, JW., Leeds, L., Thompson, PK. & Woodward, PK. (1988). Factors predictive of cytomegalovirus immune status in pregnant women. J Infect Dis., 157:172-177.

[121] Zhang, L., Li, L., Wang, B., Qian, DM., Song, XX., & Hu, M. (2014). HCMV induces dysregulation of glutamate uptake and transporter

ISSN: 2959- 7463

expression in human fetal astrocytes. Neurochem Res., 39(12): 2407–2418.

[122]Zuhair M., Smit GSA., Wallis G., Jabbar F., Smith C., Devleesschauwer B. & Griffiths, P. (2019). Estimation of the worldwide seroprevalence of cytomegalovirus: A systematic review and meta-analysis. Rev med virol., 29(3) e2034..