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DOI: 10.15225/PNN.2022.11.2.6 JNNN 2022;11(2):83–94 **Review**

Screening among Pregnant Women for Cytomegalovirus (CMV) Infection — Recommendations in Poland and Selected Countries Worldwide (a Preliminary Study to Investigate the Incidence of Neurological Complications in CMV — Infected Children)

Badanie przesiewowe wśród kobiet w ciąży w kierunku zakażenia wirusem cytomegalii (CMV) — zalecenia w Polsce i w wybranych krajach świata (opracowanie wstępne do badania występowania powikłań neurologicznych u dzieci zakażonych CMV)

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Abstract

Cytomegalovirus (CMV) is the most common cause of congenital infections worldwide, yet it remains an underestimated public health problem. There are no international standards for the prevention of vertical transmission of the infection, and the management of pregnant women as well as fetuses with symptoms of infection. The analysis was conducted between December and February 2022. The detailed criteria of inclusion in the analysis included: a separate study group, consisting only of pregnant women regardless of their stage, and statistical analysis of obtained data with particular emphasis on the result of antibodies against CMV antigens in IgG and IgM class. The introduction of universal screening is still controversial. In most countries, routine determination of IgG and IgM antibodies to CMV antigens is not recommended among pregnant women, but these tests are often offered to them independently of nationally approved screening programmes. **(JNNN 2022;11(2):83–94)**

Key Words: CMV, cytomegaly, pregmant woman, screening tests

Streszczenie

Wirus cytomegalii (CMV) jest najczęstszą przyczyną zakażeń wrodzonych na świecie, a mimo to wciąż pozostaje niedocenionym problemem zdrowia publicznego. Brak jest międzynarodowych standardów zapobiegania wertykalnej transmisji zakażenia, postępowania w stosunku do kobiet ciężarnych, jak i płodu z objawami infekcji. Analizę przeprowadzono od grudnia do lutego 2022 r. Szczegółowe kryteria włączenia do analizy obejmowały: wyodrębnioną grupę badawczą, składającą się tylko i wyłącznie z kobiet w ciąży niezależnie od jej etapu, analizę statystyczną uzyskanych danych ze szczególnym uwzględnieniem wyniku przeciwciał przeciwko antygenom wirusa CMV w klasie IgG oraz IgM. Wprowadzenie powszechnych badań przesiewowych wciąż jest kwestią sporną. W większości krajów nie zaleca się wśród kobiet w ciąży rutynowego oznaczania przeciwciał przeciwko antygenom wirusa CMV w klasie IgG oraz IgM, jednak badania te są im często proponowane niezależnie od programów skriningowych zatwierdzonych na szczeblu krajowym. **(PNN 2022;11(2):83–94)**

Słowa kluczowe: CMV, cytomegalia, kobieta w ciąży, badania przesiewowe

Introduction

Cytomegalovirus (CMV) is the most common cause of congenital infections worldwide, yet it remains an underestimated public health problem. There are no international standards for the prevention of vertical transmission of the infection, and the management of pregnant women as well as fetuses with symptoms of infection [1]. Congenital infection of the newborn with CMV (cCMV) may result from:

— primary infection among mothers with negative IgG class antibodies to CMV antigens,
— secondary infection among mothers with a positive result of antibodies against CMV antigens in IgG class as a result of virus reactivation or reinfection with another CMV strain [2,3].

In both cases, the fetus is infected via the transplacental bloodstream [3]. Primary infection of the pregnant woman carries the greatest risk of severe complications for the fetus [3,4]. Fetal infection in the first or second trimester can cause severe central nervous system (CNS) damage, even leading to a miscarriage or intrauterine fetal death [5,6]. Fetal infection in the second or third trimester usually results in organ-specific symptoms, i.e. hepatitis, myocarditis, chorioretinitis, interstitial pneumonia, seizures, bone marrow involvement, and hearing loss. Fetal infection in the third trimester generally does not cause symptoms immediately after birth [5].

Congenital CMV infections can be divided into symptomatic or asymptomatic. Infected infants with moderate to severe symptoms include those who have at least some symptoms or central nervous system involvement. Mild infection describes infants who have mild and transient isolated symptoms of one or two. Infants who have no obvious clinical signs other than hearing loss are classified as asymptomatic with isolated sensorineural hearing loss (SNHL). Infants who have normal hearing and no other abnormalities are classified as asymptomatic [5,7].

In the group of newborns with asymptomatic infection, 13.5% develop late, dangerous sequelae that most often involve the CNS, including the auditory and visual organs. Diagnoses include optic atrophy, retinochorioiditis, scarring of the macula and peripheral retina, and uveitis. The link between infection and hearing loss has only been described for about 40 years. A clear cause has still not been found. It has been assumed that the most likely cause of progressive hearing loss is a chronic inflammatory process that damages fetal tissues, especially the fetal labyrinth. It is inferred that HCMV enters the endolymphatic labyrinth through the vascular striae. The different types of hearing loss are sensorineural, conductive, central, and mixed. Damage may be unilateral or bilateral, symmetrical or asymmetrical, variable or stable, sudden or progressive. Hearing defects are of great importance for the child's overall development. Bilateral hearing loss results in poorer speech development, even if the hearing loss is described as mild to moderate. The sooner a hearing loss is identified, its aetiology determined, and appropriate treatment implemented, the better the child's chance of successful treatment and often saves them from permanent, full or partial hearing loss. A list of benefits of CMV screening for hearing has been developed. These include the ability to accurately assess the etiology of hearing loss, targeted treatment of children with hearing loss, appropriate counselling and support for parents, attention to possible neurological and behavioural complications, and prognosis of whether another child may be born with hearing loss [8].

The best method to confirm primary infection in a pregnant woman is to determine seroconversion, i.e. to detect CMV-specific antibodies in a previously seronegative pregnant woman. The presence of IgM class antibodies indicates primary infection, reactivation, reinfection with another virus strain or a false-positive test result. Antibodies of this class usually persist for 3 to 6 months, but sometimes even for more than 12 months after infection. A complementary test is the determination of the IgG antibody avidity, which allows differentiation between primary and secondary infection. High acidity is characteristic of an infection older than 3 months, a low avidity of fewer than 3 months. A borderline IgG avidity indicates an equivocal result [4]. Positive IgG antibodies are indicative of past infection, but their presence before or at the beginning of pregnancy does not rule out fetal infection [5].

Research Methods

The analysis was conducted between December and February 2022. Scientific publication databases were searched electronically: "PubMed", "Academica", "Scopus", "Google Scholar", "Europe PMC", "Cochrane Library". The search terms were CMV, HHV-5, human herpesvirus type 5, cytomegalovirus, CMV perinatal standard, CMV screening, guidelines for pregnant women, prenatal care, CMV IgM IgG antibodies, CMV seroconversion, CMV seroprevalence. Each term was searched in Polish, English, German, Italian, Spanish and French. Citation references in the retrieved articles were also analysed to find additional material. No restrictions were applied due to the language of the articles.

The detailed criteria of inclusion in the analysis included: a separate study group, consisting only of pregnant women regardless of their stage, and statistical analysis of obtained data with particular emphasis on the result of antibodies against CMV antigens in IgG and IgM class.

Screening for CMV Infection

'TORCH' pathogens are directly associated with the development of congenital disease in newborns and include a variety of bacteria, viruses and parasites. It is generally accepted that these include: Toxoplasma gondii (toxoplasmosis), Others, Rubella virus (rubella), Cytomegalovirus, and Herpes simplex virus. Hepatitis B, syphilis, and human immunodeficiency virus (HIV), among others, are assigned to the "others" category [9].

Poland

In the Republic of Poland, the regulation of the Minister of Health of 16 August 2018 on the organisational standard of perinatal care in terms of preventive services and health promotion activities, as well as diagnostic tests and medical consultations performed on women during pregnancy does not mention the recommendation of testing antibodies against CMV antigens in IgG and IgM classes (Table 1) [10].

The Polish Society of Gynecologists and Obstetricians (PTGiP) has so far not issued its position on the above [11].

Table 1. Screening tests for TORCH pathogens in Poland — own elaboration

Type of screening test	Recommended (+) Not recommended (–)
CMV	–
HIV	+
HCV	+
VDRL	+
TOXO	+
RUBV	+
HBsAg	+

Siennicka J. et al. conducted a study from 2010 to 2011 in five polish voivodeships to assess CMV seroprevalence in women of reproductive age. The prevalence of IgG class antibodies in all women was 89.1%. Among women under 30 years of age — 74.3%, between 30 and 34 years of age — 72.4%, between 35 and 39 years of age — 83.5%, between 40 and 44 years of age — 87.7%, over 45 years of age — 94.4%. It was then observed that seroprevalence in Poland is higher than in other Western European countries (among white women), which is 30.4% in Ireland, 45.6% in the Netherlands, 45.9% in the UK, 47.5% in Germany, 51.5% in France, 57.4% in Spain, 70.7% in Finland, 72% in Sweden [12]. Furthermore, the prevalence of IgG class antibodies was similar to 1979 estimates, where the seroprevalence in women aged 15 to 39 years was — 83.3% [12,13]. Higher seroprevalence indicates a higher risk of primary infection in seronegative women [12].

According to the list in the announcement of the Minister of Health on 15 February 2021 on the announcement of the consolidated text of the regulation of the Minister of Health on guaranteed benefits in the field of primary health care, guaranteed benefits do not include antibodies against CMV antigens in IgG and IgM classes [14]. For interested people, tests can be performed commercially. CMV IgG and IgM prices were compared in ten randomly selected laboratories in Mazowieckie voivodeship. The average price of CMV IgG was 40,69 PLN, while that of CMV IgM was 41,19 PLN (Table 2).

Table 2. Price list for CMV IgG and IgM tests — own elaboration [15–28]

Order No.	City	CMV IgG (PLN)	CMV IgM (PLN)
1.	Warsaw	38,00	43,00
2.	Gostynin	16,00	16,00
3.	Ciechanów	52,00	52,00
4.	Pruszków	53,39	53,39
5.	Płock	22,50	22,50
6.	Ostrołęka	65,00	65,00
7.	Warsaw	46,00	46,00
8.	Pruszków	32,00	32,00
9.	Żyrardów	45,00	45,00
10.	Sochaczew	37,00	37,00

The Racibórz District in cooperation with the Dr Józef Rostek District Hospital in Racibórz has been implementing programmes of free examinations for pregnant women since 2008. The package includes, among others, the determination of antibodies against CMV antigens in IgG and IgM classes in the first and third trimesters of pregnancy. A referral issued by a doctor specialising in obstetrics and gynaecology is necessary to perform the test. The aim of the programmes is not only to perform the tests without bearing costs but also to make society aware of the CMV virus and the risks associated with it. In the opinion of the President of the Agency for Health Technology Assessment No. 165/2013 of 10 June 2013 on the draft programme "For joyful motherhood", it would even be appropriate to consider extending the population covered by the programme to include women planning pregnancy [29,30].

Table 3. Cytomegalovirus — residents of Racibórz district — own analysis

Year	Study group size	Negative result		Positive result	
		N	%	N	%
2008	848	819	96.58	29	3.42
2009	706	672	95.19	34	4.80
2010	660	504	76.36	156	23.64
2011	741	555	74.90	186	25.10
2012	no data				
2013*	339	247	72.86	92	27.14
2014	828	624	75.36	204	24.64
2015	767	546	71.19	221	28.81
2016	no data				
2017	913	no data			
2018	850	621	73.06	229	26.94
2019	930	680	73.12	250	26.88
2020	622	454	73.00	168	27.00
Total	7 291**	5 722	78.48	1 569	21.52

*studies implemented since 1.10.2013 [29,30]; **excluding 2017

Since 2008, a total of 8204 women have been tested. Excluding 2017, since the results are not known, 5722 women were negative, which is 78.48%, while 1569 women were positive, which is 21.52% (Table 3). The results of the additional tests are not known.

United Kingdom

The Department of Health and Social Care (DHSC) is a ministerial department of the UK Government. The National Institute for Health and Care Excellence (NICE) publishes national guidance to improve healthcare. NICE is an executive, non-departmental public body sponsored by the DHSC. In addition, the DHSC supervises the work of the National Health Service (NHS) [31,32].

The guidelines published by NICE in collaboration with the Royal College of Obstetricians and Gynecologists (RCOG) do not mention the recommendation to test pregnant women for IgG and IgM antibodies to CMV antigens [33]. However, there is currently a consultation on CMV seroprevalence determination in pregnant women, with a meeting on this issue planned for March this year [34].

"CMV Action" is a UK charity whose priorities include supporting families affected by cCMV, educating the public (including healthcare professionals), and supporting the development of research into the diagnosis and treatment of CMV. According to members, seroprevalence determination should be available to all seronegative pregnant women. In addition, the organisation has commissioned an estimate of the economic costs of cCMV [34]. Retzler J. et al. state that the total cost associated with cCMV in 2016 in the UK was £732 million (estimated to be between £495 and £942 million). Roughly 40% of the cost was borne directly by the public sector, while the remaining 60% was indirect. According to the authors, it is likely that the study underestimates the true cost, due to a lack of accurate data and a resulting cost estimate that could not be accounted for [35].

Public Health England (PHE) in collaboration with the NHS has issued the 2019 UK Standards for Microbiology Investigations Investigation of cytomegalovirus infection. According to the above, CMV infection in a pregnant woman should be suspected if symptoms such as fever, myalgia of unknown aetiology, or hepatitis appear [36].

The British Paediatric Surveillance Unit (BPSU) maintained a cCMV register in the British Isles from February 2001 to February 2003 (inclusive). 93 cases were recorded, of which 81 were singleton pregnancies, and 5 were twins (both first and second infants infected). The two remaining infants infected had an uninfected twin. The twins were born between 28 and 35 weeks gestation. The gestation duration of the mothers of the above 81 infants was 36 weeks and the average birth weight was 2330 grams. Seven infants were confirmed to have died, one at birth, four in the first month, one in the sixth week and one in the eighth month [37].

Australia

The Australian Paediatric Surveillance Unit (APSU) is the surveillance authority for rare childhood diseases. Since 1999, it has conducted surveillance for cCMV in infants up to 12 months of age. A total of 399 confirmed cases have been reported over 22 years (Table 4) [38,39].

The number of doctors reporting cCMV in 2020 was 22, while in 2019 it was 14 [38].

In 2019, The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) published guidelines on the prevention of CMV infection in women during pregnancy to reduce mother-to-child transmission, and fetal infection and subsequent clinical consequences.

They recommend that all pregnant women (and those planning to become pregnant) should be provided with information on CMV prophylaxis by medical staff as part of their routine care. Hygiene practices should be recommended to all women regardless of their CMV serological status. They included specific hygiene measures in their recommendations.

Table 4. cCMV registry in Australia — last ten years — own analysis

Year	Number of confirmed cCMV	Estimated prevalence
2020	37	12,10 per 100 000 births
2019	15	5,28 per 100 000 births
2018	24	–
2017	17	5,62 per 100 000 births
2016	13	4,26 per 100 000 births
2015	18	5,93 per 100 000 births
2014	26	8,44 per 100 000 births
2013	16	5,17 per 100 000 births
2012	16	5,30 per 100 000 births
2011	24	8,1 per 100 000 births
2010	31	10,5 per 100 000 births

Universal routine CMV screening is not recommended; however, for women at high risk of infection, CMV IgG antibody determination may be considered before pregnancy or early pregnancy. In addition, women with suspected CMV infection in pregnancy should have serological tests for IgG and IgM antibodies and IgG avidity if CMV IgG and IgM are positive [40].

Germany

The Federal Joint Committee (Gemeinsame Bundesausschuss, G-BA) is the most important decision-making body in the German health care system. In 1986 (and subsequent amendments), they published guidelines entitled "Mutterschafts-Richtlinien" ("Maternity Guidelines") for medical care during pregnancy and after childbirth. The determination of antibodies to CMV antigens in IgG and IgM classes is not recommended among pregnant women [41].

The G-BA has established an independent institute called Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Healthcare (IQWiG)) to look at the quality and efficiency of the healthcare system [41]. Research is currently ongoing in the project entitled "Cytomegalievirus (CMV): Können durch einen CMV-Test bei Schwangeren Folgeschäden für das Ungeborene oder den frühgeborenen Säugling verhindert werden?". They seek to answer the question of whether screening and subsequent treatment could mitigate or prevent damage in newborns [42].

According to the Law on the Prevention and Control of Infectious Diseases in Humans, cytomegalovirus infection is not notifiable [43].

In the S2k guideline on laboratory diagnosis of viral infections associated with pregnancy, the subsection on cytomegalovirus by Prof. Klaus Hamprecht (registry number AWMF 0093/00) recommends:

— determination of IgG antibodies to CMV antigens in all pregnant women at the time of diagnosis (additional IgM antibody determination should be performed in women at increased risk of infection due to exposure to CMV through contact with children under 3 years of age);
— providing prophylactic advice to pregnant women with negative IgG antibodies to CMV antigens;
— determination of CMV serological status of women planning to use assisted reproductive technology before their initiation [44,45].

France

In 2002, the French Supreme Council for Public Hygiene (French: Conseil supérieur d'hygiène Publique, CSHPF) issued an opinion on recommendations for the prevention of CMV infection in pregnant women. They considered it a priority to focus on the main risk factors. Pregnant women with family or professional contact with children under 3 years of age should limit contact with their excretions and secretions. To do so, they recommended:

— not to take the child's dummy or spoon into their mouth, and not to finish a meal after them,
— not to share cosmetics with the baby,
— limit contact with the baby's tears and/or saliva,
— scrupulously wash hands with soap and water after each contact with the child's urine [46].

The Supreme Council for Public Health (French: Haut Conseil de la santé publique, HCSP) has established four commissions, including the Commission for Infectious and Emerging Diseases (French: Commission spécialisée maladies infectieuses et maladies émergentes, CSMIME). Further guidelines were published in December 2018. The main points concern:

— spreading information on preventive measures in all areas of life (hygiene measures),
— not to recommend routine CMV serology for pregnant women and newborns,
— in case of an abnormal result of a hearing and neonatal screening test, targeting of tests for CMV infection [47].

The High Authority for Health (French: Haute autorité de santé, HAS) is an independent public institution of a scientific nature whose main objective is to strengthen the quality and sustainability of the health system. It initiates actions to ensure that citizens have continuous and equitable access to medical care. Representatives of

the organisation are concerned that serological testing of pregnant women could lead to:

— increased maternal distress,
— increased number of amniocentesis resulting in the risk of miscarriage,
— unjustified requests for abortion.

For the future, priority was set as:

— to develop guidelines for the management of seroconversion diagnosed in a pregnant woman (treatment) and for the diagnosis of fetal infection (prognosis assessment),
— to conduct clinical trials to determine the prevalence and factors suggesting long-term problems and their consequences, the risk of transmission and the consequences of secondary infection, and the safety and efficacy of new antiviral agent therapies [48].

Portugal

The Paediatric Surveillance Unit of the Portuguese Paediatric Society (cf. Unidade de Vigilância Pediátrica da Sociedade Portuguesa de Pediatria, UVP-SPP) is a unit whose purpose is to carry out research on rare diseases. It also maintains a national registry of cCMV cases. Data are reported voluntarily by paediatricians through an electronic registration card. The inclusion criterion includes cases confirmed in the first three weeks of life. Surveillance includes completion of progress questionnaires at 6, 12, 18 months of age and 2, 3, 4, 5, 6 years of age. Partial and final results are made available to all paediatricians and are also presented at the national and international levels [49,50].

In Portugal, between 2006 and 2011, 40 cases of cCMV were reported out of 610,263 live births, which is 6.6:105 live births (95% CI 4.81 to 8.92). Asymptomatic was 55% (N-22) of newborns, while symptomatic was 45% (N-18). Primary infection was present in 52.5% (N-21) of mothers, secondary infection in 25% (N-10), and serological status was unknown in the remaining cases. The number of reports was unexpectedly low. All cases were registered by only 16 doctors. According to the authors, improved registration strategies are needed to have a good understanding of the epidemiology of cCMV in each country [51].

Belgium

In 2006, the Flemish Society of Pediatrics' Neonatology and Perinatal Epidemiology Working Group for cCMV infection [8].

In 2007, six Flemish hospitals started registering children with cCMV in Flanders. Over the years, other institutions also joined. In 14 years, 1059 children were registered, of whom 30.5% were diagnosed with symptoms (N-319): mild in 13.5%, moderate in 16%, severe in 70.5% [52]. An online registry has been maintained since 2013 [8].

According to the authors, the registration of neonates with cCMV depends mainly on the goodwill of paediatricians and otolaryngologists. Informed consent must also be given by the parents. To collect complete information, they ask that information forms be completed at 3, 6, 12, 18, 24, and 30 months of age of the child and at least once a year until 6 years of age. All registered children have their hearing checked at the age of 6 years [8].

Screening for cCMV infection is part of the diagnostic standard for children born with hearing loss [8].

Canada

The Canadian Paediatric Surveillance Program (CPSP) maintained a cCMV registry from March 2005 to February 2008. A total of 49 cases were recorded. The authors speculate that the infection rate is much higher. Only newborns with severe symptoms were reported. Many infected infants with milder symptoms were identified [53].

Between 2005 and 2010, CMV serologies of pregnant women in Canada were determined. Of 3146 women who were IgG antibody negative in the first trimester, 28 of them were IgG positive in the third trimester of pregnancy, indicating primary infection between the first and third trimesters [54,55].

Spain

The National Health Service (El Servicio Nacional de Salud) does not recommend testing pregnant women for IgG and IgM antibodies to CMV antigens for three main reasons:

— the possibility of reactivation or reinfection with another virus strain in seropositive women,
— lack of effective treatment of infection during pregnancy,
— the high rate of false-positive serological tests.

Only education of pregnant women to reduce the risk of infection has been proposed [56].

USA

In the United States, an annual celebration called National Cytomegalovirus Awareness Month is held in June to increase population awareness of CMV [57].

The American College of Obstetricians and Gynecologists along with the American Academy of Pediatrics 2007 published the eighth edition of Guidelines for perinatal care. Routine testing for IgG and IgM CMV antibodies in pregnant women is not recommended. A statement was made that:

— there are difficulties in distinguishing primary from secondary infection in a pregnant woman,
— positive IgG antibodies do not exclude infection of the newborn during pregnancy (possible reactivation, reinfection) [58].

Austria

Since 1974, the "Mutter-Kind-Pass" preventive programme has been operating in Austria to provide health care to pregnant women and children up to 62 months of age [59]. The programme is continuously adjusted to the current state of medical experience.

The Ludwig Boltzmann Institute for Health Technology Assessment (LBI-HTA), as an independent research institution, advises the government on decision-making. In 2018, they published a report showing that 11 out of 12 voters were against screening pregnant women.

Review of CMV Seroprevalence in Selected Countries

Fourteen study results from different countries around the world were analysed. The study group is 12866 women in their first, second or third trimester of pregnancy. The prevalence of IgG and IgM antibodies varies from country to country and ranges from 23% to 99.8%, 0% to 13%, respectively. A total of 65.10% (N-8376) of women had positive IgG and 4.13% (N-531) IgM antibodies (Table 5).

Table 5. Review of CMV seroprevalence in selected countries — own analysis

Author	Location	Date	Gestational age	Method	Study group size (women)	Positive IgG antibodies to CMV antigens	Positive IgM antibodies to CMV antigens
1	2	3	4	5	6	7	8
Wujcicka W. et al. [60]	Poland (Ludwik Rydygier Specialist Hospital in Kraków)	April 2010 –March 2011	I and III trimester	ELISA	1 250	780 (62.4%)	28 (2.2%)
Belegamire S.J. et al. [54]	Canada (Hospital Québec-Laval in Québec)	April 2005 –March 2010	I and III trimester	Abbott Architect Platform	4 111	965 (23.0%)	113 (11.7%)
Gaj Z. et al. [61]	Poland (ICZMPiG ICZMP and III Department of Gynaecology and Obstetrics and Obstetrics UM in Łódź)	1999–2009	not considered	EtI-Cytok G-Plus test (Diasorin, Biomedica), VIDAS test IgG and IgM test (Biomerieux, France), anti CMV IgG and IgM test (Diasorin, Biomedica)	1 332	985 (76.7%)	179 (13.0%)

Table 5. Continued

1	2	3	4	5	6	7	8
Zenebe M.H. et al. [62]	Ethiopia (Hawassa University Comprehensive Specialist Hospital)	August 2020 –October 2020	immediately before delivery	ELISA	593	532 (89.7%)	49 (8.3%)
Mhandire D. et al. [63]	Zimbabwe (Polyclinics in Harare)	February 2016 –August 2016	III trimester	ELISA	524	522 (99.8%)	39 (7.4%)
Jin Q. et al. [64]	China (Beijing Friendship Hospital, Capital University Medical)	July 2010 –June 2015	I trimester	ELISA	2 887	2 734 (94.7%)	37 (1.28%)
Porobic-Jahic H. et al. [65]	Bosnia and Herzegovina (Public Health Institution University Clinical Centre Tuzla)	June 2018 –August 2018	not considered	ELISA	300	280 (93.3%)	9 (3.0%)
Maingi Z. et al. [66]	Kenya (Thika Level 5 Hospital)	September 2012 –April 2013	I and II trimester	ELISA	260	201 (77.3%)	21 (8.0%)
Aljumaili Z.K. et al. [67]	Iraq (Kirkuk General Hospital)	–	not considered	ELISA	261	244 (93.5%)	25 (9.6%)
Abeynayake J.I. et al. [68]	Sri Lanka (De Soysa Maternity Hospital)	August 2015 –August 2016	I and II trimester	ELISA	385	374 (97.0%)	0 (0.0%)
Al-Hakami A.M. et al. [69]	Saudi Arabia (Abha Maternity and Children's Hospital)	February 2018 –May 2019	II and III trimester	ELISA	190	190 (100.0%)	18 (9.5%)
Babayo A. et al. [70]	Nigeria (Maiduguri University Teaching Hospital clinic)	December 2013 –March 2014	I, II, III trimester	No data	182	144 (79.1%)	4 (2.2%)
Hamdan H.Z. et al. [71]	Sudan (Antenatal Care Clinic at El-Rahad Hospital)	August 2009 –October 2009	I, II, III trimester	ELISA	231	167 (72.2%)	6 (2.5%)
Trombetta C.M. et al. [72]	Italy (Apulia)	August 2016 –December 2019	I, II, III trimester	ELISA	360	255 (70.8%)	3 (0.8%)
		Total			12 866	8 376 (65.10%)	531 (4.13%)

Summary

The topic of CMV screening has become a subject of the worldwide discussion. Analyses are being carried out on the validity of CMV seroprevalence determination both among pregnant women and newborns. The introduction of universal screening is still controversial. In most countries, routine determination of IgG and IgM antibodies to CMV antigens is not recommended among pregnant women, but these tests are often offered to them independently of nationally approved screening programmes. According to the literature, screening for CMV in pregnant women is not recommended because:

- it risks unwarranted termination of pregnancy because of the pregnant woman's anxiety,
- not in every case, intrauterine infection will have consequences for the fetus and later consequences for the child,
- there is no uniform standard of management to prevent mother-to-child transmission,
- there is no standardised treatment for the infected fetus,
- routine tests can cause unnecessary anxiety for the pregnant woman,
- the costs of routine testing are too high,
- documented presence of IgG antibodies does not exclude the possibility of congenital infection [4].

Clinical trials sponsored by the National Institutes of Health (NIH) on the efficacy of antiviral drugs for cCMV neonates with abnormal hearing test results are currently ongoing. The first randomised controlled trial, led by Dr Albert Park of the University of Utah, was entitled "Valganciclovir for cCMV with abnormal hearing test results". "Valganciclovir for Cytomegalovirus Infected Hearing Impaired Infants (ValEAR)", the study is expected to be completed in 2022 The second study led by a team of investigators from the National Institute of Allergy and Infectious Diseases, an open-label, multicentre study to evaluate the efficacy of 4-month valganciclovir in preventing SNHL in infants without external signs of cCMV, including normal hearing, the study is expected to be completed in 2024. However, the authors suggest that even in the absence of an effective drug, screening is cost-effective. All children with cCMV are at increased risk of vision and/or hearing loss and future developmental delays. Thus, making a diagnosis of cCMV provides an opportunity for professionals to implement appropriate control at key developmental stages [7].

Beaudoin M.L. et al. analysed women's attitudes towards CMV screening. Between June and August 2019, 234 women between 11 and 16 weeks of pregnancy participated in the study. Of these, up to 74.4% (N-174) were unaware of the risk of cCMV infection. 70.9% (N-166) of the women had a positive attitude towards screening, 20.9% (N-49) had a neutral attitude, and 7.3% (N-17) had a negative attitude. Almost all women — 94.8% (N-222) would like to be informed about CMV by the pregnancy provider. Less than half of the — 47.4% (N-111) declared their willingness to pay for screening [73].

According to the literature, diagnosis for congenital CMV infection should be initiated, among others, in newborns of mothers with primary CMV infection diagnosed during pregnancy, its reactivation or reinfection with another serotype of the virus [5]. Thus, the main benefit of screening pregnant women would be the identification of fetuses at risk of dangerous sequelae of infection. In addition, screening of mothers would enable the identification of CMV seronegative individuals. This could be the basis for familiarising them with prophylactic measures to prevent CMV infection. Informational support in this regard has been emphasised by the French National Agency for Accreditation and Evaluation in Health Care (French: Haute Autorité de Santé) [74]. Interventions to reduce the risk of CMV infection can occur as:

- primary prevention (prevention of seroconversion in the mother during pregnancy),
- secondary prevention (prevention of foetal transmission after maternal seroconversion),
- tertiary prevention (prevention of sequelae among infected fetuses).

Counselling CMV IgG seronegative pregnant women on prophylactic hygiene measures make the greatest contribution to preventing mother-to-fetus transmission of CMV [8].

Given this huge impact on society, research in the area of prevention and treatment of primary maternal CMV infection is a priority. The establishment of increasingly large cCMV registries internationally is also worth considering.

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