

## RESEARCH PAPER

# Seroprevalence of antibodies to cytomegalovirus in pregnant women in the Apulia region (Italy)

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## Keywords

Cytomegalovirus • Pregnancy • Apulia region • Italy • Seroprevalence

## Summary

**Introduction.** Cytomegalovirus is ubiquitous and easily transmitted by contact. Following the first infection, the virus becomes latent and periodic reactivation could occur due to immunosuppression. If the infection is acquired in pregnancy, especially in the first trimester, the foetal consequences could be serious. The present study was conducted to assess the serological profile of pregnant women with respect to cytomegalovirus in Apulia from 2016 to 2019.

**Methods.** Serum samples were tested by commercial ELISA kit for the detection of specific IgM and IgG antibodies against cytomegalovirus.

**Results.** The data showed that most of the pregnant women (70.8%), especially those of  $\geq 40$  years of age (80.6%), has anti-

bodies against cytomegalovirus, though these do not confer fully protective immunity against infection by different strains nor can prevent the re-activation of the latent one. Conversely, most of the youngest women are seronegative (44.4% in women  $< 25$  years of age) and vulnerable during pregnancy.

**Conclusions.** Currently, cytomegalovirus screening for pregnant women is not mandatory in Italy. Considering that congenital cytomegalovirus is the leading non-genetic cause of sensorineural hearing loss, it would be extremely useful and cost-saving to screen women of childbearing age and women at early stage of pregnancy for cytomegalovirus infection in addition to increase awareness of cytomegalovirus infection and consequences among pregnant women, health care workers and the public.

## Introduction

Congenital infections are caused by pathogens able to infect the placenta and damage the foetus. The most common are toxoplasmosis, rubella, cytomegalovirus (CMV), herpes simplex and others grouped traditionally as TORCH complex. These infections represent a major public health concern, nevertheless it seems to be poor awareness of CMV infection among pregnant women, health care workers and the public [1-3]. Prenatal screening for toxoplasmosis and rubella is usually performed at the early stage of pregnancy in Italy.

CMV, formally designated human herpesvirus 5, belongs to the *Herpesviridae* family, is ubiquitous and transmitted by contact through infected body fluids such as urine, saliva, genital secretions and breast milk. Following the first infection, the virus becomes latent and periodic reactivation could occur due to immunosuppression (i.e. stress and pregnancy) [4-8].

The worldwide seroprevalence is roughly 60-90%, however there are some differences according to geographical areas, socioeconomic level and ethnic groups [5, 9]. Low prevalence is reported in countries as North America and United Kingdom, while most of the European countries has a prevalence of 80% meaning that most of the European women has been infected by CMV [9].

During pregnancy the transmission of CMV to the fetus may occur in two setting: “primary infection” and “non-primary infection”. The first one occurs

when seronegative women contract the infection during pregnancy; the second one occurs when a woman with prior immunity to CMV experiences a re-activation of the virus from latency or an infection by different strains [10, 11].

Seronegative women who become pregnant have a 4-fold higher risk to transmit the infection to the fetus if they are infected during pregnancy [12], as the likelihood of placental transmission appears to be higher among women with primary infection (approximately 30-50%) [10, 13]. The risk of transmission to the fetus is higher in the late stage of pregnancy (58-78% of infection transmitted in the third trimester versus 30-45% in the first trimester), although the likelihood of long-term sequelae is lower (24-26% in the first trimester versus 2.5-6% after 20 weeks of pregnancy) [11, 14, 15].

Most of the infants affected by congenital CMV (cCMV) are asymptomatic, while only 10% shows symptoms at birth, of whom a high proportion (40-60%) will develop long-term sequelae such as sensorineural hearing loss (SNHL) and neurodevelopmental difficulties. Among asymptomatic infants at birth, 6-23% could develop SNHL later making of cCMV the leading non-genetic cause of SNHL [10, 11].

The cCMV prevalence in Italy is one of the lowest, ranging from 0.15% in infants born to women  $\geq 24$  years old to 0.51% in infants born to women  $< 24$  years old, suggesting that old age of the mother may be a “protective factor” against cCMV [9].

CMV screening for pregnant women is not mandatory in Italy, while it is a routine test in 8 European countries and Israel [16]. Regarding Apulia region, a large region in Southern Italy, some useful information on hygienic measures aimed at avoiding CMV infection are included in a document dedicated to pregnant women [17, 18].

The present study was conducted to assess the serological profile of pregnant women with respect to CMV in Apulia from 2016 to 2019.

## Materials and methods

### STUDY POPULATION

Serum samples of pregnant women were collected from August 2016 to December 2019 in the province of Bari, the regional capital city with the highest population density in Apulia. Serum samples were anonymously collected in compliance with Italian ethics law and stored at the Molecular Epidemiology laboratory of the University of Siena, Italy. For each serum sample, information on age, state of pregnancy, gestational week, place and year of sampling was available.

Assuming an overall CMV IgG prevalence of 64.2% [19], a precision of the estimate of 5% and a confidence interval of 95%, a sample size of 354 serum samples was required.

A total of 360 samples, available at the sera bank, were stratified by age group (< 25, 25-29, 30-34, 35-39, ≥ 40 years of age) (Tab. I). The mean age was  $32.6 \pm 5.4$  years (age range 17-46 years).

According to the USA National Institutes of Health's (NIH) definition, samples were stratified by trimester of pregnancy (Tab. II): first trimester from week 1 to week 12, second trimester from week 13 to week 28, third trimester from week 29 to week 40 [20].

Tab. I. Study population by age group; Apulia, Southern Italy 2016-2019.

Age group	N	%
< 25	27	7.5
25-29	76	21.1
30-34	120	33.3
35-39	101	28.1
≥ 40	36	10.0
Total	360	100

Tab. II. Study population by trimester of pregnancy; Apulia, Southern Italy 2016-2019.

Trimester	N	%
1°	140	38.9
2°	174	48.3
3°	46	12.8
Total	360	100

### SEROLOGICAL ASSAY

Specific IgM and IgG antibodies against CMV were detected by commercial ELISA kits (Enzywell Cytomegalovirus IgM and Enzywell Cytomegalovirus IgG; DIESSE, Siena, Italy). Testing was performed according to manufacturer's instructions. Samples were considered positive for IgM and IgG when the ratio between the optical density (OD) of the sample and that of the cut-off was > 1.2, and negative when the ratio between the OD of the sample and that of the cut-off was < 0.8. Samples with a borderline result ( $\pm 20\%$  of the cut-off) were retested, in accordance with the manufacturer's instructions. For CMV IgG ELISA, IgG concentration was determined and expressed in IU/ml. Samples with CMV IgG concentration > 1.2 IU/ml were considered as immune, as indicated by manufacturer's instructions.

### STATISTICAL ANALYSIS

Mean age of subjects was calculated along with standard deviation (SD). IgM and IgG prevalence rates were calculated along with the corresponding 95% confidence intervals (95% CI). Geometric mean titres (GMTs) with corresponding 95% CI were calculated for IgG positive samples. Chi-square test and One-Way ANOVA test were used to compare prevalence rates and GMTs, respectively. Statistical significance was set at  $p < 0.05$ , two tailed.

## Results

Out of 360 samples, 8 and 10 samples tested borderline for CMV IgM and IgG, respectively. After retest, only one sample still tested borderline for IgM.

255 samples (70.8%, 65.8-75.5 95% CI) tested positive for CMV IgG, while 105 (29.2%, 24.5-34.2 95% CI) were negative. No significant differences in prevalence rates or GMTs were found by age group (Tab. III).

Considering the CMV IgG prevalence by trimester of pregnancy, 47.8% (32.9-63.0 95% CI) of samples

Tab. III. CMV IgG prevalence (reported as number and %, 95% CI) of positive and negative samples by age group. IgG titres of positive samples are reported as GMT (95% CI).

CMV IgG	Positive			Negative	
	Age groups	N	% (95% CI)	GMT (95% CI)	N
< 25	15	55.6 (35.3-74.5)	14.0 (11.8-16.5)	12	44.4 (25.5-64.7)
25-29	60	78.9 (68.1-87.5)	12.8 (11.2-14.5)	16	21.0 (12.5-31.9)
30-34	82	68.3 (59.2-76.5)	12.9 (11.7-14.3)	38	31.7 (23.5-40.8)
35-39	69	68.3 (58.3-77.2)	12.2 (11.0-13.6)	32	31.7 (22.8-41.7)
≥ 40	29	80.6 (64.0-91.8)	14.5 (12.3-17.0)	7	19.4 (8.2-36.0)

collected during the third trimester of pregnancy was positive, significantly lower when compared to the first (79.3%, 71.6-85.7 95% CI) and the second (70.1%, 62.7-76.8 95% CI) ones ( $p < 0.001$ ). However, no significant differences were found for GMTs by trimester.

Three samples (0.8%, 0.2-2.4 95% CI) tested positive for CMV IgM, one in the first trimester ( $\geq 40$  years old age group) and 2 in the second one (1 in 35-39 and 1 in  $\geq 40$  years old age group). One sample (0.3%, 0.0-1.5 95% CI) collected in the second trimester (25-29 years old age group) tested CMV IgM borderline. All these samples were CMV IgG positive.

## Discussion

In this study a high proportion (70.8%) of pregnant women from the province of Bari had antibodies against CMV showing that almost two-thirds of pregnant women included in this study have been infected by CMV. Considering the gestational period, we found a high proportion of women in the first and second trimester of pregnancy with CMV IgG antibodies (79.3 and 70.1%, respectively), while in the third trimester a lower (47.8%) proportion of women resulted positive to CMV. We do not have a clear explanation for this difference, and it is known that although the risk of CMV transmission to the fetus is higher in late pregnancy, the probability of long-term sequelae is lower in case of infection in the later stage of pregnancy than during the first trimester [11, 14, 15].

In our study, 29.2% of pregnant women were seronegative to CMV, with the younger age group ( $< 25$  years) being more susceptible to CMV infection during pregnancy (44.4%) compared to the oldest age group ( $\geq 40$  years old, 19.4%). In a multicentre survey conducted in 4 Italian regions it was found that the frequency of cCMV infection was higher in children born to women younger than 24 years old than those born to older women [21]. Seronegative women at the beginning or during pregnancy have the greatest risk to transmit CMV infection to the foetus. Roughly 40% of the women with primary infection during pregnancy transmits CMV to the foetus and approximately 10% of the infected infants shows the disease [22]. In Italy CMV prevalence in pregnant women increases with age [23] and together to a relatively high age at first pregnancy (mean age  $> 31.1$  years) [24] it may represent a "protective factor" against cCMV [9] infection of new-born. A study conducted in 1993 focusing on infants and children reported that CMV infection was endemic in the area of Bari, was mostly acquired in early childhood once the maternal immunity waned in the first year of life [25]. Other Italian studies performed on women of childbearing age and healthy subjects from 3 to 18 years old reported a seroprevalence of 79.9 [21] and 64.2% [23] respectively. Noteworthy, the latter found a prevalence significantly higher in females and subjects resident in the South of Italy [23].

Our findings show a higher prevalence of CMV

antibodies in pregnant women than what reported from different Italian areas such as the Province of Trento (64.2%) [19], the urban area of Northern Italy (68.3%) [26] and Sicily (65.87%) [27], as well as in some European countries as in Belgium (53.9%) [28] and in London (54.4%) [29], but considerably lower than in Iran (97.69%) [30], Saudi Arabia (98.7%) [31], and Brazil (97.5%) [32].

Notably, one sample in the first trimester of pregnancy in the  $\geq 40$  age group and two samples in the second trimester in the 35-39 and  $\geq 40$  age groups tested IgM and IgG positive. These findings could suggest recent primary infection, however further investigations should be needed [33].

This study has some limitations. The serum samples are convenience samples and may not be fully representative of the Apulia region or other Italian regions.

The presence of IgM provides an indication of recent infection, however the lack of baseline serum sample did not allow to assess seroconversion, if any.

For these samples no information on maternal and/or foetal outcomes was available so further analysis could not be performed.

## Conclusions

In conclusion, our study highlights that most of the pregnant women, especially those of  $\geq 40$  years of age, has antibodies against CMV, though these do not confer fully protective immunity against infection by different strains nor can prevent the re-activation of the latent one. On the other hand, most of the youngest women are seronegative and vulnerable during pregnancy. It is acknowledged that educational and hygienic measures represent an important primary prevention strategy able to effectively reduce the rate of maternal primary infection during pregnancy and cCMV infection [18].

Considering that cCMV is the leading non-genetic cause of SNHL, whose prevalence is much higher than that of Down syndrome and spina bifida [8], as well as of other congenital anomalies and long-term sequelae in new-borns, it would be extremely important, useful and cost-saving to screen women of childbearing age and women at early stage of pregnancy for CMV infection [26, 27, 34]. In addition, increase in the awareness of CMV infection, as for other diseases representing a threat during pregnancy [35, 36], is needed to reduce the risk of congenital infection through counselling about appropriate hygienic measure to prevent infection.

Vaccination may represent the most effective way of preventing CMV infection. Despite vaccine development has been in process since the 1970s and significant progress has been made, no vaccine is yet available mainly due to the ability of CMV to evade immune mechanisms and virus genetic diversity [37]. In addition to the screening actively offered to all pregnant women, seroepidemiological studies are an important tool for monitoring not only of vaccine preventable

diseases [35, 36, 38, 39] but also of other infections that represent a potential threat for pregnant women and new-borns [40-42].

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## Conflict of interest statement

The authors declare no conflict of interest.

## Authors' contributions

Conceptualization, CMT; formal analysis, SM; investigation, CMT, SM; resources, CMT; writing, original draft preparation, CMT; writing, review and editing, SM, SV, EM; visualization, SM; project administration, CMT.

All authors have read and agreed to the published version of the manuscript.

## References

- [1] Bale JF. Congenital infections. *Neurol Clin* 2002;20:1039-60. [https://doi.org/10.1016/S0031-3955\(16\)38370-5](https://doi.org/10.1016/S0031-3955(16)38370-5)
- [2] Rasti S, Ghasemi FS, Abdoli A, Piroozmand A, Mousavi SG, Fakhrie-Kashan Z. ToRCH "co-infections" are associated with increased risk of abortion in pregnant women. *Congenit Anom (Kyoto)* 2016;56:73-8. <https://doi.org/10.1111/cga.12138>
- [3] Manicklal S, Emery VC, Lazzarotto T, Boppana SB, Gupta RK. The "silent" global burden of congenital cytomegalovirus. *Clin Microbiol Rev* 2013;26:86-102. <https://doi.org/10.1128/CMR.00062-12>
- [4] Gilden DH, Tyler KL. Herpesvirus infection and peripheral neuropathy, in *peripheral neuropathy (Fourth Edition)*. Dyck PJ, Thomas S (Eds.) 2005. Hardcover ISBN: 9780721694917
- [5] Swanson EC, Schleiss MR. Congenital cytomegalovirus infection: new prospects for prevention and therapy. *Pediatr Clin North Am* 2013;60:335-49. <https://doi.org/10.1016/j.pcl.2012.12.008>
- [6] Gwendolyn LG. Infections in pregnant women. *The Medical Journal of Australia* 2002;176:229-36. <https://doi.org/10.5694/j.1326-5377.2002.tb04381.x>
- [7] Collinet P, Subtil D, Houfflin-Debarge V, Kacet N, Dewilde A, Puech F. Routine CMV screening during pregnancy. *Eur J Obstet Gynecol Reprod Biol* 2004;114:3-11. <https://doi.org/10.1016/j.ejogrb.2003.09.016>
- [8] Gugliesi F, Coscia A, Griffante G, Galitska G, Pasquero S, Albano C, Biolatti M. Where do we stand after decades of studying human cytomegalovirus? *Microorganisms* 2020;8(5). <https://doi.org/10.3390/microorganisms8050685>
- [9] EpiCentro. L'epidemiologia per la sanità pubblica - Citomegalovirus. Available from: <https://www.epicentro.iss.it/citomegalovirus/epidemiologia#:~:text=In%20Italia%20la%20prevalenza%20dell,protettivo%20contro%20l'infezione%20congenita> (accessed on: 1 October 2020).
- [10] Coppola T, Mangold JF, Cantrell S, Permar SR. Impact of maternal immunity on congenital cytomegalovirus birth prevalence and infant outcomes: a systematic review. *Vaccines (Basel)* 2019;7(4). <https://doi.org/10.3390/vaccines7040129>
- [11] Keighley CL, Skrzypek HJ, Wilson A, Bonning MA, Gilbert GL. Infections in pregnancy. *Med J Aust* 2019;211:134-41. <https://doi.org/10.5694/mja2.50261>
- [12] Leruez-Ville M, Magny JF, Couderc S, Pichon C, Parodi M, Bussieres L, Guilleminot T, Ghout I, Ville Y. Risk factors for congenital cytomegalovirus infection following primary and nonprimary maternal infection: a prospective neonatal screening study using polymerase chain reaction in Saliva. *Clin Infect Dis* 2017;65:398-404. <https://doi.org/10.1093/cid/cix337>
- [13] Hughes BL, Gyamfi-Bannerman C; Society for Maternal-Fetal. Diagnosis and antenatal management of congenital cytomegalovirus infection. *Am J Obstet Gynecol* 2016;214: B5-B11. <https://doi.org/10.1016/j.ajog.2016.02.042>
- [14] Akpan US, Pillarisetty LS. Congenital cytomegalovirus infection (Congenital CMV Infection). *StatPearls* 2020. Bookshelf ID: NBK541003PMID: 31082047
- [15] Enders G, Bader U, Lindemann L, Schallasta G, Daiminger A. Prenatal diagnosis of congenital cytomegalovirus infection in 189 pregnancies with known outcome. *Prenat Diagn* 2001;21:362-77. <https://doi.org/10.1002/pd.59>
- [16] Lunardi S, Lorenzoni F, Ghirri P. Universal screening for congenital CMV infection, in *update on critical issues on infant and neonatal care*. Barría RM (Ed.) 2019, pp. 1-15. Available at: <https://www.intechopen.com/books/update-on-critical-issues-on-infant-and-neonatal-care/universal-screening-for-congenital-cmv-infection>. <https://doi.org/http://dx.doi.org/10.5772/intechopen.89611>
- [17] Comitato Percorso Nascita Regionale and Regione Puglia. Agenda della gravidanza. 2019. Dipartimento "Promozione della Salute, del Benessere sociale e dello Sport per tutti", pp. 1-60.
- [18] Revello MG, Tibaldi C, Masuelli G, Frisina V, Sacchi A, Furione M, Arossa A, Spinillo A, Klersy C, Ceccarelli M, Gerna G, Todros T, Grp CS. Prevention of primary cytomegalovirus infection in pregnancy. *Ebiomedicine* 2015;2:1205-10. <https://doi.org/http://dx.doi.org/10.1016/j.ebiom.2015.08.003>
- [19] Dalmartello M, Parazzini F, Pedron M, Pertile R, Collini L, La Vecchia C, Piffer S. Coverage and outcomes of antenatal tests for infections: a population based survey in the Province of Trento, Italy. *J Matern Fetal Neonatal Med* 2019;32:2049-55. <https://doi.org/10.1080/14767058.2018.1424822>
- [20] National Institutes of Health. About pregnancy. 2017. Available from: <https://www.nichd.nih.gov/health/topics/pregnancy/conditioninfo> (accessed on: 1 October 2020).
- [21] Barbi M, Binda S, Caroppo S, Calvario A, Germinario C, Bozzi A, Tanzi ML, Veronesi L, Mura I, Piana A, Solinas G, Pagni L, Bevilacqua G, Mosca F. Multicity Italian study of congenital cytomegalovirus infection. *Pediatr Infect Dis J* 2006;25:156-9. <https://doi.org/10.1097/01.inf.0000199261.98769.29>
- [22] Stagno S, Pass RF, Cloud G, Britt WJ, Henderson RE, Walton PD, Veren DA, Page F, Alford CA. Primary cytomegalovirus infection in pregnancy. Incidence, transmission to fetus, and clinical outcome. *JAMA* 1986;256:1904-8. <https://doi.org/10.1001/jama.1986.03380140074025>
- [23] de Mattia D, Stroffolini T, Arista S, Pistoia D, Giammanco A, Maggio M, Chiamonte M, Moschen ME, Mura I, Rigo G, Scarpa B. Prevalence of cytomegalovirus infection in Italy. *Epidemiol Infect* 1991;107:421-7. <https://doi.org/https://doi.org/10.1017/S0950268800049062>
- [24] European Commission, Women are having their first child at an older age. 2017.
- [25] Leogrande G. The epidemiology of childhood cytomegalovirus infections in a large city of southern Italy. *Int J Clin Lab Res* 1993;23:109-12. <https://doi.org/10.1007/BF02592292>
- [26] De Paschale M, Agrappi C, Manco MT, Paganini A, Clerici P. Incidence and risk of cytomegalovirus infection during pregnancy in an urban area of Northern Italy. *Infect Dis Obstet Gynecol* 2009;2009:206505. <https://doi.org/https://doi.org/10.1155/2009/206505>

- [27] Puccio G, Cajozzo C, Canduscio LA, Cino L, Romano A, Schimmenti MG, Giuffrè M, Corsello G. Epidemiology of Toxoplasma and CMV serology and of GBS colonization in pregnancy and neonatal outcome in a Sicilian population. *Ital J Pediatr* 2014;40:23. <https://doi.org/10.1186/1824-7288-40-23>
- [28] Naessens A, Casteels A, Decatte L, Foulon W. A serologic strategy for detecting neonates at risk for congenital cytomegalovirus infection. *Journal of Pediatrics* 2005;146:194-7. <https://doi.org/10.1016/j.jpeds.2004.09.025>
- [29] Tooke PA, Ades AE, Peckham CS. Cytomegalovirus prevalence in pregnant women: the influence of parity. *Arch Dis Child* 1992;67:779-83. [https://doi.org/10.1136/adc.67.7\\_spec\\_no.779](https://doi.org/10.1136/adc.67.7_spec_no.779)
- [30] Tabatabaee M, Tayyebi D. Seroepidemiologic study of human cytomegalovirus in pregnant women in Valiasr Hospital of Kazeroon, Fars, Iran. *J Matern Fetal Neonatal Med* 2009;22:517-21. <https://doi.org/10.1080/14767050902801678>
- [31] Almaghrabi MK, Alwadei AD, Alyahya NM, Alotaibi FM, Alqahtani AH, Alahmari KA, Alqahtani MS, Alayed AS, Moosa R, Ali AS. Seroprevalence of Human cytomegalovirus in pregnant women in the Asir region, Kingdom of Saudi Arabia. *Intervirology* 2019;62:205-9. <https://doi.org/10.1159/000506051>
- [32] Spano LC, Gatti J, Nascimento JP, Leite JP. Prevalence of human cytomegalovirus infection in pregnant and non-pregnant women. *J Infect* 2004;48:213-20. [https://doi.org/10.1016/S0163-4453\(03\)00128-2](https://doi.org/10.1016/S0163-4453(03)00128-2)
- [33] Prince HE, Lape-Nixon M. Role of cytomegalovirus (CMV) IgG avidity testing in diagnosing primary CMV infection during pregnancy. *Clin Vaccine Immunol* 2014;21:1377-84. <https://doi.org/10.1128/CVI.00487-14>
- [34] Cahill AG, Odibo AO, Stamilio DM, Macones GA. Screening and treating for primary cytomegalovirus infection in pregnancy: where do we stand? A decision-analytic and economic analysis. *Am J Obstet Gynecol* 2009;201:466 e1-7. <https://doi.org/10.1016/j.ajog.2009.07.056>
- [35] Marchi S, Monti M, Viviani S, Montomoli E, Trombetta CM. Measles in pregnancy: a threat for Italian women? *Hum Vaccin Immunother* 2019;15:2851-3. <https://doi.org/10.1080/21645515.2019.1621146>
- [36] Trombetta CM, Montomoli E, Viviani S, Coluccio R, Marchi S. Evaluation of varicella immunity during pregnancy in Apulia region, Southern Italy. *Vaccines (Basel)* 2020;8(2). [doi.org/10.3390/vaccines8020214](https://doi.org/10.3390/vaccines8020214)
- [37] Dietrich ML, Schieffelin JS. Congenital cytomegalovirus infection. *Ochsner J Summer* 2019;19:123-30. <https://doi.org/10.31486/toj.18.0095>
- [38] Wilson SE, Deeks SL, Hatchette TF, Crowcroft NS. The role of seroepidemiology in the comprehensive surveillance of vaccine-preventable diseases. *CMAJ* 2012;184:E70-6. <https://doi.org/10.1503/cmaj.110506>
- [39] Marchi S, Viviani S, Montomoli E, Trombetta CM. Elimination of congenital rubella: a seroprevalence study of pregnant women and women of childbearing age in Italy. *Hum Vaccin Immunother* 2020;16:895-8. <https://doi.org/10.1080/21645515.2019.1688041>
- [40] Marchi S, Trombetta CM, Gasparini R, Temperton N, Montomoli E. Epidemiology of herpes simplex virus type 1 and 2 in Italy: a seroprevalence study from 2000 to 2014. *J Prev Med Hyg* 2017;58:E27-E33. PMID: 28515628
- [41] Fanigliulo D, Marchi S, Montomoli E, Trombetta CM. Toxoplasma gondii in women of childbearing age and during pregnancy: seroprevalence study in Central and Southern Italy from 2013 to 2017. *Parasite* 2020;27:2. <https://doi.org/10.1051/parasite/2019080>
- [42] Gouilly J, Chen Q, Siewiera J, Cartron G, Levy C, Dubois M, Al-Daccak R, Izopet J, Jabrane-Ferrat N, El Costa H. Genotype specific pathogenicity of hepatitis E virus at the human maternal-fetal interface. *Nat Commun* 2018;9:4748. <https://doi.org/10.1038/s41467-018-07200-2>

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