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Original Article

The Frequency of Cytomegalovirus and Toxoplasma Among Microcephalic and Hydrocephalic Neonates Admitted to Pediatric Hospital in Bandar Abbas

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Abstract

Background: Congenital infection is a primary cause of malformations during infancy including hydrocephaly and microcephaly. In addition, cytomegalovirus and toxoplasma are the two prevalent causes of congenital infections. The present research aimed to investigate the prevalence of cytomegalovirus and toxoplasma infections among neonates afflicted with microcephaly and hydrocephaly in a pediatric hospital in 2018.

Materials and Methods: The present descriptive, cross-sectional research was conducted on all neonates diagnosed with microcephaly and hydrocephaly hospitalized in the pediatric hospital of Bandar Abbas in 2018. Blood samples were taken from the neonates to be analyzed for cytomegalovirus and toxoplasma serology, followed by statistically analyzing the information describing 11 subjects including 5 hydrocephaly and 6 microcephaly cases.

Results: The mean gestational age was estimated at 35.8±4.08 and 37.16±1.32 weeks in hydrocephaly and microcephaly groups, respectively (P=0.507). In both groups, the female population was larger than the males. In addition, blood relations among parents were stronger in the microcephaly group (40%) compared to the microcephaly group (83.3%). Moreover, the anomaly was found to be more in the microcephaly group. This rate was 60% and 16.7% in the hydrocephaly and microcephaly groups, respectively. The serology of cytomegalovirus and toxoplasma in neither groups showed to be positive. One hundred percent of patients with an anomaly were term although 50% of those without any anomaly belonged to the term group. It appears that the presence of an anomaly was positively correlated with term birth. One hundred percent of patients with an anomaly were found to have parents who were close relatives. However, 50% of patients with no anomaly showed to have parents closely related in the family. Finally, heart problems were found to prevail in the group diagnosed with an anomaly.

Conclusion: In the present research, the prevalence of cytomegalovirus and toxoplasma infections was reported to be zero in neonates who were afflicted with microcephaly and hydrocephaly.

Keywords: *Toxoplasma gondii*, Cytomegalovirus, Hydrocephaly, Microcephaly

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Introduction

Most women at the age of fertility in low- or moderate-income countries enjoy long-term immunity to prior cytomegalovirus infections. In African, Latin American, and South Asian countries, more than 90% of the public have immunoglobulin G (IgG) antibodies and 40%-60% of the public have IgG antibodies in comparison to high-income countries (1-6). The prevalence of congenital cytomegalovirus (CMV) in high-income countries is 7% of all live births but between 1 and 5% in low-income countries (1, 4, 7). The risk of transmission grows with an increase in gestational age. In fact, among mothers with a primary infection, 35% of transmissions occur in the first trimester while this rate raises to 65% in the third trimester. The majority of neonates afflicted with CMV are asymptotic. However, the common symptoms among neonates are intrauterine growth restriction (IUGR), sensorineural hearing loss, petechial, and jaundice. Further, neural side effects are observed in 60%-90% of those diagnosed with clinical symptoms upon birth. Up to

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15% of asymptotic neonates upon birth could develop the symptoms during childhood (8). According to (9), most women at the age of fertility in Latin America, Central Europe, and West Africa possess specific antibodies against *Toxoplasma gondii* (IgG type). On the contrary, in the south-east of Asia, China, and South Korea, as well as Scandinavia and the United States, the immunity level is extremely lower (9, 10). Transmission from the mother to the child often occurs after affliction with the infection during pregnancy. The global occurrence rate of congenital toxoplasmosis has been estimated at 1.5 cases per 1000 live births. The highest rate of occurrence in some Latin American countries is 3.4 per 1000 live births while its lowest rate is reported in some parts of Europe as 0.5 per 1000 live births (11). Furthermore, the classical consequences of congenital toxoplasma are chorioretinitis, hydrocephaly, intracranial calcification, and epilepsy. It can also cause infant mortality. Contrary to cytomegalovirus, congenital toxoplasma does not transmit the infection to the child if the mother is immune. The risk of fetal infection following pregnancy progress can increase to 60% in the third trimester although the risk of fetal consequences is significantly lowered along the pregnancy progress (12). Microcephaly is a clinical diagnosis upon birth and describes a smaller than normal head. Nonetheless, this diagnosis does not necessarily point to abnormal brain growth as some children afflicted with microcephaly are healthy. Microcephaly is defined as the head occipitofrontal circumference more than 2 standard deviations (SDs) smaller than the mean size for the gestational age and the gender of a properly healthy population (8). Hydrocephaly is the hydrodynamic disorder of the cerebrospinal fluid (CSF) that can increase the volume taken by this fluid in the central nervous system (13). Moreover, congenital hydrocephaly occurs in 1 per thousand births (14). Considering the above-mentioned explanations, the present research aimed to explore the frequency of cytomegalovirus and toxoplasma among patients afflicted with microcephaly and hydrocephaly.

Materials and Methods

The present descriptive, cross-sectional research was conducted on neonates who were diagnosed with hydrocephaly or microcephaly in Bandar Abbas pediatric hospital in 2018. Throughout this year, 5 and 8 neonates were hospitalized for hydrocephaly and microcephaly, respectively. In the computed tomography (CT)-scan result of 2 cases with microcephaly, cerebral dysgenesis was observed which led to the exclusion of these subjects and 11 neonates were included in the research. Informed consent was obtained from all subjects' parents. Before study initiation, an ethical code was obtained from the Ethics Committee of Hormozgan University of Medical Sciences. Blood samples were taken from neonates with microcephaly lower than 3 SD below the head circumference growth curve and hydrocephaly (even mild) that were hospitalized in 2017 with no known infection but suspected of infections with cytomegalovirus and toxoplasma. The samples were then tested for cytomegalovirus and toxoplasma serology. If the result was positive, the CSF was sent for polymerase chain reaction (PCR) for cytomegalovirus and toxoplasma. Ultrasonography and CT scan were used to determine hydrocephaly. To check toxoplasma and cytomegalovirus serology, the luminance quantitative method was used in this research. In this method, minerals such as luminol, isoluminol, and acridinium esters are oxidized in the presence of an oxidant (e.g., hydrogen peroxide), a catalyst (e.g., the microperoxidase enzyme), and metal ions and then the produced light is further stimulated and appears as a sudden flash read by the luminometer. Eventually, microcephaly was set based on Stark's manual of neonatal care.

Statistical Procedures

The data were analyzed using SPSS software (version 19.0) and descriptive tests such as frequency, percentage, mean and, SD. Moreover, the t-test and Fisher's exact test were run to analyze the data and the *P* value was set at or below 0.05.

Results

The information describing 11 subjects (5 hydrocephaly and 6 microcephaly cases) were analyzed. The description of these patients is summarized in Tables 1 and 2. Table 3 presents the information bout gestational age upon

Table 1. Patients' Hydrocephaly Description

Gender	Gestational Age	Parents' Blood Relation	Head Circumference	Heart	Concomitant Anomaly	Epilepsy
Female	30	No	33	PDA	No	Yes
Female	39	No	40	Small PDA, followed by mild MR and TR	No	No
Female	38	Yes	38	VSD	Anomaly in limbs, ultrasound and no ventriculomegaly and dilated lateral ventricles	No
Male	33	No	41	Normal	In the brain CT scan: severe hydrocephaly and cerebral atrophy	No
Male	39	Yes	40	Normal	myelomeningocele	No

Note. PDA: patent ductus arteriosus; MR: mitral regurgitation; TR: tricuspid regurgitation; VSD: ventricular septal defect; CT: computed tomography.

Table 2. Patients' Microcephaly Description

Gender	Gestational Age	Parents' Blood Relation	Head Circumference	Heart	Concomitant Anomaly	Epilepsy
Female	35	Yes	28	Left ventricular hypertrophy	No	No
Female	38	Yes	28	Normal	No	No
Male	36	Yes	26	Normal	No	No
Female	38	Yes	30	Normal	No	No
Male	38	Yes	29	PS , VSD	Various limb anomalies	No
Female	38	Yes	29	Normal	No	Yes

Note. PS: Pulmonary stenosis ; VSD: ventricular septal defect;

birth and the head circumference of the two groups. The two groups were compared in terms of gestational age at the time of birth. This mean score was 35.8 ± 4.08 and 37.16 ± 1.32 weeks in the hydrocephaly and microcephaly groups, respectively, although the difference between the two groups was not statistically significant ($P = 0.507$). The comparative information of some qualitative features is provided in Table 4. In addition, anomaly-related information, along with several qualitative features is reported in Table 5.

Table 3. Head Circumference and Gestational Age at Birth

Group	Variable	Mean	SD	Minimum	Maximum
Hydrocephaly	Gestational age at birth	35.8	4.08	30	39
	Head circumference (cm)	38.4	3.2	33	41
Microcephaly	Gestational age at birth	37.16	1.32	35	38
	Head circumference (cm)	28.33	1.36	26	30

Note. SD: Standard deviation.

Table 4. Comparison of the 2 Research Groups in Terms of Qualitative Features

Variable	Sub-group	Research Group			
		Hydrocephaly		Microcephaly	
		No.	%	No.	%
Gender	Male	2	40	2	33.3
	Female	3	60	4	66.7
Gestational age	Term	3	60	4	66.7
	Preterm	2	40	2	33.3
Parents' close family relation	Yes	2	40	5	83.3
	No	3	60	1	16.7
Heart problem	Yes	2	40	4	66.7
	No	3	60	2	33.3
Epilepsy	Yes	1	20	1	16.7
	No	4	80	5	83.3
Concomitant anomaly	Yes	3	60	1	16.7
	No	2	40	5	83.3
Cytomegalovirus serology	Positive	0	0	0	0
	Negative	5	100	8	100
Toxoplasma serology	Positive	0	0	0	0
	Negative	5	100	8	100

Discussion

In the present research, heart problems reached 40% and 66.7% in the hydrocephaly and microcephaly groups, respectively. One hundred percent of patients with an anomaly were term cases while 50% with no anomaly belonged to the term group. It seems that anomaly is more associated with term birth. Moreover, 100% of patients with an anomaly reported their parents' close blood relation. However, 50% of patients with no anomaly reported a close family relation. Based on the results, heart problems were more prevalent in the group with an anomaly. Thus, in the case of anomalies, it is recommended that patients should be checked for heart conditions.

Congenital toxoplasmosis engagement patterns can be divided into four categories. In the first category, the most severe side effects occur, including cerebral calcification, hydrocephaly, encephalomyelitis, and even abortion. The second category is marked by severe systematic infections, hepatosplenomegaly, pneumonia, myocarditis, and the like. What usually occurs in the third category includes hyperbilirubinemia, epilepsy, purpura, chorioretinitis, lymphadenitis, and fever. Further, subclinical toxoplasmosis or generalized symptoms may occur in the fourth category (15). The congenital infection of cytomegalovirus is asymptotic in the majority of cases and symptomatic only in 11% of them. Even when the secondary maternal infection is the cause, the prevalence of symptoms at birth reaches the rate below 2%. However, in the related body of literature, a correlation has been reported between preterm birth, low birth weight, and the congenital infection of cytomegalovirus. The congenital infection of cytomegalovirus is the main cause of child hearing loss and other neurological disorders such as cognitive and visual disorders. A mild sensory-neural hearing loss is observed in about one-eighth (12.5%) of neonates afflicted with the infection. In a case series study, the hearing problem was reported to be improved after treatment with ganciclovir and valganciclovir. Moreover, research has shown a higher occurrence rate of the congenital infection of cytomegalovirus in congenital hypothyroid cases and Down Syndrome (16). In another

Table 5. Correlation of Anomaly and Several Qualitative Features in the Two Research Groups

Variable	Sub-group	Concomitant Anomaly			
		Yes		No	
		No.	%	No.	%
Gender	Male	2	66.7	2	25
	Female	1	33.3	6	75
Gestational age	Term	3	100	4	50
	Preterm	0	0	4	50
Parents' close family relation	Yes	3	100	4	50
	No	0	0	4	50
Prior condition	Normal	1	33.3	5	62.5
	Abnormal	2	66.7	3	37.5

research concerning congenital toxoplasmosis, the most prevalent engagement symptoms were found in the eyes and brain (17).

In the present research, toxoplasma and cytomegalovirus serology were negative in neonates with hydrocephaly and microcephaly. This difference can be explained by the smaller sample size. Concerning the serology of the blood sample, in the present research, the luminance quantitative method was used to check serology. The sensitivity of this test is lower than its specificity which leaves the chance of a false negative.

In another research on 64 neonates born with congenital anomalies, the ELISA method was used to investigate the antibody level against TORCH (Toxoplasma gondii, other, rubella virus, cytomegalovirus, and herpes simplex virus). Based on the findings, 6% of neonates and 14% of mothers showed an anti-toxoplasma immunoglobulin M (IgM), rubella, and positive cytomegalovirus (18). In another investigation for the screening of all neonates, the cytomegalovirus serology was analyzed via the ELISA technique in order to check IgG and IgM and in terms of the DNA virus through PCR. Overall, the prevalence of cytomegalovirus was reported as 12.57% out of which 5.71% pertained to congenital cause and 8.86% was explained by prenatal infections. In neonates with a CMV infection, 80% were milk-fed and 30% had a concomitant congenital anomaly. On the contrary, in neonates with a prenatal infection, 75% were breast-fed and 16.67% were diagnosed with anomalies. It was concluded that low birth weight, congenital anomalies, and breastfeeding were among the risk factors of cytomegalovirus infection in the neonatal intensive care unit (NICU) neonates. The CMV infection was more prevalent in preterm neonates or those of a low birth weight in the NICU. No evidence was found for the transmission of nosocomial cytomegalovirus in the NICU (19).

Based on the findings of another research, the overall prevalence of cytomegalovirus infection in neonates was reported to be 0.49%. In this research, 3 neonates were males and 5 were females. Moreover, 3 cases were born in natural delivery and 5 of them underwent a cesarean section. Additionally, 2 neonates (25%) were preterm and 3 were symptomatic upon birth and were sent for the urine test. Thus, the prevalence was rather lower (16). However, in another study, in which the mother's blood sample and umbilical cord were used for serology via the ELISA technique and urine was cultured, a total number of 988 neonates participated among whom 27 cases showed cytomegalovirus infections. Similarly, 12 cases (1.2%) were found with CMV. The risk of congenital infection in neonates whose mother had a positive serology was 3.4% (20). In another study aimed to explore the prevalence of cytomegalovirus, 75 pregnant women were aminosynthesized and all showed a negative IgM CMV. In addition, 56 cases of 75 mothers (74.7%) were positive at the time of amniocentesis. The amniotic fluid underwent a PCR to check the DNA CMV which revealed no positive cases. Further, 65 fetuses were followed up until birth and their urine samples within the first 2 weeks underwent a PCR but yielded no positive cases (21).

The related body of literature has reported the prevalence of cytomegalovirus in Iran from 0.3% in saliva samples to 4% in the PCR of the sample blood taken from the umbilical cord. The positive serology of the cytomegalovirus antibody of the IgG type in Iranian pregnant women was reported to range from 70% to 98%. However, IgM was found to range between 2.5 and 4.3, indicating that the majority of pregnant women in Iran got afflicted with cytomegalovirus before pregnancy. Nonetheless, several researchers believe that in developing countries, CMV infection is induced by non-preliminary congenital infections. The prevalence of serology and CMV infection among mothers varies across different areas (16).

In an investigation among neonates, the serology of IgG toxoplasma was positive in 35.9% of cases and that of IgM was positive in 3.2% of them. In their research among neonates below one year of age and suspected with intrauterine infection, Khosravi et al (22) found acute toxoplasmosis (IgM) in 10% of cases (23). In another study, the rate of congenital toxoplasmosis was reported to be 1.5%, which is equal to 14.8 cases per thousand live births (17). Based on the findings of another research, the risk of affliction among negative serum mothers during pregnancy was estimated at 14 per thousand cases and the probability of the toxoplasmosis of the neonates of mothers at risk was reported to be 7 per thousand (15). In an investigation exploring the prevalence of cytomegalovirus among neonates whose birth weight was lower (with no specific reason) than their IUGR, PCR was performed on 25 sample placenta which revealed no cases of infection (24). In the present research, the PCR technique was used, which is of high sensitivity and specificity, but the technique was not effective in IUGR neonatal screening. Neither was it economical nor logical. In a study of neonates with encephalopathy, the prevalence

of cytomegalovirus was estimated at 1.5% (25). The prevalence of toxoplasmosis varies across different parts of the country. Such different factors as different climates and cultural styles can account for this divergence (26).

Given that many prenatal infections with severe side effects including cytomegalovirus and toxoplasma are asymptomatic, the present research began to look into the screening of severe infections during pregnancy. If such infections are screened during pregnancy and under certain conditions such as IUGR, microcephaly, and hydrocephaly, severe side effects can be prevented at higher ages. In the current study, the applied laboratory investigation method was luminance quantitative serology and its sensitivity and specificity in examining IgM were 92% and 97.3%, respectively. It seems that the sensitivity of ELISA tests in examining serology or performing PCR is higher. This could be one reason for the negative result.

Therefore, it is suggested that more detailed research be conducted following more reliable serology methods or through PCR and microarray for a more comprehensive outlook. A longer time period needs to be spent on sampling as well.

Conclusion

In general, the frequency of congenital infections, cytomegalovirus, and toxoplasma varies as reported in different investigations conducted in different times and places and using various testing methods. The prevalence of the two target infections among microcephaly and hydrocephaly neonates in the child hospital was found to be zero in the present study. Thus, it seems that investigating and screening neonates affected by microcephaly and hydrocephaly is not economical.

Conflict of Interest Disclosure

The authors declare that they have no conflict of interests.

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Ethical Statement

The study was approved by the Ethics Committee of Hormozgan University of Medical Sciences (IR.HUMS.REC.1397.029). Patients' information was kept confidential all through research procedures.

Authors' contribution

All the authors made contributions to the proposal and design of the study, the acquisition of the data, as well as the analysis and interpretation of the data. Furthermore, they cooperated on drafting the article and revising it critically for important intellectual content, along with approving the final version of the study for submission.

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Informed Consent

The present study was conducted after informed consent was obtained from all participants.

References

1. Manicklal S, Emery VC, Lazzarotto T, Boppana SB, Gupta RK. The "silent" global burden of congenital cytomegalovirus. Clin Microbiol Rev. 2013;26(1):86-102. doi: 10.1128/cmr.00062-12.
2. Sheevani, Jindal N, Aggarwal A. A pilot seroepidemiological study of cytomegalovirus infection in women of child bearing age. Indian J Med Microbiol. 2005;23(1):34-6. doi: 10.4103/0255-0857.13870.
3. Schoenfisch AL, Dollard SC, Amin M, Gardner LI, Klein RS, Mayer K, et al. Cytomegalovirus (CMV) shedding is highly correlated with markers of immunosuppression in CMV-seropositive women. J Med Microbiol. 2011;60(Pt 6):768-74. doi: 10.1099/jmm.0.027771-0.
4. Cannon MJ, Schmid DS, Hyde TB. Review of cytomegalovirus seroprevalence and demographic characteristics associated with infection. Rev Med Virol. 2010;20(4):202-13. doi: 10.1002/rmv.655.
5. Alanen A, Kahala K, Vahlberg T, Koskela P, Vainionpää R. Seroprevalence, incidence of prenatal infections and reliability of maternal history of varicella zoster virus, cytomegalovirus, herpes simplex virus and parvovirus B19 infection in South-Western Finland. Bjog. 2005;112(1):50-6. doi: 10.1111/j.1471-0528.2004.00320.x.
6. Seo S, Cho Y, Park J. Serologic screening of pregnant Korean women for primary human cytomegalovirus infection using IgG avidity test. Korean J Lab Med. 2009;29(6):557-62. doi: 10.3343/kjlm.2009.29.6.557.
7. Kenneson A, Cannon MJ. Review and meta-analysis of the epidemiology of congenital cytomegalovirus (CMV) infection. Rev Med Virol. 2007;17(4):253-76. doi: 10.1002/rmv.535.
8. Devakumar D, Bamford A, Ferreira MU, Broad J, Rosch RE, Groce N, et al. Infectious causes of microcephaly: epidemiology, pathogenesis, diagnosis, and management. Lancet Infect Dis. 2018;18(1):e1-e13. doi: 10.1016/s1473-3099(17)30398-5.
9. Tenter AM, Heckeroth AR, Weiss LM. Toxoplasma gondii: from animals to humans. Int J Parasitol. 2000;30(12-13):1217-58. doi: 10.1016/s0020-7519(00)00124-7.
10. Jones JL, Kruszon-Moran D, Wilson M, McQuillan G, Navin T, McAuley JB. Toxoplasma gondii infection in the United States: seroprevalence and risk factors. Am J Epidemiol. 2001;154(4):357-65. doi: 10.1093/aje/154.4.357.
11. Torgerson PR, Mastroiacovo P. The global burden of congenital toxoplasmosis: a systematic review. Bull World Health Organ. 2013;91(7):501-8. doi: 10.2471/blt.12.111732.
12. Wong A, Tan KH, Tee CS, Yeo GS. Seroprevalence of cytomegalovirus, toxoplasma and parvovirus in pregnancy. Singapore Med J. 2000;41(4):151-5.
13. Shariatpanahi G, Nejat F, Pourpak Z. Effects of ventriculoperitoneal shunt on the neutrophil chemotaxis and NBT in hydrocephalic children. Iran J Pediatr. 2005;15(4):361-6. [Persian].
14. Nomura ML, Barini R, De Andrade KC, Milanez H, Simoni RZ, Peralta CF, et al. Congenital hydrocephalus: gestational and neonatal outcomes. Arch Gynecol Obstet. 2010;282(6):607-11. doi: 10.1007/s00404-009-1254-2.
15. Gharavi MJ. Seroepidemilogical survey of toxoplasmosis in pregnant women in Tehran. Hakim Research Journal.

2002;5(2):91-7. [Persian].
16. Karimian P, Yaghini O, Nasr Azadani H, Mohammadizadeh M, Arabzadeh SA, Adibi A, et al. Prevalence, characteristics, and one-year follow-up of congenital cytomegalovirus infection in Isfahan City, Iran. Interdiscip Perspect Infect Dis. 2016;2016:7812106. doi: 10.1155/2016/7812106.
17. Noorbakhsh S, Kalani M, Aliakbari AM, Tabatabaei A, Ehsanipour F, Taghipour R, et al. Prevalence of congenital toxoplasmosis in two university hospitals: a brief report. Tehran University Medical Journal. 2013;71(6):410-4. [Persian].
18. Golalipour MJ, Khodabakhshi B, Ghaemi E. The prevalance of TORCH antibodies among newborns with congenital malformations and their mothers in Gorgan, Iran. Journal of Gorgan University of Medical Sciences. 2008;10(3):45-50. [Persian].
19. Morgan MA, el-Ghany el SM, Khalifa NA, Sherif A, Rasslan LR. Prevalence of cytomegalovirus (CMV) infection among neonatal intensive care unit (NICU) and healthcare workers. Egypt J Immunol. 2003;10(2):1-8.
20. Lamberson HV Jr, McMillian JA, Weiner LB, Williams ML, Clark DA, McMahon CA, et al. Prevention of transfusion-associated cytomegalovirus (CMV) infection in neonates by screening blood donors for IgM to CMV. J Infect Dis. 1988;157(4):820-3. doi: 10.1093/infdis/157.4.820.
21. Nishimura N, Kimura H, Yabuta Y, Tanaka N, Ito Y, Ishikawa K, et al. Prevalence of maternal cytomegalovirus (CMV) antibody and detection of CMV DNA in amniotic fluid. Microbiol Immunol. 1999;43(8):781-4. doi: 10.1111/j.1348-0421.1999.tb02470.x.
22. Khosravi N, Farhadi SN, Tabatabaei A. Congenital infection with Toxoplasma gondii: a case control study of Tehran, Iran. Journal of Public Health and Epidemiology. 2011;3(2):68-72.
23. Golalipour MJ, Khodabakhshi B, Ghaemi E. Possible role of TORCH agents in congenital malformations in Gorgan, northern Islamic Republic of Iran. East Mediterr Health J. 2009;15(2):330-6.
24. Byrne J, Stephens A, Dinsmoor M. 25: Prevalence of cytomegalovirus infection (CMV) in placentas of unexplained small for gestational age (SGA) neonates: a pilot study. Am J Obstet Gynecol. 2015;213(6):905-6. doi: 10.1016/j.ajog.2015.09.056.
25. Tann CJ, Nkurunziza P, Nakakeeto M, Oweka J, Kurinczuk JJ, Were J, et al. Prevalence of bloodstream pathogens is higher in neonatal encephalopathy cases vs. controls using a novel panel of real-time PCR assays. PLoS One. 2014;9(5):e97259. doi: 10.1371/journal.pone.0097259.
26. Khosravi S, Eslamirad Z, Rafiei F. The Overview on studies related to the prevalence of neonatal toxoplasmosis in Iran. Journal of Iranian Clinical Research. 2016;3:91-6.