

Prevalence of Cytomegalovirus among pregnant women relation to congenital abnormalities in embryos and children in Wasit province

انتشار الإصابة بالفيروس المضخم للخلايا المفاوية في النساء الحوامل وعلاقته بالاجهاض والتشوهات الخلقية للاجنة والاطفال في محافظة واسط

Rasha Noori Al-shammary
Wasit University/college of medicine

Abstract

Serological examination to detect CMV virus and ultrasound examination to known congenital anomalies in embryos among aborted and pregnant women blood sample of 750 and children blood sample of 36 was carried out in Al – karama hospital and AL-Zahra hospital of Wasit province from January to July 2012. Overall prevalence of CMV (positive cases) was 345 (43.9%). Prevalence of virus increased in age (23-29) and there were highly significantly ($P < 0.001$) between age (23-29) and age (36-40). The highest infection in no aborted time (51.3%) and with highly significantly ($P < 0.001$) compared with lowest in fifth aborted times. CMV infection increased in embryos at (22-26) weeks of pregnancy and there were highly significantly ($P < 0.001$) between fetuses (22-26) weeks and children at aged 2 years, types of congenital anomalies caused by aborted is Hydrocephalus or Microcephally (%57.2), Hearing loss and vision loss(%66.6), Delayed mile stones (%80).

الخلاصة

تم إجراء الفحص المصلي لايجاد فايروس الخلايا العملاقة وفحص سونار لمعرفة التشوهات الخلقية للاجنة بين 750 عينة دم لنساء المجهضات وحوامل و36 عينة دم اطفال الدين راجعوا مستشفى الكرامة و مستشفى الزهراء في محافظة واسط من كانون الثاني ولغاية تموز 2012 بلغت عدد العينات المصابة (الموجبة) 345 (%43.9) ، كانت نسبة انتشار الفايروس اكبر بين الاعمار (23-29) ، كما أشارت الدراسة الى وجود فروقات معنوية عالية ($p < 0.001$) بين الاعمار (23-29) والاعمار (36-40) ، اظهرت النتائج اعلى نسبة اصابة للنساء بدون الاجهاض بنسبة 51.3% بفرق معنوي عالي ($P < 0.001$) مقارنة مع اقل نسبة و هي النساء ذات خمس اجهاضات. مرض الخلايا العملاقة يزداد في الاجنة في (22-26) اسبوع من الحمل وفروقات معنوية عالية بين الاجنة (22-26) اسبوع من الحمل والاطفال في سنة 2. وانواع التشوهات الخلقية المتسببة من الاجهاض ، فهي كبر اوصغر حجم الرأس وفقدان البصر او السمع وتاخر النمو و بالنسب (%57.2) ، (%66.6)(%80) على التوالي.

INTRODUCTION

Cytomegalovirus (CMV) is herpes virus and a leading biological factor causing congenital abnormalities, intra-uterine death (IUD) of the fetus and Recurrent spontaneous miscarriage (RSM) [1]. CMV is spread from one person to another through contact with saliva, semen, vaginal fluid, blood, urine, tears, feces, or breast milk [2,3]. Symptoms of congenital CMV were jaundice, thrombocytopenia, hepatomegaly, petechiae, purpura and splenomegaly. These symptoms may cause significant, life-threatening problems; however, they also may resolve without permanent damage to the infant. In contrast, CNS disease in infants may have a permanent effect on the outcome of the child, such as delayed mental development, deafness, seizures, cerebral palsy and blindness[4-5]. Congenital infections are the result of transplacental transmission of CMV to the fetus [6,7]. The mechanisms by which the mother accepts the implanting fetus as an allograft remain unexplained. Mononuclear cytotrophoblasts, the specialized cells of the placenta that invade the uterus, play an important role. Cytotrophoblasts secrete IL-10, the immunosuppressive cytokine that modulates immune responses, helping to protect the fetal hemiallograft from rejection.

IL-10 is involved in the maintenance of normal pregnancy, perhaps by suppressing IFN- γ and TNF- α production by TH1 cells. Moreover, IL-10 may influence the histocompatibility leucocytic antigen (HLA) class I expression pattern at the feto-maternal barrier, contributing to the maternal tolerance of the allogenic fetus [8,9]. Human cytomegalovirus (CMV) is often detected at the uterine-placental interface, impairing cytotrophoblast differentiation and invasion. Infected cytotrophoblasts express CMV IL-10 which upregulates human IL-10 and decreases matrix metalloproteinase-9 activity, an enzyme which degrades the extracellular matrix and increases the depth of invasion. The diminished degradation of extracellular matrix could contribute to the shallow invasion of the uterus and restriction of fetal growth in pregnancies affected by CMV. Although the mechanisms causing reproductive failure remain speculative, recent evidence suggests that a specific uterine immune-endocrine network play a pivotal role in the continuation of pregnancy. Soluble intercellular adhesion molecule-1 (sICAM-1), a cytokine inducible molecule is released by the endometrium in a hormone-dependent manner and is able to interfere with several immunological responses. Its reduced levels in some patients with unexplained recurrent miscarriage may reflect the presence of an altered immunological environment during early gestation [10,11].

The first step in the prenatal diagnoses of congenital CMV infection is determination of maternal primary and secondary infection by serological testing [12]. In women with proven CMV infection, the second step is to identify fetal infection by non-invasive (ultrasound examination) and invasive (amniocentesis) prenatal tests [13]. Treatment is the use of CMV-specific hyperimmune globulin for the treatment and prevention of fetal CMV infection [14,15]. The ultimate goal in prevention of congenital CMV infection is to develop a vaccine, which would be administered to seronegative women of childbearing age to prevent the occurrence of primary CMV infection during pregnancy until an effective vaccine is available, recommendations for seronegative pregnant women with respect to CMV infection include practising good personal hygiene such as avoiding intimate contact with salivary secretions and urine from young children and careful hand washing after changing diapers and wiping secretions [16,17].

This work aimed to detect CMV virus among aborted women and relate to congenital anomalies embryos and children

Material & method

From January to July 2012, seven hundred and fifty aborted women and thirty six children attending the virology unit of Al-Karama hospital of Wasit province were investigated in this study. The women aged between 17 years to 40 years, children ages ranged from (1- 4) years. The diagnosis of these patients was established on the basis of thorough clinical and serological examination. In most of these cases samples were found positive for CMV Virus. For each sample should be examined by: ELISA Test for the Detection of IgM Antibodies to CMV Virus in Human Serum. Human GMBH according to [18-19]

Statistical analysis :

Data were coded and fed to SPSS/Win (Version 6.4). Data were presented as numbers, percentages, means and standard deviations ($X \pm SD$). Analysis of data was done using independent T-test [20].

Result & Discussion

Table (1) Prevalence of infected women & children with cytomegalovirus

Total no.	+ve	%	-ve	%
786	345	43.9	441	56.1

Table (1) show the distribution of positive and negative cases .These result showed the highest infection percentage 56.1% in negative cases compared with 43.9% infection in positive cases.

Table (2) The infected women group with cytomegalovirus according age.

Group	Age interval (years)	+ve %		-ve %		Total
1	17-22	75	33.3	150	66.7	225
2	23-29	105	60.3	69	39.7	174
3	30-35	33	32.1	70	67.9	103
4	36-40	25	22.7	85	77.3	110
	Total					750

Table (2) shows the distribution CMV infection according to the age group .These results showed the highest infection was 60.3 %in group 2(23 -29) years and the lowest was 22.7% in group 4(36-40). When compared between highest infection and lowest infection highly significant ($P < 0.001$) difference was found between then.CMV detection in blood of individuals of age range between 17 to 45 years [21].intrauterine transmission of human cytomegalovirus (CMV) has been recognized as the major cause of congenital defects in countries for over 20 years. High prevalence was recorded in the age group of 21 to 30 years, followed by the age group of <20 years, then the age group of 31 to 40 years and 0% was recorded in the age group of >40 years [22-23].

Table (3) Aborted times per infected women with cytomegalovirus engaged in our study

Aborted times	No. of women+ve %		No. of women -ve		Total
0	100	51.3	95	48.7	195
1	75	42.8	100	57.2	175
2	65	34.3	125	65.7	190
3	20	30.7	45	69.3	65
4	10	14.3	60	85.7	70
5	5	9.1	50	90.9	55
Total	275	36.7	475	63.3	750

Table(3)indicates the distribution of aborted woman according to the number of abortions .These results showed that the highest infection in non aborted women (51.3%) and the lowest in fifth abortion (9.1%). When comparison was made between highest infection and lowest infection we found that highly significant ($P < 0.001$) between then .From a total of individuals, showed highest infection in no abortion. Followed pregnant women who had abortion once was CMV -PCR positive and were CMV antibodies positive , then women who had abortion two, thrice women were CMV-PCR positive were CMV antibodies positive, and in women who had abortion 4 times [24] . Treatment is the use of CMV-specific hyperimmune globulin for the treatment and prevention of fetal CMV infection .The ultimate goal in prevention of congenital CMV infection is to develop a vaccine to prevent the occurrence of primary CMV infection during pregnancy [25]. This treatment and vaccine lead to decrease the percent of CMV infection with increase times of aborted fetuses.

Table no (4) The infected women group with cytomegalovirus according months.

Month	+ve	%	-ve	%	Total	%
January 2011	64	53.7	55	46.3	119	15.2
February 2011	64	53.7	55	46.3	119	15.2
March 2011	88	53.7	76	46.3	164	20.8
April 2011	18	18.4	80	81.6	98	12.4
May 2012	11	13.7	70	86.3	81	10.3
Jun	34	25.7	100	74.3	134	17.2
July	15	23.1	50	76.9	65	8.2
Total	441	56.1	345	43.9	786	

Monthly distribution is represented in table (4). These results showed the highest infection in January 2011 (53.7%) and the lowest in May 2012 (13.7%). When compared between highest infection and lowest infection we found highly significant ($P < 0.001$) between them. CMV virus spread during the winter and spring [26,27]

(Table no. 5):- Times per children engaged and type of congenital anomalies in our study

Times	No. of children +ve		No. of children -ve				Type congenital abnormalities a of children
	No.	%	No.	%	No.	%	
Embryo+ Fetus(8-9)	2	66.6	1	33.4	3	10.	Microcephally Oligohydroaminos polyhydriaminos
1 year	3	42.8	4	57.2	7	19.5	Asymptomatic Hydrocephalus Microcephally
2 year	4	20	16	80	20	55.5	Delayed mile stones
3-4 years	1	33.4	2	66.6	3	10.	Hearing loss and vision loss Hearing loss and vision loss
Total	10	27.7	26	72.2	36		

Table no (5) Shows the distribution of congenital CMV according to ages children. These results showed the highest infection of congenital CMV were reported in fetuses at last two months of pregnancy (66.6%) and the lowest at 2 years (20%). When compared between highest infection and lowest infection we found highly significant ($P < 0.001$) between them. Through active national surveillance 70 cases of congenital CMV were reported 3- 4-year period, Of the 85–90% fetus and children born with asymptomatic congenital CMV, up to 15-30% will develop symptoms in later life, the most common being sensorineural hearing loss after three years [28]. Cytomegalovirus is the most common cause of intrauterine infection, occurring in 0.2% to 2.2% of all live births, and is a common cause of sensorineural hearing loss and, vision loss and mental retardation [29]. Syndrome with symptoms including malaise, persistent fever, myalgia, cervical lymphadenopathy, and, less commonly, pneumonia and hepatitis [30]

Conclusion

- 1- The infection of CMV increased between the ages 23 -39 and decreased between upper and lower this rang
- 2- January recorded highest infection rats
- 3-CMV infection increased in woman had suffering from no abortion and decreased with increased numbers of abortion
- 4- CMV infection increased in fetuses at last two months of pregnancy compared with children at age 2years

Recommendations

CMV infections are prevented by a vaccine, which would be administered to seronegative women of childbearing age to prevent the occurrence of primary CMV infection during pregnancy

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