

Research Article**Screening of Cytomegalo Virus Antibodies among Sudanese Children with Congenital Malformation****Alakbash Khaliefa^{1*}, Mohammed Abbas², Mohammed J. El-Mak¹, Mohammed Nafia¹**¹ Microbiology Department, Faculty of Medical Laboratory Sciences, Al-Neelain University, Sudan² Medical Laboratory Department, College of Applied Medical Sciences, Salman bin Abdulaziz University, Saudi Arabia***Corresponding author**

Alakbash Mosaad Alakbash Khaliefa

Email: agbash1978@gmail.com

Abstract: Human cytomegalo virus (CMV) is a double stranded DNA belongs to Herpesviridae family that is restricted to humans. CMV can be transmitted from infected to non infected individuals through various types of body fluids; the infection can also be transmitted from infected women to her fetus during pregnancy. The prevalence of congenital CMV infection ranges from 0.3 to 2.3% of live births in different populations. A high prevalence of CMV infection was demonstrated among pregnant women in Sudan. The aim of the current study was to screen the presence of CMV IgG and IgM in Sudanese children with congenital malformation. It was a descriptive, cross sectional study performed in the period between May and July 2014 at Academy charity hospital, Sudan. 90 of Sudanese children with congenital malformation (46 male and 44 female) were included in this study. The patients were classified into three age groups: below 2 years, between 2 and 4 years and more than 4 years. Questionnaires were used to collect the patients' data. The IgM and IgG antibodies against CMV in patients' samples were detected by using ELISA technique. The results showed that 93.3% of the patients were seropositive for CMV IgG, and 90% of them had CMV IgM in their serum. The major malformation observed among patients was hydrocephaly (46.7%), microcephaly was observed in only 5.6% of the patients. (71.1%) of the tested malformation child mothers had history of abortion; 93.8% of their child had CMV IgG. Human cytomegalo virus (CMV) infection was frequent among Sudanese patients with congenital malformation, especially in the age group below 2 years. We recommended the gynecologists and the pediatrians to investigate their pregnant women for CMV routinely and especial care should be taken to investigate the neonates of infected mothers. We suggest developing a wide scale epidemiological screening program to investigate in depth this problem especially because there was no CMV vaccine discovered and to overcome CMV infection malformation among Sudanese children.

Keywords: CMV, Malformation, Congenital.

INTRODUCTION

Human cytomegalo virus (CMV) is a double stranded DNA belongs to Herpesviridae family that is restricted to humans. The major targets of CMV in *in vivo* infection include: Epithelial cells, endothelial cells and fibroblasts [1]. CMV can be transmitted from infected to non infected individuals through various types of body fluids; the infection can also be transmitted from infected women to her fetus during pregnancy. The prevalence of congenital CMV infection ranges from 0.3 to 2.3% of live births in different populations [2]. At birth the infected neonates may have symptoms such as: neonatal sepsis, intrauterine growth retardation, jaundice, petechiae, thrombocytopenia, hepatosplenomegaly and/or microcephaly. Asymptomatically infected children have a 10% chance to develop neurodevelopment squealer later in childhood [3]. Maternal recurrent CMV infection can also result in congenital CMV [4]. In order to minimize the risk of congenital CMV infection, numbers of

European countries such as (France, Belgium, Spain, Italy, Germany, Austria, Portugal, and the Netherlands) routinely screen the majority of pregnant women serologically for CMV [5, 6]. CMV is a slow replicating virus, infecting only as many as few percentages of all neonates in developed countries, but demonstrating up to 90% IgG - positivity in developing countries [7].

A high prevalence of CMV infection was demonstrated among pregnant women in Sudan [8-10]. Recent study conducted in Sudan by Khairi *et al.* noticed 97.5% of tested pregnant women were CMV IgG positive [10]. Furthermore, Nahla *et al* elucidated that 94.3% of congenially infected neonates were CMV IgM positive [11].

The aim of the current study was to determine the serofrequency of CMV IgG and IgM positivity among Sudanese children with congenital malformation.

MATERIALS AND METHODS

It was a descriptive, cross sectional study performed in the period between May and July 2014 at Academy charity hospital, Sudan. 90 of Sudanese children with congenital malformation (46 male and 44 female) were included in this study. The patients were classified into three age groups: below 2 years, between 2 and 4 years and more than 4 years. Questionnaires were used to collect the patients' data. The study was approved from the ethical committee of EL Neelain University. After appropriate ethical approval and written consent form from participants prior the commencement of the study, 3 ml of blood were collected into plain container and allowed to clot, and then serum was separated at room temperature by centrifugation at 5000 rpm for 10 min, and kept frozen at - 20° C until immediately before assay. The IgM and IgG antibodies against CMV in patients' samples were detected by using ELISA technique the method used as recommended by the manufacturer. Data was entered in the computer and Statistical software packages (Excel 5.0, Microsoft, Redmond, WA; and Statistical Package for the Social Sciences 20.0, SPSS, Inc., Chicago, IL) were used for data management and analysis.

RESULTS

A total of 90 patients with congenital malformation were enrolled in the study. Forty four (48.9%) were females and sixty four (51.1%) of the patients were male.

Regarding age distribution, 64 of the patients were below 2 years, 18 were between 2 and 4 years, and 8 were above 4 years, figure 1 shows the seropositivity to CMV among different age groups in this study.

The results showed that 93.3% of the patients were seropositive for CMV IgG, and 90% of the study subjects had CMV IgM in their serum. Table 1 showed the presence of CMV antibodies in children of mothers with history of miscarriage.

The predominant malformation observed among patients was hydrocephaly (46.7%), microcephaly was observed in only 5.6% of the patients, Fig. 2.

71.1% of the tested malformation child mothers had history of abortion; 93.8% of their child had CMV IgG. Table 1 show IgM & IgG CMV among patients of mothers with history of miscarriage.

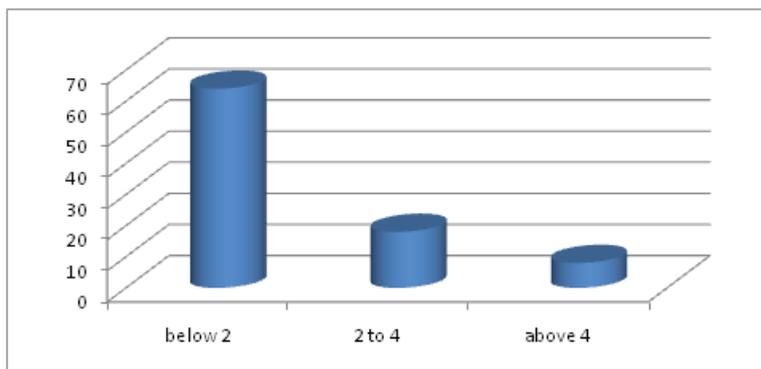


Fig. 1: Age group distribution among study population

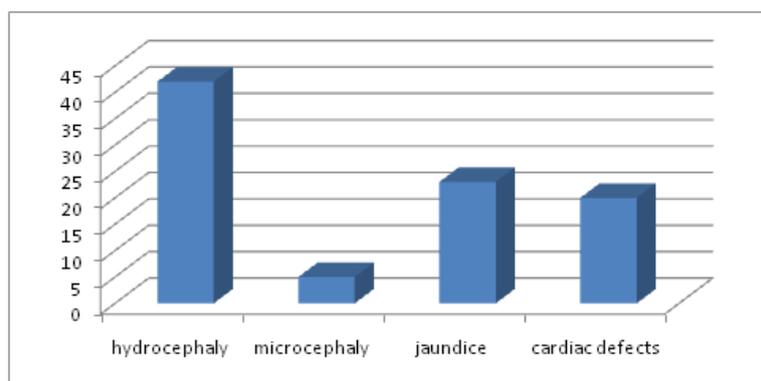


Fig. 2: Congenital malformations observed in selected patients

Table 1: The presence of CMV antibodies in children of mothers with history of miscarriage

Mothers with history of miscarriage	CMV IgM	CMV IgG
Yes	57	60
No	24	24
Total	81 (90%)	84 (93.3%)

DISCUSSION

The CMV infection can be transmitted from infected mothers to their fetus; the infected neonates may develop many congenital abnormalities. A majority of infants with congenital CMV, who are born to women with preconceptional immunity, acquire the virus as a result of recurrent maternal infection: reactivation of endogenous virus or reinfection with a new strain of CMV. Asymptomatic neonates have a chance to develop malformations later. The current study revealed the high percentage of CMV IgG & IgM antibodies in congenitally malformation Sudanese children samples.

In this study, 93.3% of tested children with malformation were seropositive for CMV IgG, and 90% were seropositive for CMV IgM. A high percentage (94.3%) of CMV IgM in neonates with malformation was also observed in a study conducted in Sudan by Nahla *et al.* The reported congenital infections among neonates between 2004 -2007 from Soba Hospital and Omdurman Hospital, Khartoum – Sudan were 276 and 3189 respectively [11].

Anti-CMV IgG antibodies were found in 97.5% in pregnant women attending Omdurman Maternity Hospital between Januarys – June 2012 [10], the high prevalence of CMV infection among Sudanese pregnant women support our findings in this study. Furthermore, the history of miscarriage in children mothers may give a clear sign of previous CMV infection.

Transplacental transfer of maternal IgG to the fetal blood stream is mediated by neonatal Fc receptor in syncytiotrophoblast of the placenta and contributes to the passive immunity of newborns to pathogen. Maternal IgG antibodies in full-term newborns are usually higher than those in their mother [12], in agreement with previous studies [13, 14] we found that the seroprevalence of anti-CMV IgG was much higher in infant (less than 2 years old) as compare to older children, Fig. 1.

In conclusion, the study showed that CMV infection was frequent among Sudanese patients with congenital malformation, especially in the age group below 2 years. We recommended the gynecologists and the pediatrians to investigate their pregnant women for CMV routinely and especial care should be taken to investigate the neonates of infected mothers. We suggest developing a wide scale epidemiological screening program to investigate in depth this problem especially because there was no CMV vaccine discovered and to overcome CMV infection malformation among Sudanese children.

ACKNOWLEDGMENT

The authors sincerely thank the staff of the Academy charity hospital and laboratory department, Khartoum-Sudan.

REFERENCES

1. Stagno S; Cytomegalovirus. In Remington JS, Klein JO editors; Infectious diseases of the fetus and newborn infant. Philadelphia Saunders WB, 2001: 389-424.
2. Lazzarotto T, Lanari M; Why is cytomegalovirus the most frequent cause of congenital infection? Expert Rev Anti Infect Ther., 2011; 9(10): 841-843.
3. Jones CA; Congenital cytomegalovirus infection. Curr Probl Pediatr Adolesc Health Care, 2003; 33(3):70-93.v
4. Wang C, Zhang X, Bialek S, Cannon MJ; Attribution of congenital cytomegalovirus infection to primary versus non-primary maternal infection. Clin Infect Dis., 2011; 52:e11–e13.
5. Adler SP; Screening for cytomegalovirus during pregnancy. Infect Dis Obstetric Gynecol., 2011; 2011: 942937.
6. Forsgren M; Prevention of congenital and prenatal infections. Euro Surveillance, 2009; 14: 2–4.
7. Cannon MJ, Schmid DS, Hyde TB; Review of cytomegalovirus seroprevalence and demographic characteristics associated with infection. RMV, 2010; 20(4): 202- 213.
8. Kafi SK, Eldouma EY, Saeed SBM, Musa HA; Seroprevalence of Cytomegalovirus among blood donors and antenatal women attending two hospitals in Khartoum State. Sudan J Med Sci., 2009; 4(4): 399-401.
9. Hamdan ZH, Abdelbagi IE, Nasser NM, Adam I; Seroprevalence of cytomegalovirus and rubella among pregnant women in western Sudan. Virol J., 2011; 8: 217-220.
10. Khairi SI, Intisar KS, Enan KH, Ishag MY, Baraa AM, Ali YH; Seroprevalence of cytomegalovirus infection among pregnant women at Omdurman Maternity Hospital, Sudan. Journal of Medical Laboratory and Diagnosis. 2013; 4(4): 45-49.
11. Nahla Kh. M, Ali YH, Enan KA; Studies on congenital infections in infants in Sudan: Seroprevalence of cytomegalovirus. Journal of Science and Technology, 2011; 12(4): 83–90.
12. Simister NE; Placental transport of immunoglobulin G. Vaccine, 2003; 21(24): 3365-3369.
13. Chen MH, Chen PC, Jeng SF, Hsieh CJ, Su FC, Liao HF *et al.*; High prenatal seroprevalence of Cytomegalovirus in northern Taiwan. J Paediatr Child Health, 2008, 44(4):166-169.
14. Nozawa N, Fang-Hoover J, Tabata T, Maidji E, Pereira L; Cytomegalovirus-specific, high-avidity IgG with neutralizing activity in maternal circulation enriched in the fetal bloodstream. J Clin Virol., 2009; 46(Suppl 4): S58-S63.