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RESEARCH ARTICLE

IgG AVIDITY AS A DIAGNOSTIC TOOL FOR HUMAN CYTOMEGALOVIRUS INFECTION IN ABORTED WOMEN IN AL-KUT DISTRICT – IRAQ

[1*]Ansaf Abdulhussein Mahoor Chlaibawi and [2]Qasim Dawood Yasir Altameemi

[1]Senior Gynecologist in Al-Kut Hospital for Gynecology and Pediatrics, Iraq
[2]Assist. Prof. and Consultant Pediatrician in Faculty of Medicine, Wasit University, Iraq

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ABSTRACT

Human cytomegalovirus (HCMV) is a world widely distributed among pregnant ladies and it is considered the most prevalent congenital viral infection in the developed countries where acute infection during pregnancy is a leading cause of deafness and serious neurologic manifestations in the newborn babies and a questionable cause for recurrent abortions. This study conducted on two groups of women aged between 16 to 46 years selected from the gynecology clinic of Al- Kut hospital for gynecology and pediatrics (the patients group consists of 60 women with a history of recurrent miscarriages while the control group consists of 60 healthy pregnant women with no history of previous abortion) for the period between February 2016 to February 2017 to seek for serum anti-human CMV IgG and IgG avidity levels using the ELISA test and genetic test for detection of gB gene after DNA extraction using PCR technique. The serum anti-HCMV IgG Ab was detected in 54 (90%) of women in the patients group while it was detected in 45(75%) of women in the control group. the serum IgG avidity for anti-HCMV IgG Ab was positive in 18(30%) of women in the patients group while it was positive in 3(5%) of women in the control group. the DNA extraction for PCR glycoprotein B gene revealed a positive results in 15 (25%) of women from the patients group while non (0%) was positive in the control group. These results proved that IgG avidity is a dependable indicator for diagnosis of primary CMV infection in pregnant ladies.

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INTRODUCTION

Human cytomegalovirus (HCMV) is an enveloped DNA virus from the herpes virus family characterized by a long life latency after a primary infection (Mocarski, 2001). Human CMV is a world widely distributed with 40 – 90% of adults carrying the virus (Cannon *et al*., 2010). The vast majority of people who are immunocompetent and acquire the virus typically have no symptoms of infection or may develop a mild disease (Soderberg, 2006) while individuals with weakened or immature immune system; such as patients who undergo organ transplantation and patients who are infected with human immunodefiency virus (HIV); may have a severe life threatening disease and the virus can be a leading cause of morbidity and mortality (Steininger, 2007). Transmission of CMV can occur throughout life by contact with a person who is excreting the virus and it can be transmitted through the placenta. blood transfusion. organ transplantation. breast milk. and sexual contact (Alder, 2007; Zeimann *et al*., 2010).

****Corresponding author:*** **Ansaf Abdulhussein Mahoor Chlaibawi,**
Senior Gynecologist in Al-Kut Hospital for Gynecology and Pediatrics, Iraq.

Human CMV infection is considered the highly prevalent congenital viral infection in the developed countries. e.g. in the United States, about 8000 infants born with deafness and neurologic manifestations each year due to vertical transmission of CMV infection from mothers acquired the primary infection during pregnancy (Stagno, 2001). It is proved that the CMV infection in utero is less severe in products of ladies with recurrent rather than primary maternal infection (Griffiths, 2000). Primary CMV infection is defined as infection in an individual who was seronegative for the virus and during primary infection. HCMV immunoglobulin M (IgM) can be detected as early as 4 weeks after initial infection and may persist up to 20 weeks. IgM antibodies are produced during primary but not recurrent infection (Landolfo *et al*., 2003). Antibodies of IgG class can be detected early and quickly at the onset of primary infection and persist for life and women who transmit the virus in uterus have high levels of total IgG characterized by low avidity and neutralizing activity (Naessens *et al*., 2005). Many CMV proteins are recognized by the humoral immune system and the envelop glycoproteins (mainly gG and gH) are the targets of virus-neutralizing antibody (Pass, 2011).

The IgG avidity means the strength of binding of IgG to antigenic epitopes synthesized by a certain protein, encoded by a gene. Whereas low avidity(less than 30%) indicates a recent acute viral infection during the antecedent three months while high avidity(more than 40%) rules out primary infection during this period. Recurrent abortion usually referred to as three or more consecutive abortions prior to 22nd gestational weeks, is one of the most frustrating and difficult areas in reproductive medicine. Studies found more frequent seropositivity and higher levels of antibodies in women with recurrent abortion than controls and suggested that abortion might have resulted from fetal infection due to reactivation of CMV infection (12).

MATERIALS AND METHODS

This is a case – control study was conducted on two groups of women (patients group and control group) in Al Kut hospital for gynecology and pediatrics for the period between February 2016 to February 2017. Each group consists of 60 women aged between 16 to 46 years selected from the genecology clinic of Al Kut hospital. The patients group consists of 60 women with a history of recurrent miscarriages while the control group consists of 60 healthy pregnant women with no history of previous abortion . Five milliliters of venous blood aspirated from each candidate in the studied groups under fully aseptic technique and divided in sterile EDTA and plain tubes for laboratory investigations which included serological tests for serum anti-human CMV IgG and IgG avidity levels using the Enzyme Linked Immuno-Sorbent Assay (ELISA) test and genetic test for detection of glycoprotein B (gB) gene after DNA extraction using Polymerase Chain Reaction (PCR) technique.

Statistical analysis: The results of this study were statistically analyzed using the Statistical Package for the Social Science (SPSS) software (version 23). using Chi-square test and a P value <0.05 was considered as statistically significant.

RESULTS AND DISCUSSION

The serum anti-HCMV IgG Ab was detected in 54 (90%) of women in the patients group while it was detected in 45(75%) of women in the control group. These results indicate that IgG Ab against HCMV is a common finding in pregnant women regardless of their obstetric history and it reflects the wide prevalence of this virus among people in the developing countries including Iraq.

Table 1. Results of serological tests and PCR (Polymerase Chain Reaction)

Test	Patients (No. = 60)		Control (No. = 60)	
	Positive No. (%)	Negative No. (%)	Positive No. (%)	Negative No. (%)
IgG	54 (90)	6 (10)	45 (75)	15 (25)
IgG avidity	18 (30)	42 (70)	3(5)	57 (95)
PCR glycoprotein B gene	15 (25)	45 (75)	0 (0)	60 (100)
P value	<0.05		<0.05	

Alwan 2011 found that the prevalence rates of HCMV IgG in non pregnant women to be 84% and 90% in pregnant women. Edmunds 2000(14) in Iran found that anti-HCMV IgG was detected in 94% of women who had a history of abortions. Mahdi 2011 reported that anti- HCMV IgG seropositivity increased in relation to abortion and infection. Ali 1992 stated that the majority of Iraqi women of child bearing age are seropositive for HCMV and they may contract the infection either prenatally or through postnatal transmission during early childhood. Jahromi 2010 stated that the poor living conditions and bad hygienic practices facilitate transmission of HCMV by many routes ; sexual and non sexual. The serum IgG avidity for anti-HCMV IgG Ab was positive in 18(30%) of women in the patients group while it was positive in 3(5%) of women in the control group. The DNA extraction for PCR glycoprotein B gene revealed a positive results in 15 (25%) of women from the patients group while non (0%) was positive in the control group. Previously. Many laboratories depended on detection of CMV IgM Ab to confirm the presence of recent (primary) infection with CMV; but later on. they discovered that IgM for CMV has a low specificity because it is also produced during viral replication so that studies on the last two decades focused on the detection of IgG avidity for CMV as a sensitive and specific tool for confirmation of primary CMV infection in pregnant women which carries the risk of vertical transmission to the fetus where the possibility of carrying the virus is estimated to be 40% in infants delivered to women who got infection by the virus after becoming pregnant ; while the possibility is estimated to be 1% in the products of women who were seropositive for CMV before getting pregnant (Coll *et al*., 2009).

Most pregnant ladies who had a primary infection with CMV have no signs and symptoms so that. it is very difficult to diagnose them clinically ; and because of the strong evidence that a higher prevalence of infection with CMV in infants delivered to ladies who got infection with the virus during current pregnancy. the diagnosis of recent infection as early as possible is considered an essential strategy for treatment to prevent the serious long term sequelae on the fetus (Revello, 2002). Abortion is a commonly occurring phenomenon during pregnancy with an estimated rate of one in each five pregnancies which implies a significant burden on the patient regarding physiological**.** psychological and economic aspects and there is an evidence based data suggested that preventable infections including CMV may constitute 15% of etiologies for early miscarriages (pregnancy loss prior to 12 weeks of gestation) and 66% of etiologies for late miscarriages (pregnancy loss between 12 to 24 weeks of gestation)**.**

These considerable data necessitated the need to seek for the provision of newly advanced screening and management schemes to lessen the impact of this health problem (Sevi, 2016)**.** Studies revealed a low avidity of IgG during a recent infection with CMV had a very high sensitivity and specificity and it can be dependable as the cornerstone to differentiate the primary infection by the virus from recurrent ones so that this test is recommended now to be used widely for confirming the diagnosis of primary infection with virus in pregnant ladies (Lazzarotto *et al*., 2008; Hazell, 2007; Munro *et al*., 2005). In women with high possibility of transmitting CMV to their fetuses. a prenatal diagnosis could be achieved between 21st and 22nd weeks of pregnancy. through examination of amniotic fluid to ascertain vertical transmission of the virus (Lazzarotto *et al*., 2008). Although CMV can transmit vertically and may affect off springs of ladies with an initial (or primary) infection where affected babies may suffer serious or fatal; women who contract CMV infection during early pregnancy may be candidates for early miscarriage and there is no established correlation between primary or reactivated infection with CMV and recurrent pregnancy loss(20).

Conclusion

- The high prevalence of anti-HCMV IgG in recurrently aborted women suggests that HCMV plays an important role in abortion.
- There is a strong correlation between IgG avidity detected by ELISA and glycoprotein B gene estimated by PCR for viral detection.
- HCMV IgG avidity is a reliable indicator for diagnosis of primary CMV infection in pregnant women.
- Further studies are recommended to clarify whether latent infection with CMV induce an indirect process of autoimmune mechanism in recurrent abortion or women with recurrent abortion have recurrent or reactivation of CMV infection.

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