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Seroprevalence of *Cytomegalovirus* among pregnant women in Islamabad, Pakistan

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Abstract
A cross-sectional study was carried out in Islamabad city to investigate the prevalence and risk factors associated with CMV infection among pregnant women. Blood samples of 172 pregnant women visiting Mother and Child Healthcare, Pakistan Institute of Medical Sciences (PIMS) Islamabad were obtained during the period from September 2013 to March 2014. In the present study, serum samples were analyzed for CMV-specific IgG and IgM antibodies by enzyme linked immunosorbent assay (ELISA). Clinical, obstetrical and socio-demographical characteristics of the women were collected by using structured questionnaires. Out of 172 pregnant women included in the study, 171 (99.4%) were CMV specific IgG positive and 30 (17.4%) were found positive for CMV-IgM antibodies. There was no significant association between CMV positivity rate with any socio-demographical and obstetrical characteristic. The CMV has a very high prevalence and taken an endemic form in Pakistan so, routine screening of CMV among pregnant women is recommended.

Keywords: *Cytomegalovirus*, Seroprevalence, ELISA, Blood transfusion, Pakistan

1. Introduction
Human *Cytomegalovirus* (HCMV) is a beta human *herpesvirus* type 5 (HHV-5). CMV is known to be one of the significant causes of morbidity and mortality among the infants and in patients with compromised immune system [1]. It has a ubiquitous distribution with 40-90% of adults carrying the virus throughout the world [2]. CMV was first isolated by Craig *et al*. in 1957 but its histopathology was described back in 1904 [3]. CMV can infect people of different age, race and socio-economic status. The clinical manifestations of CMV may include fever, bone-marrow suppression and organ invasive diseases [4]. In healthy individuals infection is mostly asymptomatic but can be life threatening in immune compromised individuals like HIV patients, fetuses and transplant recipients who are on immunosuppressive therapy [5].
HCMV reservoirs are human beings. Mode of transmission of this virus can either be horizontal via infected secretions like saliva, semen, blood etc. or vertical via genital tract, breast milk etc. The most significant mode of post-natal spread is through blood transfusion [6]. HCMV is one of the major causes of birth defects and can be transmitted from mother to fetus during gestation period. It is mainly detrimental when the mother, during the pregnancy, experiences a primary infection [7]. Congenital CMV can cause permanent physical disabilities like hearing and neurological impairment in the fetus [8].
There is no effective therapy for congenital CMV infection and pregnancy is mostly terminated whenever, fetal infection is detected [9]. At present, no vaccine is available for the prevention of CMV but phase 3 clinical trials are in process for seronegative women of the child bearing age [10]. Promising strategies have been proposed for the control of congenital CMV infection such as hand washing or hand hygiene education [11], maternal screening for the identification of women with hyperimmune globulin [10] and screening of newborns for the early diagnosis of sensory impairments [12]. However, these strategies are seldom implemented mainly due to unawareness of the magnitude of disease burden and due to concerns of the general public about their cost, effectiveness and safety [13]. The present study was designed to determine the seroprevalence of CMV among pregnant women in Pakistan.

2. Materials and Methods
2.1 Socio-demographic and clinical characteristics
Blood samples of 172 pregnant women were collected from Pakistan Institute of Medical Sciences (PIMS) Islamabad during the period of 21 January to 27 February 2013.

The study was approved by Hospital Ethics Committee and oral consent was also taken from each patient before taking their blood. Taking all aseptic precautions, about 2-3 mL blood from each woman was taken in EDTA blood vacutainers. Structured questionnaires were used to collect the clinical, obstetrical and sociodemographical characteristics of the women. After the collection of blood, the samples were transported to laboratory. The blood samples were centrifuged at 3000 rpm for 10 minutes. Sera was separated in micro-centrifuge (1.5mL) tubes and stored at -20˚C, until further analyzed [5].

2.2 Laboratory analysis

The serum samples were checked for the presence of CMV specific Immunoglobulin G and Immunoglobulin M (IgG & IgM) antibodies by enzyme linked immunosorbent assay (ELISA)[5] using EIA kits (Human® Gesellschaft fűr Biochemica und Diagnostica mbH. Germany) following manual instructions. After the termination of reaction, cut-off value was calculated. Absorbance of samples was measured at 450nm using ELISA reader (Multi-Skan) within 30 minutes. Samples with absorbance 15% or more above the cutoff were recorded as positive, those with absorbance between 15% below and 15% above the cutoff were equivocal, and all others were negative.If the sample's optical density was within 15% of the cutoff level the sample was retested and classified on the basis of latest results.

2.3 Statistical analysis

Data were analysed using Epi info version 7.1.5 program (CDC Atlanta USA). Pearson chisquare test was used to determine associations between seroprevalence and the socio-demographic variables.

3. Results

3.1 Socio-demographic and clinical characteristics

A total of 172 women were included in the study. Quarter of the women were Illiterate, 64 (37.2%) were from rural back ground, 52 (30.2%) had a history of anemia and 66 (38.4%) had a past history of miscarriage. The mean (SD) of age, parity and gestational age were 26.1 (4.4) years, 1.0 (1.2), 23.1 (9.8) weeks, respectively (Table1).

3.2 Seroprevalence of CMV

Except one all women were positive for CMV-IgG antibodies i.e. the prevalence rate was 99.04%. Only 30 (17.4%) women were found to be positive for CMV specific IgM antibodies. All the CMV-IgM positive women were also CMV-IgG positive. No significant association was found between any of the risk factor and CMV specific antibodies except parity i.e. women having one or more children were found to be more susceptible to IgM positivity than those without any child (Fig.1) The IgG test result shows that 82 (100%) pregnant women having no child and 89 (98.9%) pregnant women having one or more children tested positive while the IgM test result shows that 13 (15.9%) pregnant women having no child and 17 (18.9%) pregnant women having one or more children tested positive.

4. Discussion

To our knowledge this is the first published study regarding the epidemiology of CMV among pregnant women in Pakistan. The prevalence of CMV specific antibodies alters in different parts of the world. A review of CMV seropositivity shows that residents of developing countries have higher rates of CMV seroprevalence in comparison to those of developed countries [4]. The results of our study are in accordance with the developing countries. Seroprevalence of CMV among voluntary blood donors in Ghana and Malaysia was 93.2% and 97.6% respectively [14]. Similarly, CMV seroprevalence among haemodialysis patients in Turkey was recorded to be 99.6% [15]. However, in developed countries the CMV seroprevalence rate was significantly low [16]. European countries had also shown low CMV prevalence [17].

This difference of CMV seropositivity was perhaps due to the effect of factors, such as hygiene, breastfeeding, and safe sexual contacts, ethnic and socioeconomic factors. All the anti-CMV IgM positive samples were also positive for anti-CMV IgG antibodies so there is no primary infection found in any of the women included in the study. All the 30 active infections found were secondary or recurrent infections. Thus, it can be conferred that majority of the women in Pakistan were seropositive for CMV specific IgG antibodies before their child bearing age. A lot of debate regarding maternal age and CMV infection was going on; while many studies showed that, elder women were more susceptible to CMV infection [18], others observed the reverse [19].

The endemicity of the virus was so high (99.04%) that we couldn't associate CMV specific IgG with age or any other risk factor. As far as, anti-CMV IgM is concerned, it is relatively low (15.9%) in women having no children than those having one or more children (18.9%). This could be due to expected increase in sexual activity as a result of usual longer marriage time among women having one or more children. Extended sexual activity and the direct contact of women with the contagious secretions of seropositive children is a major risk factor for CMV infection in women with increasing parity [18]. Multiple sexual partnerships could also be the reason behind this trend but in Pakistan multiple sexual partnerships of women are limited mainly due to cultural, social and religious constraints. This could also be backed by other studies where sexually transmitted infections were higher among promiscuous people having STDs [20].

5. Conclusıon

The data in our study strongly suggests that, in Pakistan, there should be a base line test or screening of CMV specific antibodies for the women of childbearing age, including pregnant women, so that checks could be placed on the transmission of the virus. The screening of females for CMV specific IgM antibodies would be of immense help in lessening the fatal outcomes of the pregnancy and would also promote follow up of the newborns delivered by the infected mothers. The very high seropositivity rate also suggests the need for the development of a vaccine against CMV. Thus, results of our study are helpful for health planners and care providers in making future vaccination strategies and public policy.

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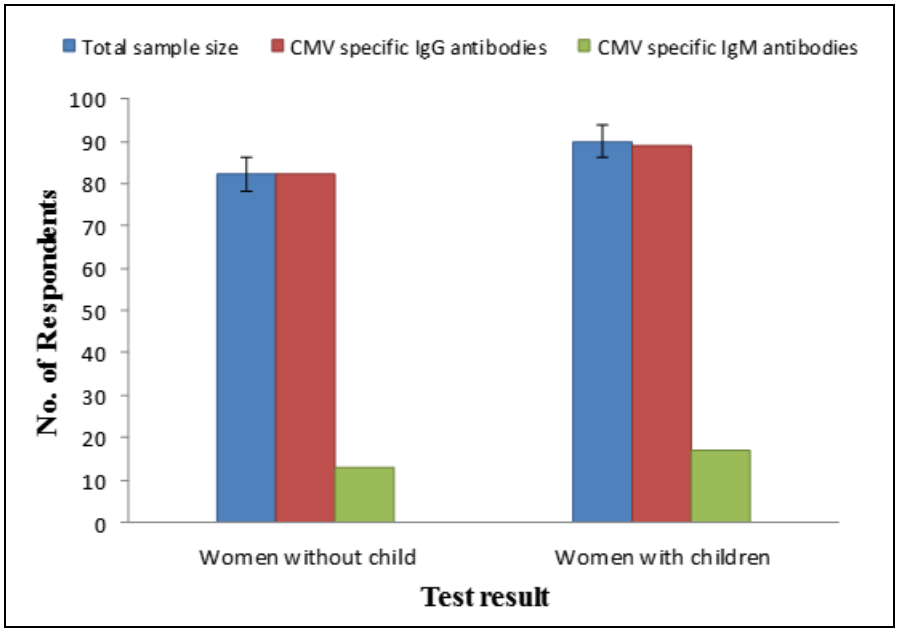

Fig 1: Distribution of CMV-specific IgG and IgM in the sera of pregnant women with or without any child (N= 172).

This fig shows the Distribution of CMV-specific IgG and IgM in the sera of the pregnant women participated in the study. Women were divided into two categories one having no child and the other having one or more children. The IgG test result shows that 82 (100%) pregnant women having no child and 89 (98.9%) pregnant women having one or more children tested positive while the IgM test result shows that 13 (15.9%) pregnant women having no child and 17 (18.9%) pregnant women having one or more children tested positive

Table 1: Clinical, Obstetrical and Socio-demographical characteristic of the pregnant women in PIMS Hospital Islamabad

Variables	Total(N=172)	CMV-IgG Positive (N=171)	CMV-IgM Positive (N=30)
Age (years)	26.1 (4.4)	26.1 (4.4)	26.5 (5.0)
Gestation age (weeks)	23.1 (9.8)	23.0 (9.7)	23.2 (10.7)
Parity	1.0 (1.2)	0.9 (1.2)	1.2 (1.5)
Education level			
sIlliterate	42 (24.4)	42 (24.5)	6 (20)
Middle	30 (17.4)	30 (17.5)	5 (16.7)
Matric	44 (25.6)	44 (25.7)	9 (30)
Intermediate	16 (9.3)	16 (9.4)	4 (13.3)
Graduation	26 (15.1)	25 (14.6)	4 (13.3)
Masters	14 (8.1)	14 (8.2)	2 (6.6)
Occupation			
House wife	163 (94.8)	162 (94.7)	28 (93.3)
Employee	9 (5.2)	9 (5.3)	2 (6.6)
Residence			
Urban	108 (62.8)	107 (62.6)	17 (56.7)
Rural	64 (37.2)	64 (37.4)	13 (43.3)
History of Miscarriage			
Yes	66 (38.4)	66 (38.6)	11 (36.7)
No	106 (61.6)	105 (61.4)	19 (63.3)
History of Anemia			
Yes	52 (30.2)	52 (30.4)	8 (26.7)
No	120 (69.8)	119 (69.6)	22 (73.3)

*Data is expressed as Mean (SD) or number (percentage)

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