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Full Length Research Paper

Serostatus of cytomegalovirus among population, Jazan region, Saudi Arabia

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A high prevalence of Cytomegalovirus (CMV) was detected to be spreading fast in the Jazan region in Saudi Arabia. CMV has the ability to remain latent within the body over a long period. CMV is a life-threatening infection to the immunocompromised persons, such as organ and bone marrow transplant recipients and cancer patients. It can cause a wide spectrum of infections in immunocompetent hosts as; hepatitis, colitis, and encephalitis. It is the most common cause of congenital infection. It can cause intrauterine growth retardation, microcephaly, retinitis and hearing defects. CMV is found throughout all geographical locations, but it is more widespread in developing countries. The main objective of the study is to assess the prevalence of CMV in Jazan region, Saudi Arabia. A total of 486 (315 non-pregnant females, 87 pregnant females and 48 males) random serum samples were collected. The samples were screened for anti-CMV IgM and IgG antibodies using the enzyme-linked immunosorbent assay (ELISA). CMV IgG antibody was positive in 64.28% of males and 78.35% in females. CMV IgM antibody was positive in 25% of males and in 3.73% of females. Prevalence of CMV in all age groups was generally high but in older age reached 100% in both male and female. Positive seroprevalence of the CMV antibody in the randomly selected representative sample was 83.3%, 75% of the seropositive female were pregnant in age at 20 - 40 year and seropositivity among pregnant women was 93.10% and non-pregnant women were 79.05%. The high prevalence of CMV is an indication that the virus is spreading fast in the Jazan region and it is a warning sign to anticipate its serious complications. Accordingly, it is recommended to set up appropriate plans and preventive measures by decision makers of health authorities to reduce the spread of the virus and to raise the public awareness of the disease among the population in the Jazan region.

Key words: Cytomegalovirus, antibodies, seroprevalence, population.

INTRODUCTION

Cytomegalovirus is a member of a family of 8 human Herpesviridae or herpesviruses. It is a common opportunistic infection (Hizel et al., 1995; Ryan, 2004). It is found throughout all geographic locations but it is more widespread in developing countries and in communities of low socioeconomic status. CMV spreads directly through body fluids such as urine, blood, breastfeeding and through the placenta of a pregnant mother ~~to~~ her baby (Cunha, 2010). After infection, CMV usually causes asymptomatic infection in a healthy person. It has an ability to remain latent within the body over long periods (Yamanishi et al., 2007). In rare cases in which CMV causes a healthy person (Immune competent) to become very sick, the infection may lead to some complications, such as; diarrhea, fever, abdominal pain, liver complication, encephalitis, pneumonitis and CMV

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mononucleosis (Mayo Clinic, 2011). The infection is life-threatening for the immunocompromised persons, such as organ and bone marrow transplant recipients and cancer patients (Cunha, 2010), and may cause visual impairment and blindness, pneumonia, diarrhea, ulcers in the digestive tract, possibly causing bleeding, hepatitis, encephalitis, behavioral changes, seizures and coma (Mayo Clinic, 2011). Also the complications arising from newborn CMV infection include; hearing loss, eye abnormalities (including central vision loss, scarring of the retina, retinitis, uveitis), mental disability, attention-deficit/hyperactivity disorder, autism, lack of coordination, small head, seizures, and death (CDC, 2010). The risk of serious complications from CMV infection is the highest among the infants born to women who had a primary CMV infection during pregnancy (Mayo Clinic, 2011). In newborns, CMV is a leading cause of congenital infection worldwide (Mussi-Pinhata and Yamamoto, 1998). In a study of seroprevalence rates of IgG to common toxoplasmosis and other infections, including; syphilis, rubella, CMV, and HSV (TORCH) agents in pregnant Saudi women using indirect enzyme-linked immunosorbent assay (ELISA) CMV total IgG antibodies were found to be 92.1% (Hani, 2002). The congenital CMV infection is one of the TORCH infections, which carry a risk of significant symptomatic disease and developmental defects in newborns Mussi-Pinhata and Yamamoto, 1998). Antibodies bind to CMV, thereby inhibiting its ability to infect new cells and marking it for removal from the body. The first type of antibody to develop in response to CMV is the IgM, which develops within a few days following primary infection. The second antibody type to respond to CMV is the IgG. This antibody develops within 1 to 2 weeks after infection and once developed, it will be detected throughout life. Consequently, IgG is a commonly used and widely accepted measure of previous CMV infection (Ljungman and Griffiths, 2002). The risks of serious complications from CMV infection among the infants born to women who had a primary CMV infection during pregnancy are high (CDC, 2010). Considering the wide range of the clinical significance of CMV and its similarity with symptoms of other diseases; in addition, there are rare data about the sound of CMV in the Jazan region and consequently we studied this deficient point to explore the prevalence of CMV in the Jazan region.

Although only 0.5 to 1% of children in the USA acquire CMV in utero, 40% of the children got the infection within the first ten years of life. Seroprevalence increases to >80% by the age of 60 (Kenneson and Cannon, 2007; Staras et al., 2006).

The percentage of seroprevalence is affected by many factors. It depends on the socioeconomic status and ethnic background. It increases among workers or teachers with proximity to infected children (Fowler et al., 2006; Ornoy and Diav-Citrin, 2006). It is well known that the risk of congenital CMV is more serious if the woman has it for the first time and it is called primary infection during pregnancy. The rate of transmitting the virus through the placenta occurs in one-third of the pregnant ladies studied with primary CMV infection (Boppana et al., 2001; Fowler, 2003), and it causes asymptomatic clinical syndrome in about one-half of these infections (17). The timing of having the primary CMV infection in relation to the start of pregnancy is very crucial in determining the risk to the fetus in utero infection (18). Women who are CMV-positive before pregnancy (seropositive) have less chances of having a baby with congenital CMV than women who have a primary CMV infection during pregnancy and the transmission rate of CMV infection through the placenta in seropositive women is 1.4% (Kenneson and Cannon, 2007),

There are very limited publications investigating congenital CMV in Saudi Arabia. For this reason, there is a high demand to investigate the prevalence of congenital CMV. A few years ago, one group investigated TORCH in Saudi pregnant women and they showed that CMV IgG antibodies were found in 92.1% of the selected pregnant women (Hani et al., 2002).

MATERIALS AND METHODS

Study population

The study was conducted in the Jazan region, Saudi Arabia. The target population were of both males and females with different age groups from different districts, who attended King Fahd Central Hospital, Jazan, KSA.

Sample collection

A total of 486 serum samples was tested for CMV seroprevalence using an enzyme-linked immunosorbent assay (ELISA). Samples were collected from the laboratory of King Fahd Central Hospital, Jazan, KSA. Sera from subjects who were known to be infected with human immunodeficiency virus, hepatitis B virus, and hepatitis C virus were excluded. Sera were identified by the sex of the subject, age, and date of collection. The samples were coded by sample number. All serum samples were stored at -20°C until use.

Study design

A cross-sectional study was used to study the prevalence of CMV infection in the Jazan region, Kingdom of Saudi Arabia. In which serum samples were randomly collected during the period of March 27th, 2015, to May 28th, 2015.

Table 1. Demographic characteristics and types of antibodies of the studied population.

Sex	Age	Presence of antibodies			Total	Percentage of positive Abs	Percentage of positive IgG Abs	Percentage of positive IgM Abs	Pregnant
		IgG	IgM	-ve					
Females	1m-9Y	33	9	12	54	77.77%	61.1%	16.66%	NA
	10-19	9	0	0	9	100%	100%	0%	**2**
	20-29	129	3	30	162	81.48%	79.62%	1.85%	**45**
	30-39	105	3	15	123	87.8	85.36%	2.44%	**35**
	40-49	21	0	9	30	70%	70%	0%	**5**
	50-59	9	0	6	15	60%	60%	0%	NA
	60-70	9	0	0	9	100%	100%	0%	NA
	Total	315	15	72	402	82.**29**%	78.35%	3.73%	NA
Males	1m-9Y	15	9	6	30	80%	50%	30%	NA
	10-19	6	0	3	9	66.7%	66.7%	0%	NA
	20-29	9	6	0	15	100%	60%	40%	NA
	30-39	9	3	0	12	100%	75%	25%	NA
	40-49	6	3	0	9	100%	66.66%	33.33%	NA
	50-59	6	0	0	6	100%	100%	0%	NA
	60-70	3	0	0	3	100%	100%	0%	NA
	Total	54	21	9	84	89.29%	64.28	25%	NA
Total		369	36	81	486	83.3%	75.9%	7.4%	87
pregnant	Females	81	0	6	87	93.1%	93.1%	0%	
Non Females	pregnant	234	15	66	315	79.05%	74.28%	4.76%	
Total		315	15	72	402	82.08%	78.35%	3.73%	

Ethical considerations

Consent was taken from all participants and personal information had been coded on the sample and maintained secretly.

Detection of antibodies (IgM, IgG)

The evaluation of anti-CM V IgM and IgG were carried out with a commercial ELISA kit (Genesis Diagnostics Ltd, UK). The ELISA is based on the principle that Cytomegalovirus IgG and IgM specific antibodies are detected by the addition of diluted sera to wells coated with purified CMV antigen. If the specific antibody is present, they will bind to the antigen. An enzyme conjugate is added to bind the antigen-antibody complex if it is present. A substrate to the enzyme is added and a hydrolytic reaction between the enzyme and its substrate resulting in a colour formation, that its intensity is proportional to the amount of specific antibody in the tested sera (Drew, 1988; Conti and Freed, 2006).

Statistical analysis

The collected data were analyzed by Statistical Package for Social Studies (SPSS) version 17.0 (SPSS Inc, Chicago, Ill, USA). The differences in proportions were evaluated by Pearson's chi-square and $p < 0.05$ considered to be statistically significant. The results are presented in table, bar and pie charts.

RESULTS

The results were presented in the following table and figures. Their characteristics are described in Table 1.

The total number of females examined in this study was 402. A 330 (82.29%) out of 402 were seropositive for CMV antibody. A 315 (78.35%) out of 402 were IgG positive while 15 (3.73%) were IgM positive. A 72 (17.91%) out of 402 were CMV negative.

Regarding the pregnant females included in the study, 81 (93.10%) out of 87 are IgG positive, whereas no IgM positive in the pregnant females. 6 (6.90%) out of 87 are negative for CMV antibody.

In non-pregnant females, 234(74.28%) out of 315 are IgG positive whereas 15 (4.76%) out of 315 are IgM positive. A 66 (20.95%) out of 315 are negative for CMV antibody.

The total number of males examined in this study was 84. A 75 (89.29%) out of 84 were seropositive for CMV antibody. 54 (64.28%) out of 84 were IgG positive while 21 (25%) were IgM positive. A 9 (10.70%) of 84 were CMV negative (Table1) (Figure1).

There is disparity in the results of IgG and IgM in female and male results. In female samples, 78.35% are IgG positive and 3.73% are IgM positive while in male

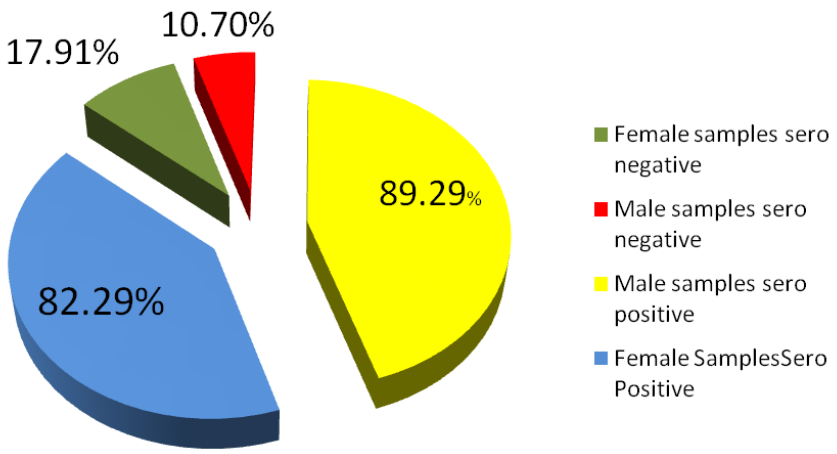

Figure 1. Percentage of positive and negative CMV antibodies among males and females.

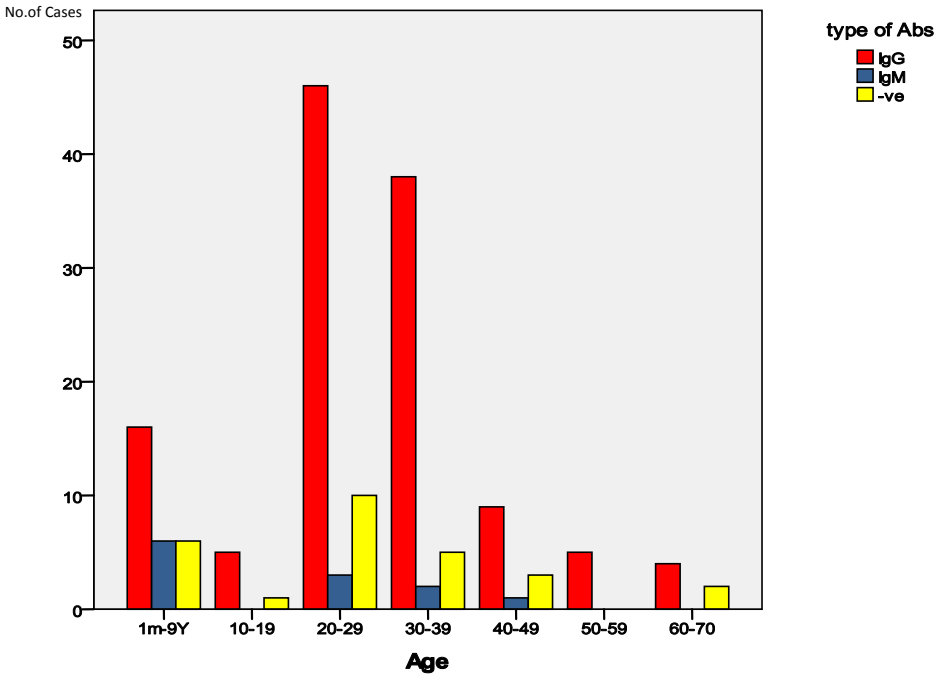

Figure 2. Prevalence of CMV by age groups from 1 month to 70 years old.

samples, 64.28% are IgG positive and 25% are IgM positive.

It was clear from the results that the age group from 20 to 39 years old was the highest prevalence of positive CMV IgG antibodies for both sexes, whereas the lowest prevalence of positive CMV IgG antibodies age group was between 50 and 70 years old people (Figure 2).

For females, the highest prevalence of CMV IgG antibodies was in the age group between 20 and 39 years old females whereas the lowest prevalence of CMV IgG antibodies was in the age group between 50 and 70 years old females (Figure 3).

For males, the highest prevalence of CMV IgG antibodies was in the first year of life and gradually decreases with increasing age of the males (Figure 4).

DISCUSSION

CMV is one of the most common viral infections. Most people develop the infection during early childhood or as

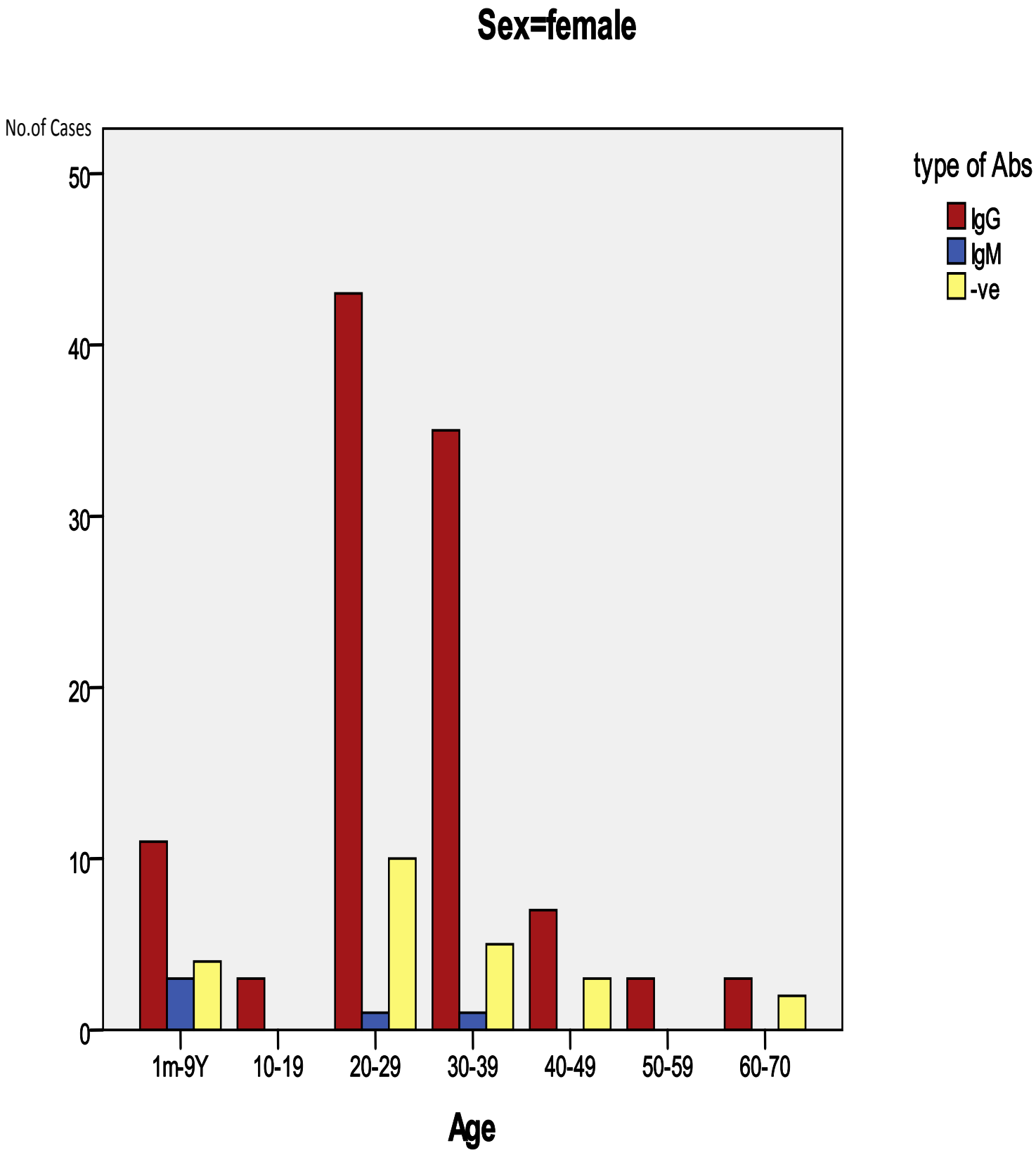

Figure 3. Prevalence of CMV among females by age groups from 1 month to 70 years old.

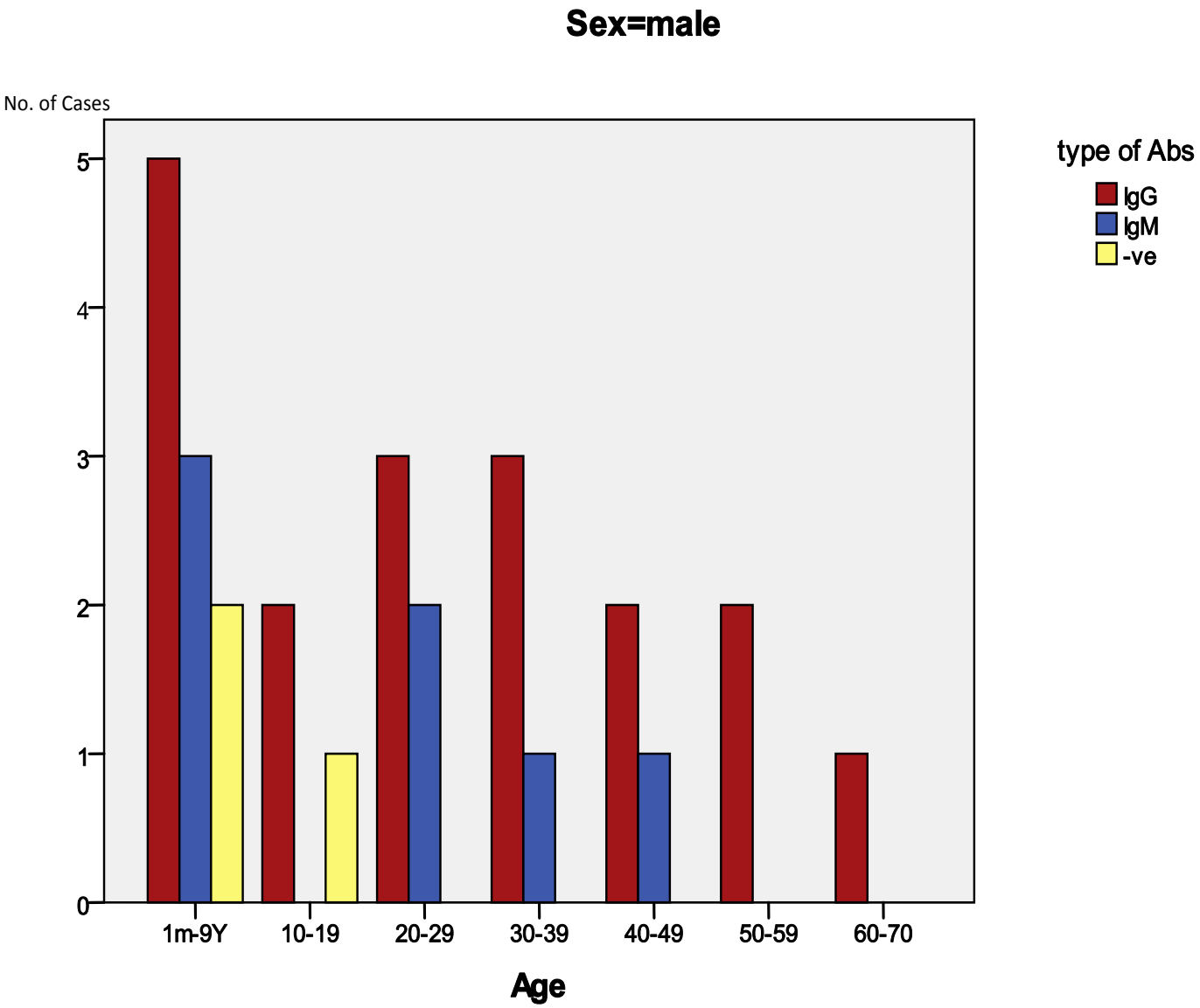

Figure 4. Prevalence of CMV among males by age groups from 1 month to 70 years old.

a teenager. It is a serious pathogenic disease especially in immunocompromised individuals and can be found all over the world. CMV has been linked to inflammatory processes, cardiovascular diseases, cognitive outcomes and Alzheimer's diseases (Söderberg-Nauclér, 2006). For these reasons, it is important to examine the prevalence of CMV at various life stages within the diverse socioeconomic and racial groups. In the Kingdom of Saudi Arabia, the Ministry of Health has plans to prevent the spread of the virus where it has made the TORCH analysis mandatory for pregnant women.

Solid phase sandwich or antibody capture ELISAs is being routinely used in CMV diagnosis. However, the best method for diagnosing CMV infection is still the virus isolation in cell cultures (http:// Derek Wong virology-online.com/viruses/CMV.htm), but, cell culture needs time for viral induced changes to appear which usually takes a few days or weeks, and requires an experienced personnel to perform. Thus, ELISA had been applied in this study.

CMV infection is usually asymptomatic in healthy humans but its reactivation occurs mostly in immune-compromised persons (Ray and Mahajan, 1997). CMV seropositivity rates are higher in females, older people, those of lower socioeconomic status and residents of

developing countries at all age groups (Cunha, 2010; Yamanishi et al., 2007).

In this study, the positive percentage of CMV IgG was 75.9%, which is more than in Australia (57%) entire population (Seale and MacIntyre, 2006), and in Canada (57%) among day care educators (Joseph and Beliveau, 2005). The prevalence of CMV antibodies during childbearing age is variable in the world. IgG prevalence is between 40% to100%; while, the IgM seroprevalence rate is between 0% to 10% (Joseph and Beliveau, 2005). This result is similar to our results wherein women IgG was 78.35% and IgM 3.73 %, which indicates that primary infection had occurred mostly in the younger age (1m- 9yrs). Another finding corresponds with the present findings, there were 97.0% and 3% of the studied participants who tested positive and negative respectively, for anti-CMV IgG antibodies and those who tested positive for anti-CMV IgM were 3.5% while 96.5% tested negative (Joseph and Beliveau, 2005). The association between the prevalence of cytomegalovirus and sex in the study indicates that the prevalence of CMV was slightly higher in men 89.28% than in females 82.29%. On the contrary, the overall seroprevalence of CMV was 87.9%; seroprevalence was statistically higher in women (94.7%) than in men (84.6%) (Gargouri et al., 2000). The reason could be due to the small number of male samples used in our work. Also, our study is compatible with the findings of the prevalence of CMV infection among foreign manpower in Jeddah,–Saudi Arabia. The investigators found the prevalence of CMV infection to be 80.7% in the studied population and the prevalence of CMV was significantly higher in females (86.8%) than in males (75.0%) (Redwan et al., 2011). They also found the seroprevalence of CMV- IgG among the studied population increased gradually with age from 50.8% in 20 to 24 year age group to 95.2% in the 50 to 54 and 55 to 60 year age groups (http:// Derek Wong virology-online.com/viruses/CMV.htm; Redwan et al., 2011). However, it is in complete concordance with our findings, that indicated that the prevalence of CMV by age groups is found with children at high levels (78.50%) and then decrease in 10-19 years after that increase with age in adult 20 - 30 years (83 %) to 50 to 60 years (100%). This can be attributed to old age, because, in old age the immune response becomes less than in youth. The seroprevalence of CMV in pregnant women in Ireland using the ELISA test also reported that only 30.4% of Irish women were CMV antibody positive compared to 89.7% of non-Irish women (Knowles, 2005). While on our findings, it was 93.10%, which is similar to the previous study among pregnant Saudi women, which, was 92.1% (9) and in Yemen was 96% (IgM 28% and IgG 68%) positive (Idris, 2010). The possible reason could be due to the differences in the living standers between the populations. In all, the total prevalence of CMV in the Jazan region was high (89.29%) which coincide with several studies globally, such as in Ghana (93.2%) (Adjei et al., 2006), India (95.0%) (Kothari et al., 2002), Turkey (97.2%) (Mutlu et al., 2008), Nigeria (92.0%) (Alao et al., 2008), Tunisia (97.14%) (Gargouri et al., 2000), and in the USA (50 – 80 %) were infected with CMV by the time they are 40 years old (CDC, 2010).

We observed a wide disparity in CMV seroprevalence in IgM and IgG between male and female but there is no apparent reason. This results consistent with many studies which showed the same disparity between male and female. Some of the disparities could be explained by differential exposure to CMV through differences in sexual behavior. Although all participants are Saudis by nationality, differential exposure to young children may also contribute to CMV seroprevalence differences by race/ethnicity. One way exposure to young children may differ by race/ethnicity is through differential birth rates (Staras et al., 2006).

Although the serological screening for TORCH agents among pregnant women and follow-up examinations until delivery are routine procedures in Saudi Arabia, but this care cannot reach to all pregnant women because of different socioeconomic status in different sites. A consistent health education to people may contribute to the control and prevention of infections.

Conclusion and recommendation

We recommend:

I.) The adoption of appropriate plans and preventive measures to be made by healthcare professionals.
ii.) Public enlightenment of the dangers of the CMV infection, its control, and preventive measures must be taken seriously by specialists, in order to protect mothers from the CMV infection and subsequent disability in their children.
iii.) Further investigation must be done in more samples to detect the virus by isolation on tissue cultures and identify the viral genome by polymerase chain reactions to assess the prevalence of CMV in the Jazan region.

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