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RESEARCH ARTICLE

STUDY THE PREVALENCE OF CYTOMEGALOVIRUS AND RUBELLA VIRUS IN ABORTED WOMEN IN THAMAR GOVERNORATE, YEMEN

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ABSTRACT

A total 453 Serum Samples from Women in Thamar with history of one or more unexplained abortion were screened for the presence IgG and IgM antibodies against Cytomegalovirus and Rubella virus by (ELISA). About 71 % (322/453) of the screened females were positive for either Cytomegalovirus or Rubella antibodies. Cytomegalovirus Ig M positive were (4.9 %) , Rubella IgM positive were (28.6 %) were positive CMV IgG (98.7 %) were positive Rubella IgG (27 %) ,and aborted women showed mixed infection with CMV IgM, with Rubella IgG. The rate of one miscarriage abortive women was 4.3 % (14/322) higher than to two and three miscarriage 1.5 % (5/322), 1.5 % (5/322), respectively.

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INTRODUCTION

Children born with some deformities or disabilities or who develop disabilities later in life has been documented in the world over and this have become a major public health concern. These disabilities may be the result of exposure to congenital infections from certain microorganisms including viral infections during pregnancy (*Jamison et al,. 2006*). Tow of such viral infections includes the Cytomegalovirus, Rubella virus. When these viruses infect immunocompetent individuals, their outcomes are usually mild and in most cases are asymptomatic or without any signs or symptoms. This has contributed to majority of infected individuals being unaware of their infection status (*Brooks et al,. 2010*). However, when such infections occur in pregnant women especially at certain stage of gestation, these viruses are able to cross the placenta and infect the fetus causing fetal damage thereby resulting in spontaneous abortion (miscarriage), stillbirth and wide range of malformations in newborns such as hearing loss, mental retardation, developmental delay, cerebral palsy, epilepsy, ocular abnormality, microcephaly, hydrocephaly, hydranencephaly (absence of the cerebral hemispheres), porencephaly (cavities in the brain), heart disease, cataract, intracranial calcification, microphthalmia, chorioretinitis, skin aplasia (failure of skin to develop).Cytomegaloviruses, also known as salivary gland viruses are widely distributed species-specific herpes viruses. Human cytomegalovirus) HCMV (formally called human herpes virus 5) (infects a majority of the world population by adulthood, but causes acute disease in only a small proportion of immunocompetent individuals. Developing areas of the world typically exhibit widespread transmission early in life, whereas more developed areas show a broader range of patterns, individuals may escape infection early in life and remain susceptible during the childbearing years. HCMV emerged as the major infectious cause of congenital hearing loss preventable by vaccination HCMV is an opportunistic pathogen associated with disease in immunocompromised hosts, predominating in the settings of genetic or acquired immunodeficiency, allograft tissue and organ transplantation and pregnancy. Disease pathogenesis requires active viral replication and focuses on different target tissues and organs in different clinical settings, particularly in circumstances where the ability to mount a cellularimmune response has been compromised. Transmission of this virus in the general population depends on direct contact with infected bodily secretion (*Brian et al,. 2010*).

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Rubella virus (RUBV) infection causes a benign disease known as rubella or German measles that can result in profound birth defects if contracted in utero. Norman Gregg, an Australian ophthalmologist, first reported the association of congenital cataracts as a consequence of gestational rubella in 1941, establishing RUBV as a major teratogen. The last major epidemic of rubella to impact the United States occurred in 1964–65, resulting in 20 000 congenital rubella syndrome (CRS) cases. Currently, _50% of countries has national rubella vaccination programs, but the majority of the world's population is not covered and rubella thus remains a worldwide challenge (*Brian et al., 2010).* The aim of the study determine the prevalence of CMV and Rubella virus antibodies infection among aborted women in Thamar Governorate.

MATERIALS AND METHODS

Study population: This study screened pregnant women consulting and childhood Hospital for the period of 8 months between 14.11.2017 to 11.6. 2018. Demographic data were obtain via questionnaire filled by members of the research group .The data included age, residence, pregnancy status, and abortion details (time and frequency if any). The subjects were ascertained into two groups; 339 suspected cases of CMV infections and 114 cases of Rubella infections.

Sample Collection

- Blood samples were collected according to standard technique.
- The immunoassays were carried on Cobas e411®; a fully automated system employing the Electro chemo luminescence (ECL) technology.
- After the daily preparation procedures, the corresponding reagents (for CMV & Rubella antibodies) were previously loaded into the system as specified by the manufacturer (Roche Diagnostics, Germany)
- About 0.5 ml of the serum was obtained into a tube and loaded into the allotted compartment of the Cobas e411®.
- Required tests were selected and preformed fully automated.

Electrochemoluminescence

Electrochemiluminescence or electro generated chemiluminescence (ECL) is a kind of luminescence produced during electrochemical reactions in solutions. In electro generated chemiluminescence, electrochemically generated intermediates undergo a highly exergonic reaction to produce an electronically excited state that then emits light upon relaxation to a lower-level state. This wavelength of the emitted photon of light corresponds to the energy gap between these two states. ECL excitation can be caused by energetic electron transfer (redox) reactions of electro generated species. Such luminescence excitation is a form of chemiluminescence where one/all reactants are produced electrochemically on the electrodes (*Forster et al., 2009; Valenti et al., 2016*). It generally uses Ruthenium complexes, especially $[Ru(Bpy)_3]^{2+}$ (which releases a photon at ~620 nm) regenerating with TPrA (Tripropylamine) in liquid phase or liquid–solid interface. It can be used as monolayer immobilized on an electrode surface (made e.g. of nafion, or special thin films made by Langmuir–Blogett technique or self-assembly technique) or as a reactant or more commonly as a tag and used in HPLC, Ru tagged antibody based immunoassays, Ru Tagged DNA probes for PCR etc., NADH or H_2O_2 generation based biosensors, oxalate and organic amine detection and many other applications and can be detected from Pico molar sensitivity to dynamic range of more than six orders of magnitude. Photon detection is done with photomultiplier tubes (PMT) or silicon photodiode or gold coated fiber-optic sensors. The importance of ECL techniques detection for bio-related applications has been well established. ECL is heavily used commercially for many clinical lab applications (*Miao, 2008).*

Anti –Rubella IgM assay: The analyzer automatically calculates the cutoff based on the measurement of RUBIGM Cal1 and RUBIGM Cal2 .The result of a sample is given either as reactive or non-reactive as well as in the form of a cutoff index .(signal sample /cutoff). Results obtained with the Elecsys Rubella IgM assay are interpreted based on lower cutoff index (COL) values as follows :

Non –reactive :<0.8 COL

Indeterminate :≥ 0.7 -<1.0 COL

Reactive :≥1.0 COL

Anti –CMV IgM assay

Results obtained with the Elecsys CMV IgM assay are interpreted as follows:

Non-reactive: < 0.7 COL
Indeterminate: 0.5 -<1.0U/ml
Reactive: ≥1.0 COL

Anti-CMV IgG assay: The analyzer automatically calculates the analytic concentration of each sample in U/ml. Results obtained with the Elecsys CMV IgG assay are interpreted as follows:

Non –reactive: < 0.5 U/ML

Indeterminate: 0.5 -<1.0U/ML

Reactive: ≥1.0 U/ML

Anti –Rubella IgG assay: The analyzer automatically calculates the analytic concentration of each sample in 1U/ML. Results obtained with the Elecsys Rubella IgG assay can be interpreted as follows:

Non –reactive :< 10 IU/ML

Reactive: >10 IU/ML

Intermediate samples' results were re-tested to be as curtained into reactive or non- reactive categories.

RESULTS

Sample study: A Total of (453) specimen were collected from female patients consulting Maternity and Childhood Hospital .322 specimens were seropositive for either of the targeted viruses tested by ELISA (Cobas 411) at AL-Dubai Medical Laboratories'. Study population: The study sample is drawn from the population of pregnant women ranged in age between 15 to 45 years old .CMV cases were 339, Rubella cases were only.

Glassware	Instruments and sets	Others
Tube	ELIZA System	Serum
		Reagent (ELIZA System)
	Centrifuge	Distal water
		Cotton
		Micro pipettes
		Disinfectant solutions(spirit, Dettol, chloroform)
		Cups
		Tips
		Syringe
		Tornika
		Gloves

Table 1. Showing overall prevalence of CMV and Rubella antibodies among screened population

Virus	Residence area	No. of samples	No. of positive	%
CMV	City	163	112	33
	Countryside	176	126	37
	Total	339	238	70
Rubella	City	50	36	32
	Countryside	64	48	42
	Total	114	84	74
Grand Total		453	322	71.1

Table 2. Showing seroprevalence of CMV and RV antibodies (IgG and IgM)

Sero-criteria		Cytomegalovirus (%)	Rubella virus (%)	Total
IgG	Positive	233 (98.7)	27 (100)	260 (98.9)
	Negative	3 (1.3)	0 (0)	3 (1.1)
	Total	236	27	263
IgM	Positive	5 (4.9)	12 (28.6)	17 (11.7)
	Negative	98 (95.1)	30 (71.4)	128 (88.3)
	Total	103	42	145

Table 3. Showing distribution of abortion incidences among pregnant females

Viruses	Residence area	No. of abortion incidences				Total (%)
		1	2	3	More	
CMV	City	5	0	1	1	7 (41.2)
	Countryside	4	2	1	3	10 (58.8)
	Total	9	2	2	4	17 (53.1)
Rubella	City	3	1	1	1	6 (40)
	Countryside	2	2	2	3	9 (60)
	Total	5	3	3	4	15 (46.9)
Grand Total		14	5	5	8	32(100)

Table 4. Showing Abortion time during pregnancy course

Viruses	Residence area	Abortion trimester (%)			Total (%)
		1st trimester	2nd trimester	3rd trimester	
CMV	City	6 (17)	6 (17)	3 (8.8)	15 (44.1)
	Countryside	13 (38.2)	4 (11.8)	2 (5.9)	19 (55.9)
	Total	19 (55.9)	10 (29.4)	5 (14.7)	34 (53.1)
Rubella	City	1 (3.3)	3 (10)	3 (10)	7 (23.3)
	Countryside	11 (36.7)	4 (13.3)	8 (26.7)	23 (76.7)
	Total	12 (40)	7 (23.3)	11 (36.7)	30 (46.9)
Grand Total		31	17	16	64(100)

Distribution of CMV and Rubella infection among females: The percentage of seropositive females reside in urban and rural areas for CMV was 70 % (238/339), while Rubella seropositive percentage was 74 % (84/114). In term of incidence rates for Cytomegalovirus and Rubella viruses, about 71% (322/453) of the screened females were positive for either Cytomegalovirus or Rubella antibodies. Moreover, females residing in countryside are the most effected group. The proportion of seropositive this group was 53% while the counterpart proportion of urban females was 47% .Table summarizes the distribution of seropositive cases among the studied population.

Distribution of Sero-diagnostic Antibodies among infected women: The sero-diagnosis revealed that 4% of the samples were living with the acute phase of the viral infection .Table 2 summarizes the employed serological tests and their results for the sample.

Abortion Rate among Infected Females: The abortion rate, that CMV or Rubella viruses may have been the cause, was 9.9 %. It is worth mentioning that in CMV-positive females, 59% of rural females had at least single abortion incidence, while only about 41% of urban pregnancies ended in abortion. On the other hand, 60% of Rubella-associated abortions were in

rural areas. Table 3 details the Abortion rates among females under study.

Abortion Period during Pregnancy: In terms of abortion time, the results showed that 48% of the seropositive females had the Incidence in the first trimester. About 66% of this group of females is rural residents and the remaining portion is urban residents. Strikingly, 55.9 % of CMV seropositive females experienced an abortion episode in the first trimester, while 36.7% of Rubella-seropositive females experienced abortion in the third trimester. Table 4 details the timing of abortion during pregnancy course.

DISCUSSION

Human cytomegalovirus (CMV) and Rubella virus are increasingly being recognized as important causes of congenital infection. Intrauterine transmission of CMV to the baby can occur irrespective of prior maternal exposure; whereas, in rubella, a previous exposure actually prevents the virus from crossing the placenta by generating protective antibodies. There are great variations in rates of seroprevalence among countries due to many factors including; sex, socioeconomic status, geographical location, and accessible healthcare services *(Cannon et al., 2010).* It became apparent that CMV infections are more common than Rubella infections especially in rural areas. This could be ascribed to the shortage of the required healthcare services. The results also showed that great proportion of pregnant women may abort for at least one time, mostly during the first trimester. This observation could be explained by reactivation of latent infections due to pregnancy-induced immune suppression (*Kourtis et al., 2014*). The seroprevalence of congenital viral infections in Yemen has not been well-documented. Consequently, findings of the present study will be compared to surveys from different countries around the globe. In terms of CMV seroprevalence, a study from UK found the rate to be 56% of screened pregnant women tested by complement fixation assay designed to detect IgG antibodies (*Peckham et al., 1983*).

On the contrary, the counterpart finding in this study is extremely high (98.7%). This variation could be attributed to the absence of vaccination programs in our society, individual attempts to seek regular check-up, reduced sensitivity of the employed diagnostic assay (*Booth et al., 1989*), and/or geographical area. Indeed, it is well-known that around 90% of the Asian population is infected with CMV and acquired antibodies in early childhood (*Schopfer et al., 1978; CDC, 2010*).In France, the prevalence of CMV-IgM in pregnant women was reported to be about 3% (Mace et al., 2004), which is in good agreement with the finding of this study (5%). However, a higher rate was documented in the USA (73%) detected by ELISA (*Stango et al., 1985*). Yet, for Rubella-IgM prevalence, a study from Kashmir *(Fomda et al., 2004*) found the rate to be 16.7%, which is quite high than we found. Moreover, an ELISA-based study from western Sudan found that rates of CMV-IgG and Rubella-IgG in pregnant women were 72% and 65% respectively. On the other hand, the rates of CMV-IgM and Rubella-IgM were only 2.5% and 3.4% (*Hamdan et al., 2011*). These findings are roughly similar to the rate of CMV antibodies reported in the present study. Strikingly, the seroprevalence of CMV-IgG reported in the present study greatly matched the rate reported in two different Turkish studies (97-98%) despite their large samples sizes (*Karabulut et al., 2011; Uyar et al., 2008*).

The ability of CMV or Rubella viruses to cause abortion is still controversial *(Sunanda et al., 1994; Yasodhara et al., 2001; and references therein*). It should be mentioned that abortion has been reported to result from multiple infections alongside the CMV or Rubella infection (*Yasodhara et al., 2001*). As a consequence, caution must be considered when ascribing the cause of abortion to either CMV or Rubella infections. Maternal infection especially during the first trimester associated with adverse neonatal outcome which encompass heart disease, cataract and deafness collectively known as congenital rubella syndrome which had a major neonatal morbidity and burden to families (*Ojala et al., 1973*). If primary rubella infection occurs during the first trimester of pregnancy, the incidence of congenital rubella is 90% and the risk decreases to 25% during the third trimester. Additionally, if contracted during the first trimester of pregnancy, it can infect the fetus leading to congenital rubella syndrome (*Singh et al., 2009*).In term of CMV-associated abortion, the rate of abortion in CMV-positive women (14.3%) was in good agreement with a study from Greece that found 16% of fetal death cases were positive for CMV (*Syridou et al., 2008*). Nonetheless, an Iraqi study reported a higher rate (34.2%) of association between Rubella-IgG and abortion (*Abdul-Karim et al.,* 2009). Furthermore, a Palestinian study detected CMV and Rubella IgM antibodies by ELISA reported the seroprevalence to be 6% and 7% respectively (*Al-Hindi et al., 2010*). The findings of first trimester abortion are supported by an Iraqi study that screened 210 pregnancies and found most of abortion cases occurred within the first three months (*Basim.M.Hussan.2013*). However, the study did not specify the residential areas of the screened women. Additionally, the same study also found the prevalence of CMV-IgG and Rubella-IgG to be 29% and 8.5% respectively, while prevalence of CMV-IgM and Rubella-IgM were 12% and 7%. These are lower than the rates found by the present study. These variations are possibly due to differences in sample size or socioeconomic standards and vaccination practice.

Conclusion

Most of seropositive women, for both CMV and Rubella, are residents of rural areas. Additionally, many women experienced abortion incidences occurred at least once during pregnancy. The percentage of seropositive females reside in urban and rural areas for CMV was 70 % (238/339), while Rubella seropositive percentage was 74 % (84/114). In term of incidence rates for Cytomegalovirus and Rubella viruses, about 71% (322/453) of the screened females were positive for either Cytomegalovirus or Rubella antibodies. Moreover, females residing in countryside are the most effected group. The proportion of seropositive this group was 53% while the counterpart proportion of urban females was 47%. The sero-diagnosis revealed that 4% of the samples were living with the acute phase of the viral infection. The abortion rate, that CMV or Rubella viruses may have been the cause, was 9.9 %. It is worth mentioning that in CMV-positive females, 59% of rural females had at least single abortion incidence, while only about 41% of urban pregnancies ended in abortion. On the other hand, 60% of Rubella-associated abortions were in rural areas**.** In terms of abortion time, the results showed that 48% of the seropositive females had the Incidence in the first trimester. About 66% of this group of females is rural residents and the remaining portion is urban residents. Strikingly, 55.9 % of CMV seropositive females experienced an abortion episode in the first trimester, while 36.7% of Rubella-seropositive females experienced abortion in the third trimester**.**

REFERENCES

Abdul-Karim, E. T., Abdul-Muhymen, N., & Al-Saadie, M. 2009. Chlamydia trachomatis and rubella antibodies in women with full-term deliveries and women with abortion in Baghdad. *Eastern Mediterranean Health Journal*, 15(6), 1407-1411.

Acosta, E. P., R. C. Brundage, J. R. King, P. J. Sanchez, S. Sood, V. Agrawal, J. Homans, R. F. Jacobs, D. Lang,J. R. Romero, J. Griffin, G. Cloud, R. Whitley, and D. W. Kimberlin. 2007. Ganciclovir population pharmacokinetics in neonates following intravenous administration of ganciclovir and oral administration of a liquid valganciclovir formulation. *Clin. Pharmacol. Ther*., 81: 867–872.

Al-Hindi, A., Al-Helou, T., & Al-Helou, Y. 2010. Seroprevalence of Toxoplasma gondii, cytomegalovirus, rubella virus and Chlamydia trachomatis among infertile women attending in vitro fertilization center, Gaza strip, Palestine. *Journal of the Egyptian Society of Parasitology*, 40(2), 451-458.

Anonymous. 1992. Mortality in patients with the acquired immunodeficiency syndrome treated with either foscarnet or ganciclovir for cytomegalovirus retinitis. Studies of Ocular Complications of AIDS Research Group, in collaboration with the AIDS Clinical Trials Group. N. Engl. J. Med. 326:213–220. (Erratum, 326: 1172.)

Balfour, H. H., Jr., B. A. Chace, J. T. Stapleton, R. L. Simmons, and D. S. Fryd. 1989. A randomized, placebocontrolled trial of oral acyclovir for the prevention of cytomegalovirus disease in recipients of renal allografts. N. Engl. J. Med. 320:1381–1387.

Best JM, Castillo-Solorzano C, Spika JS, et al. 2005. Reducing the global burden of congenital rubella syndrome: Report of the World Health Organization steering committee on research related to measles and rubella vaccines and vaccination, June 2004. International Journal of Infectious Diseases 192: 1890–1897.

Boppana, S. B., L. B. Rivera, K. B. Fowler, M. Mach, and W. J. Britt. 2001. Intrauterine transmission of cytomegalovirus to infants of women with preconceptional immunity. N. Engl. J. Med. 344:1366–1371

Boppana, S. B., L. B. Rivera, K. B. Fowler, M. Mach, and W. J. Britt. 2001. Intrauterine transmission of cytomegalovirus to infants of women with preconceptional immunity. N. Engl. J. Med. 344:1366–1371.

Boppana, S. B., R. F. Pass, and W. J. Britt. 1993. Virus specific antibody responses in mothers and their newborn infants with asymptomatic congenital cytomegalovirus infections.J. Infect. Dis. 167:72–77.

Cannon, M. J., Schmid, D. S., & Hyde, T. B. 2010. Review of cytomegalovirus seroprevalence and demographic characteristics associated with infection. Reviews in medical virology, 20(4), 202-213.

Dolan A, Cunningham C, Hector RD, et al. 2004. Genetic content of wild type human cytomegalovirus. Journal of General Virology 85: 1301–1312.

Dollard, S. C., S. D. Grosse, and D. S. Ross. 2007. New estimates of the prevalence of neurological and sensory sequelae and mortality associated with congenital cytomegalovirus infection. Rev. Med. Virol. 17:355–363.

Douglas. D. Richman Richard J. Whitley Frederick G. Hayden 2003. Clinical Virology. Third Edition., Washington 2009, USE United States of America ., Cytomegalovirus p. 475-506.,Rubellavirus p.1275-1289.

Drew, W. L., R. C. Miner, D. F. Busch, S. E. Follansbee,J. Gullett, S. G. Mehalko, S. M. Gordon, W. F. Owen,Jr., T. R. Matthews, W. C. Buhles, et al. 1991. Prevalenceof resistance in patients receiving ganciclovir for serious cytomegalovirus infection. J. Infect. Dis. 163:716–719.

Emery, V. C., C. A. Sabin, A. V. Cope, D. Gor, A. F.Hassan-Walker, and P. D. Griffiths. 2000. Applicationof viral-load kinetics to identify patients who develop cytomegalovirus disease after transplantation. Lancet 355: 2032–2036.

Fomda, B. A., Thokar, M. A., Farooq, U., & Sheikh, A. 2004. Seroprevalence of rubella in pregnant women in Kashmir. Indian journal of pathology & microbiology, 47(3), 435-437.

Forster, R.J., Bertoncello, P, & Keyes, T.E. 2009. Electrogeneratedchemiluminescence .Annual Review of Anaiytical chemistry, 2,359-383.

Fowler, K. B., S. Stagno, and R. F. Pass. 2003. Maternal immunity and prevention of congenital cytomegalovirus infection. *JAMA* 289:1008–1011.

Griffiths, P. D., and C. Baboonian. 1984. A prospective study of primary cytomegalovirus infection during pregnancy: final report. Br. J. Obstet. Gynaecol. 91:307–315.

Grundy, J. E., S. F. Lui, M. Super, N. J. Berry, P. Sweny, O. N. Fernando, J. Moorhead, and P. D. Griffiths. 1988. Symptomatic cytomegalovirus infection in seropositive kidney recipients: reinfection with donor virus rather than reactivation of recipient virus. *Lancet* ii: 132–135.

Guerra, B., G. Simonazzi, A. Banfi, T. Lazzarotto, A. Farina, M. Lanari, and N. Rizzo. 2007. Impact of diagnostic and confirmatory tests and prenatal counseling on the rate of pregnancy termination among women with positive cytomegalovirus immunoglobulin M antibody titers. Am. J. Obstet. Gynecol. 196:221–226.

Hamdan, H. Z., Abdelbagi, I. E., Nasser, N. M., & Adam, I. 2011. Seroprevalence of cytomegalovirus and rubella among pregnant women in western Sudan. Virology journal, 8(1), 217.

Kimberlin, D. W., C. Y. Lin, P. J. Sanchez, G. J. Demmler, W. Dankner, M. Shelton, R. F. Jacobs, W.Vaudry, R. F. Pass, J. M. Kiell, S. J. Soong, and R. J. Whitley. 2003. Effect of ganciclovir therapy on hearing in symptomatic congenital cytomegalovirus disease involvingthe central nervous system: a randomized, controlled trial. J. Pediatr. 143:16–25.

Kourtis, A.P., Read, J.S., Jamieson, D.J. 2014. Pregnancy and infection – New England Journal of medicine, 370(23)2211-2218.

Mace, M., Sissoeff, L., Rudent, A., & Grangeot-Keros, L. 2004. A serological testing algorithm for the diagnosis of primary CMV infection in pregnant women. Prenatal diagnosis, 24(11), 861-863.

Metselaar, H. J., P. H. Rothbarth, R. M. Brouwer, G. J. Wenting, J. Jeekel, and W. Weimar. 1989. Prevention of cytomegalovirus-related death by passive immunization. A double-blind placebo-controlled study in kidney transplant recipients treated for rejection. Transplantation 48:264–266.

Mocarski ES, Jr. 2007. Betaherpesvirus-common genes and their functions. In: Arvin AM, Mocarski ES, Moore P, et al. (eds.) Human Herpesviruses: Biology, Therapy and Immunoprophylaxis, pp 202–228. Cambridge: Cambridge University Press.

Mocarski, E. S. 1993. Cytomegalovirus biology and replication, p. 173–226. In B. Roizman, R. J. Whitley, and C. Lopez (ed.), The Human Herpesviruses. Raven Press, New York, NY.

Ojala. P, Vesikari, T, Elo. O. Rubella during pregnancy as a cause of congenital hearing loss. Am J Epidemiol. 98(5):395–401 (1973)

Peckham, C., Coleman, J., Hurley, R., Chin, K. S., Henderson, K., &Preece, P. 1983. Cytomegalovirus infection in pregnancy: preliminary findings from a prospective study. The Lancet, 321(8338), 1352-1355.

Plotkin SA. 2006. The history of rubella and rubella vaccination leading to elimination. Clinical Infectious Diseases 43(supplement 3): S164–S168.

Reef SE, Frey TK, Theall K, et al. 2002. The changing epidemiology of rubella in the 1990s: On the verge of elimination and new challenges for control and prevention. JAMA 28(7): 464–472.

Sanchez, V., E. Sztul, and W. J. Britt. 2000. Human cytomegalovirus pp28 (UL99) localizes to a cytoplasmic compartment which overlaps the endoplasmic reticulum-Golgi-intermediate compartment. J. Virol. 74: 3842–3851.

Schopfer, K. U. R. T., Lauber, E. D. G. A. R., &Krech, U. L. R. I. C. H. 1978. Congenital cytomegalovirus infection in newborn infants of mothers infected before pregnancy. Archives of disease in childhood, 53(7), 536-539.

Singh MP, Arora S, Das A, Mishra B, Ratho RK. Congenital rubella and cytomegalovirus infections in and around Chandigarh. *Indian J Pathol Microbiol.,* 2009;52:46-48

Spector, S. A., R. Merrill, D. Wolf, and W. M. Dankner. 1992. Detection of human cytomegalovirus in plasma of AIDS patients during acute visceral disease by DNA amplification. J. Clin. Microbiol. 30:2359–2365.

Stagno, S., D. W. Reynolds, A. Tsiantos, D. A. Fuccillo, W. Long, and C. A. Alford. 1975. Comparative serial virologic and serologic studies of symptomatic and subclinical congenitally and natally acquired cytomegalovirus infections. J. Infect. Dis. 132:568–577.

Stagno, S., Tinker, M. K., Elrod, C., Fuccillo, D. A., Cloud, G., &O'Beirne, A. J. (1985). Immunoglobulin M antibodies detected by enzyme-linked immunosorbent assay and radioimmunoassay in the diagnosis of cytomegalovirus infections in pregnant women and newborn infants. Journal of clinical microbiology, 21(6), 930-935.

Sunanda N, Thakar VS, Joshi SG, Saoji AM. Seroprevalence of cytomegalovirus specific IgM antibodies in pregnant women. A preliminary study. Indian J Med Microbiol 1994; 12: (1) 65-67.

Syridou, G., Spanakis, N., Konstantinidou, A., Piperaki, E. T., Kafetzis, D., Patsouris, E., &Tsakris, A. 2008. Detection of cytomegalovirus, parvovirus B19 and herpes simplex viruses in cases of intrauterine fetal death: association with pathological findings. Journal of medical virology, 80(10), 1776-1782.

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