

Epidemiological study of Cytomegalovirus (CMV) ,Toxoplasma gondii(T.g) and Rubella virus among aborted women in Misan province, Iraq

Assist Lecture: Mustafa ,A.Al-Norri

M.Sc. Microbiology Basic medical science department /Nursing college

Abstract

The aim of this study was to determine the seroprevalence of these infections and more effect in aborted women in different period of gestation. Prenatal screening for antibodies to Toxoplasma gondii (T.g) rubella virus and cytomegalovirus (CMV) infectious agents provided good information about effective treatment which decrease abortions women.

The data obtained from the records at Al -sader hospital in misan province.

The total number of sera collected and tested for serum samples was 1143 samples. antibodies to Toxoplasma gondii (T.g) rubella virus and cytomegalovirus (CMV) IgM and IgG which were caused serious congenital infections of Pregnant women were assayed by ELISA method using Abbott kits (AxSYM, Abbott, USA) according to the manufacturer's instructions. From all 1143 pregnant women, seropositivity for anti-toxoplasma IgG+IgM antibodies together was found in 389 (34.03%) while The seropositivities for anti-CMV IgG+IgM together was found in 901 (78.82%) Whilst The seropositivities for anti-rubella IgG+IgM together were found in 626 (54.76 %). from among 1143 of samples which recorded in hospital about 97 (8.48%) of women had abortion with infections . Whilst the number of abortion women without any infections of these diseases was 12 (1.04%) women .the age of aborted women which was most abortion was limited in (21 to 30). Out of the total number of women tested the number of women who had previous abortion in their disease history was 150.the number of women who live in rural area with previous miscarriage 150 women while the number Of women who live in urban area was 44.

the IgG titer was significantly higher in seropositive cases with aborted women than seropositive controls (5.18 ± 1.99 vs. 2.00 ± 0.81 , $P < 0.001$).

Key words: Aborted women, T. gondii, CMV, rubella, Missan province.

الخلاصة

لتقييم نسبة انتشار الفيروس المضخم للخلايا (cytomegalovirus)، وطفيلي داء المقوسات (*Toxoplasma gondii*) وفيروسات الحصبة الألمانية (rubella virus). أجريت دراسته استعاديّة retrospective بالتعاون مع المختبر الداخلي لمستشفى الصدر التعليمي في محافظة ميسان والتي هدفت لجمع معلومات كافية والتي من خلالها يمكن الوقاية والعلاج من هذه الأمراض ذات الأهمية الصحية الكبيرة. التحري عن وجود الاضداد المتكونة نتيجة الاصابه بطفيلي *Toxoplasma gondii* و cytomegalovirus و rubella virus. قبل الولادة يوفر معلومات قيمة عن تحديد العلاج المناسب لتقليل حالات الاجهاض عند النساء. وكان عدد عينات مصل الدم المفحوصه (١٤٣) عينه. كانت هناك علاقه سببيه بين ارتفاع مستوى الاجسام المناعيه ضد الاصابات المذكوره اعلاه وحصول اصابات شديده في النساء الحوامل ادت الى حالات الاجهاض، حيث استعمل فحص الممتز المناعي المرتبط بالانزيم (ELISA). للتحقق عن وجود الاجسام المناعيه واعتمادا على التعليمات المذكوره في الفحص. كان عدد النساء الحوامل التي اظهرت الاجسام المناعيه بنوعيهها IgG, IgM معا ضد طفيلي داء المقوسات (*Toxoplasma gondii*) ٣٨٩ (٣٤,٠٣٪). في حين كانت عدد النساء الحوامل الحامله للاجسام المناعيه بنوعيهها IgG, IgM ضد فيروس المضخم للخلايا (CMV) حوالي ٩٠١ (٧٨,٨٢٪). وكانت عدد النساء الحامله الاجسام المناعيه بنوعيهها IgG, IgM ضد فيروس الحصبة الألمانية (rubella virus) حوالي ٦٢٦ (٥٤,٧٦٪). من مجموع العينات التي اظهرت الاصابه كان عدد حالات الاجهاض عند النساء حوالي ٩٨ (٨,٤٨٪) حاله مع ظهور العدوى لهن. في حين كان عدد حالات الاجهاض عند النساء مع عدم ظهور العدوى لهن حوالي ١٢ (١,٠٤٪). وكانت اعمار النساء اللواتي اجهضن بين عمر (٢١ الى ٣٠) حسب الجدول (٢). من مجموع العينات الكلي للنساء المفحوصه كان عدد النساء اللواتي تعرضن لحالات اجهاض سابقه حوالي (١٥٠) حاله. من هذا العدد (١٥٠) كانت عدد النساء من المناطق الريفيه (١٠٦) اللاتي تعرضن الى عملية اجهاض سابقه في حين كان عدد النساء اللاتي يعشن في المدينه واللاتي تعرضن الى حالة اجهاض سابقه حوالي (٤٤) حاله.

INTRODUCTION

The first trimester of pregnancy is an important period often replete with complications like bleeding and pain, leading to severe anxiety in the mother(1). Pregnancy loss has been attributed to several factors involved in human

reproduction. Genetic and uterine abnormalities, endocrine and immunological dysfunctions, infectious agents, environmental pollutants, psychogenetic factors and endometriosis are most important causes of spontaneous abortion(2). Spontaneous abortion is a new issue in periods of its social and economic impact (3). Today majority of women decide to conceive in their thirties or forties because they are career-oriented during the age of maximum fecundity. After the age of 30-35 years, potential fertility descend and the rate of spontaneous abortion increases (4). The pregnant teenagers are at greater risk and require additional care. Stress, pollutants, smoking etc (4,5,6). also increase the risk of miscarriage. Some maternal infections, especially during the early gestation, can result in fetal loss or malformations because the ability of the fetus to resist infectious organisms is limited and the fetal immune system is unable to prevent the dissemination of infectious organisms to various tissues (6). Infections with various pathogens cause miscarriage or may lead to congenital anomalies in the fetus while others are associated with neonatal infectious morbidity(6). most of the information obtained about abortions cases in women in misan province was showing that one of the causative agent was Toxoplasmosis, Rubella and (CMV) Cytomegalovirus are reported to cause damage to the fetus if acquired during pregnancy (1,7). These maternal infections with adverse outcome are initially unapparent or asymptomatic and are thus difficult to diagnose on clinical grounds(6,7). widespread population screening may contribute to the prevention of congenital infections Because of the high seropositivity of T.gondii, rubella and CMV in pregnant women(8,9,10) , protective methods should be taken. The aim of this study was to determine the seroprevalence of T. gondii, rubella and CMV infections through antenatal screening in misan province.

Materials and methods

The study protocol was approved by local research ethics committees and informed consent was obtained from all tested women between November 2014

to October 2015, a total of 1143 serum samples were tested for antibodies against *T. gondii*, rubella and CMV. The records of pregnant women in their first trimester who had come for their first antenatal visit to the hospital were included in the study. Anti-Toxoplasma, anti-rubella and anti-CMV IgM and IgG antibodies were assayed by an enzyme linked immunosorbent assay method using Abbott kits (AxSYM, Abbott, USA) according to the manufacturer's instructions. Anti-Toxoplasma IgM antibody titers greater than a 0.490 index and anti-Toxoplasma IgG antibody titers greater than 3.0 IU/ml were considered positive. Anti-rubella IgM antibody titers greater than 0.600 and anti-rubella IgG antibody titres greater than 10.0 IU/ml were considered positive. Anti-CMV IgM antibody titers greater than 0.500 and anti-CMV IgG antibody titres than 15.0 IU/ml were considered positive. Statistical Package for Social Sciences (SPSS, ver 10.0) software was used to calculate descriptive statistics.

The results

The mean age of the tested women according to gestation period was 28.5 years, (min 14 years, max 47 years). Of 1143 pregnant women, positivity for anti-Toxoplasma IgM+IgG together antibodies was 389 (34.03%). The seropositivities of the pregnant women for anti-rubella IgM+IgG, antibodies together was 626 (54.77%). The seropositivities of the pregnant women for anti-CMV IgM+ IgG antibodies were 901 (78.82%). The total number of abortions women was 97 (8.49%). Spontaneous abortions women without any infections were 12 (1.05%) from all these infections women. The IgM+IgG levels observed against these pathogens are represented in table (1). The incidence of miscarriages in various age groups was as 14.43% in 14 - 20 years group (teenagers); 43.3% in 21 – 30 years group; 30.9% in 31 - 40 years and 11.34% in the 41-50 years group. The categories of abortions women age with infections are represented in table (2). The number of aborted women without any Toxoplasma, CMV and rubella infections was 12 women compared

with 1143 total number of infection women and comparison with 97 abortion women which were caused by infections .as well as there were women had previous miscarriages which have 150 from total samples as illustrate on table(1).the table (4) showed about 106 of rural women which had aborted whatever about (44) of urban women were aborted.

Table 1. Seropositivity of anti-Toxoplasma, anti-rubella and anti-CMV antibodies in pregnant women.

NO.anti-(IgM +IgG)	NO. seropositive	Percentage %	NO. seronegative	Percentage %
Anti-Toxoplasma Seropositive IgM +IgG	389	34.03%	754	65.97%
Anti-CMV Seropositive IgM +IgG	901	78.82%	242	21.17%
Anti- Rubella Seropositive IgM +IgG	626	54.76%	517	45.23%
Previous miscarriages with T.gondii	75	50%	75	50%
previous miscarriages with CMV	120	80%	30	20%
previous miscarriages with Rubv	97	64.67%	53	35.33%

Table 2.The age of aborted women (year)

Categories of aborted women age	No. aborted women	percentage%
14-20	14	14.43%
21-30	42	43.30%
31-40	30	30.90%
41-50	11	11.34%

total	97	100%
--------------	-----------	-------------

Table 3. Illustrate total number of infections women with threat abortion and complete abortion.

Total number of infection samples	1143
Total number of Threat Abortion with infection	1046
Total number of complete Abortion with infection	97
Total number of complete Abortion without infection	12
Total number of women previous miscarriages	150
Total number of rural women previous miscarriages	106
Total number of urban women previous miscarriages	44

Table 4. Illustrate number and percentage of rural aborted women and urban aborted women with infections.

NO. of women previous iscarriages	NO. SAMPL ES	NO. Seropositive TOX	percenta ge %	NO. Seropositive CMV	percent age %	NO. Seropositive RUB	percent age %
urban women previous miscarriages	44	10	22.7 %	20	45.4%	14	31.9%
rural women previous miscarriages	106	13	26.84%	55	51.88%	38	35.87%

Discussion

Toxoplasma, Rubella and CMV are known to cause infection in uterus and are often responsible for abortion, still birth, premature delivery and congenital malformation(3,6,8)

In this study, the determined anti-Toxoplasma IgM+IgG seropositivities in pregnant women was 34.03% . The seroprevalence of *T. gondii* infections ranges between 7.7 and 76.7% in different countries: United Kingdom, 9.1-7.7%; France, Indian, 45% ; Iran, 51.8%; Sweden, 14-25.7% (14,15). The National Health and Nutrition Examination Survey (NHANES), found that the prevalence of toxoplasmosis has declined in the past decade. This reduction prevalence was likely related to a reduction of *T. gondii* in cysts in meat through the efforts of meat producers, education of physicians and the public and other food-related factors(17), as at table (1). (389) cases of *T. gondii* infections. The high seroprevalence of *T. gondii* in Misan is related to the presence of a great number of stray cats in both rural and urban areas of the country. The Iraq diet, which consists of large amounts of raw, wild vegetables, salads and undercooked meats that could easily be contaminated with parasite. Also why number of abortion rural women was high from urban women in table (3), which were rural women (106) and urban women (44). In this study can see the seropositivities of the pregnant women for anti-rubella IgG+IgM were 54.76%. Seropositivities of rubella were reported to be 87 % in USA(14); 93.3-94% in Saudi Arabia,(18). The epidemiology of rubella infection has been modified ever since the introduction of the rubella vaccination. Danovaro-Holliday et al (18) have reported that childhood immunization strategies alone may not be enough, and that workplace vaccination of high-risk adults needs to be considered. There are still unvaccinated women in childbearing age. Did not collect information on rubella vaccination and so the effect of rubella vaccination on rubella seropositivity could not be determined. This reason it can explain why number of abortion rural women higher than *T. gondii* as in table (3), which were rural aborted women(13) with percentage (26.84%) whilst urban aborted women were (10) with (22.7%) percentage.

In this study, the seropositivities of the pregnant women for anti-CMV both IgG+IgM were 78.82%. Seropositivities of CMV were reported in pregnant women as 39%-94.7% in USA(18) and 100% in Thailand.(19). Although, there is a high prevalence of CMV all over the world, there is no available vaccine for CMV up to the moment this is explain why high rate of infection than other infection with T.gondii and Rub virus also give us good imagination to explain raising incidence on abortion women as in table (3) On the basis of these results, we estimate that each year in the iraq ~800,000 from of childbearing age experience a primary CMV infection. given the number of women at risk and the significance of congenital disease, development of programs for the prevention of CMV infection, such as vaccination or education, is of considerable public health importance(9,10,13).most infections that are high efficacy on rural aborted women

Than urban aborted women as in table (4),Which were for toxoplasmosis (26.84%) ,CMV (51.88%) rubella virus (35.87%) whilst urban women were for toxoplasmosis (22.7%),CMV (45.4%) and rubella virus (31.9%) ,resulting to illiterate women and women with high parity were at higher risk for rubella virus and cytomegalovirus infections(19,20).High parity and illiteracy were observed before as risk factors for increased susceptibility to acquisition Toxoplasma gondii infection, rubella virus and cytomegalovirus infections, perhaps through the direct contact with contagious secretions from their own children and poor hygiene practiced by these women (15,18,19,22).Likewise, low socio-economic status has been found as a strong risk factor for acquisition these infections also presence of a great number of stray cats in rural regions (17 ,23,24,25).

Conclusion

Widespread population screening may contribute to the prevention of congenital infections Because of the high seropositivity of T. gondii, rubella

and CMV in pregnant women . protective methods should be taken. Primary infections with *T. gondii*, rubella virus and cytomegalovirus (CMV) in pregnant women can lead to serious complications that are initially unapparent or asymptomatic these organisms cause only asymptomatic or mild infection in the mother but can cause much more serious consequences in the fetus. A very important component of prenatal care is the to recognition of these infections in the mother and fetus. Identification of susceptible women is essential so that early treatment can be offered.

References

- 1-Florence RG, Marie FG, Thierry A, Josette R, Claudine TS, Jean DC (1999). Value of prenatal diagnosis and early postnatal diagnosis of congenital toxoplasmosis. Retrospective study of 110 cases. *J Clin. Microbiol.* 9: 2893-2898.
- 2-Rock JA, Zacur HA (1983). The clinical management of repeated early pregnancy wastage. *Fertil. Steril.* 39:123-140.
3. Levine ND. Sarcocystis.(1961). *Toxoplasma and related protozoa.* Vol. 12. Minneapolis: Burgess Publishing Company;. *Protozoan Parasites of domestic animals and of man*; pp. 317–46.
- 4-Lopez A, Dietz VJ, Wilson M et al.(2004). Preventing congenital toxoplasmosis, *Morb Mort Week Report*;49:59-68.
5. Dubey JP, Lindsay DS, Speer CA. (1998). Structures of *Toxoplasma gondii* tachyzoites, bradyzoites, and sporozoites and biology and development of tissue cysts. *Clin Microbiol Rev.* ;11:267–99.
- 6 . CA Alford, S Stagno, RF Pass, WJ Britt. (1998). Congenital and perinatal cytomegalovirus infections. *Rev Infect Dis.* 12(7):745–753
doi:10.1093/clinids/12.Supplement_7.S745
7. MJ Cannon, DS Schmid, TB Hyde. (2014). Review of cytomegalovirus seroprevalence and demographic characteristics associated with infection. *Rev Med Virol.* 20(4):202–13 doi:10.1002/rmv.655
- 8-P Ojala, T Vesikari, O Elo. (1973).Rubella during pregnancy as a cause of congenital hearing loss. *Am J Epidemiol .* 98(5):395–401
9. Peckham CS, Chin KS, Coleman JC. (1983).Henderson K, Hurley R, Preece PM. Cytomegalovirus infection in pregnancy: preliminary findings from a prospective study. *Lancet*;8338:1352e5.
10. Peckham CS. (1999). Cytomegalovirus infection: congenital and neonatal disease. *Scand J Infect Dis Suppl*;80:82e7.

11. Ahlfors K, Ivarsson SA, Johnsson T. (1982). Svanberg L. Primary and secondary maternal cytomegalovirus infections and their relation to congenital infection. Analysis of maternal sera. *Acta Paediatr Scand*;71:109e13.
12. Stagno S, Pass RF, Dworsky ME. (1989). Congenital cytomegalovirus infection, the relative importance of primary and recurrent maternal infection. *N Engl J Med*, 306:945e9.
13. Boppana SB, Fowler KB, Britt WJ, Stagno S.(1999). Pass RF. Symptomatic congenital cytomegalovirus infection in infants born to mothers with preexisting immunity to cytomegalovirus. *Pediatrics*;104:55e60.
14. Sugita K, Ando M, Makino M, Takanashi J, Fujimoto N, Niimi H.(1991). Magnetic resonance imaging of the brain in congenital rubella virus and cytomegalovirus infections. *Neuroradiology*; 33:239e42.
15. Jeannel D, Niel G, Costagliola D, Danis M, Traore BM, Gentilini M. (1988). Epidemiology of toxoplasmosis among pregnant women in the Paris area, *Int J Epidemiol*; 17:595-602.
- 16-Jenum PA, Stray-Pedersen B, Malby B et al. (1998) Incidence of *Toxoplasma gondii* infection in 35 940 pregnant women in Norway and pregnancy outcome for infected women, *J Clin Microbiol*;36:2900-6.
- 17- Jones JL, Kruszon-Moran D, Sanders-Lewis K, Wilson M.(1999-2004). *Toxoplasma gondii* infection in the United States, decline from the prior decade, *Am J Trop Med Hyg* 2007;77:405-10.
- 18-Danovaro-Holliday MC, LeBaron CW, Allensworth C et al.(2011). Large rubella outbreak with spread from the Work place to the community, *JAMA*;284:2733-9.
- 19-Wong A, Tarik KH, Tee CS, Yeo GSH. Seroprevalence of cytomegalovirus, *Toxoplasma* and parvovirus in pregnancy. *Singapore Med J* 2000;41:151-5.
- 20-. Al-Nakib W , Ibrahim ME , Hathout H , Moussa MA , Deverajan LV , Thorburn H , Yousof AM , 1983 . Seroepidemiology of viral and toxoplasma infections during pregnancy among Arab women of child-bearing age in Kuwait . *Int J Epidemiol* 12: 220 – 223 .
- 21- el-Moukdad AR , 2002 . Serological studies on prevalence of *Toxoplasma gondii* in Awassi sheep in Syria [German]. *Berl Munch Tierarztl Wochenschr* 115: 186 – 188 .
- 22- Bonyadian M , Hematzade F , Manuchehri K , 2007. Seroprevalence of antibodies to *Toxoplasma gondii* in sheep in the center of Iran . *Pak J Biol Sci* 10: 3228 – 3230 .
- 23- Sanad MM, I-Ghabban AJ , 2007 . Serological survey on toxoplasmosis among slaughtered sheep and goats in Tabouk, Saudi Arabia. *J Egypt Soc Parasitol* 37: 329 – 340 .

24- Sharif M , Gholami S , Ziaei H , Daryani A , Laktarashi B , Ziapour SP , Rafiei A ,

Vahedi M , 2007 . Seroprevalence of *Toxoplasma gondii* in cattle, sheep and goats slaughtered for food in Mazandaran province, Iran, during 2005 . *Vet J* 174: 422 – 424 .

25- Zia-Ali N , Fazaeli A , Khoramizadeh M , Ajzenberg D , Dardé M , Keshavarz-Valian H , 2007 . Isolation and molecular characteristics of *Toxoplasma gondii* strains from different hosts in Iran . *Parasitol Res* 101: 111 – 115 .