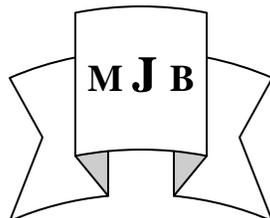


A Study of the Some Causes Associated with Single and Recurrent Spontaneous Abortion in Al-Hindia City

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Abstract

A total of 87 consecutive women (mean age 26 years; SD 6 years) had history of abortion (single or recurrent) ,were undergo details of their previous reproductive history and complete investigations in order to detect an underlying cause of their pregnancy losses. All women were asked about if they complained from infertility (primary or secondary) or had history of diabetes mellitus (type 1 or type 2).

Fasting blood sugar (FBS) was performed looking for any hidden cases of diabetes mellitus, while abdominal ultrasonography was done to determine if there is any abnormalities in there genital tract ,also ELISA technique was used looking for anti-Toxoplasma and anti-cytomegalovirus antibodies in the sera of those women who visited the gynecological department in AL-Hindia General hospital during the period from November / 2009 to May / 2010.

We found that 27(31%) of those women had anti-Toxoplasma antibodies and 15(17.2%) had anti-CMV antibodies in their sera; 11 (12.6%) women had anomalies in their genital tract (uterine anomalies and cervical incompetence), 10 (11.4%) were infertile (primary or secondary); and 6(6.8%) were diabetic. The rest of the studying group (18) were normal.

دراسة لبعض الاسباب المتعلقة بحدوث الاسقاطات التلقائية المفردة والمتكررة في قضاء الهندية

الخلاصة

اجريت هذه الدراسة على ٨٧ امرأة (متوسط العمر ٢٦ سنة) كانت قد عانت من الإجهاضات (المفردة أو المتكررة)، حيث خضعت جميع هؤلاء النسوة الى مجموعة من التحليلات المخبرية وسئل جميع النساء حول ما إذا اشتكوا من العقم (الابتدائي أو الثانوي) أو كانت قد عانت من مرض السكري (نوع ١ أو نوع ٢)، من أجل الكشف عن الاسباب الكامنة وراء حالات خسائر الحمل. ومن ضمن التحليلات المخبرية التي اجريت هو قياس نسبة السكر في الدم في حالة الصيام (FBS) للبحث عن حالات مخفية من داء السكري، وكذلك اجراء فحص السونار للبطن (abdominal ultrasonography) لتحديد ما إذا كان هناك أي خلل في الجهاز التناسلي، في حين استخدمت تقنية فحص ارتباط الخميرة للادمصاص المناعي (ELIZA) لتخمين وجود الاجسام المضادة للمقوسات الكونديه (Toxoplasma gondii) و للفايروس المضخم للخلايا (Cytomegalovirus) لدى هؤلاء النساء الذين زاروا قسم أمراض النساء في المستشفى الهندية العام خلال الفترة من نوفمبر/٢٠٠٩ إلى أيار/مايو ٢٠١٠.

وكانت نتائج هذه الدراسة اننا وجدنا أن ٢٧ (٣١٪) من هؤلاء النساء تعرضن الأجسام المضادة التوكسوبلازما و ١٥ (١٧,٢٪) للأجسام المضادة للفايروس المضخم للخلايا (CMV) ؛ ١١ (١٢,٦٪) من النساء كان لديهن تشوهات في المسالك التناسلية (شذوذ الرحم و عدم الكفاءة عنق الرحم) وكانت ١٠ (١١,٤٪) يعانون من العقم (الابتدائي أو الثانوي)، و ٦ (٦,٨٪) من مرض السكري. وكانت بقية مجموعة دراسة (١٨) طبيعية.

Introduction

Abstortion is defined as termination of pregnancy resulting in expulsion of an immature,

nonviable fetus. A fetus of less than twenty week's gestation or a fetus weighing less than 500 gm is considered an abortus [1].

Recurrent abortion or recurrent pregnancy loss (RPL) (medically termed habitual abortion) is defined as three or more spontaneous abortions [2]. However, some authors suggested that even two spontaneous pregnancy losses constitute recurrent miscarriage and deserve evaluation [3].

Miscarriages can occur for many reasons, not all of which can be identified. Some of these causes include infections (including listeriosis, toxoplasmosis, and certain viral infections such as rubella, herpes simplex, measles, cytomegalovirus and coxsackie virus), genetic causes, hormonal or reproductive tract abnormalities, and tissue rejection [4].

According to Stirrat (1990) [5]; Bricker and Farquharson (2002) [6]; about 50% of cases have no cause or association found and are classified as idiopathic.

Between 15% and 40% of women of reproductive age have antibody (IgG) to *Toxoplasma gondii* and therefore are immune to future infection. [7]. The risk of transmission to the fetus is 15 % in the first trimester, 25 % in the second trimester and 65 % in the third trimester [8,9].

Regarding CMV infections about half of pregnant women have had CMV in the past and most do not need to be concerned about it during pregnancy. However, an infected woman can pass the virus on to her fetus during pregnancy and breastfeeding [10].

Uterine malformation is considered to cause about 15% of recurrent miscarriages [11]. These anatomic abnormalities can be congenital, or acquired, such as intrauterine adhesions or leiomyoma [12]. In the second trimester a weak cervix can become a recurrent problem.

Such cervical incompetence leads to premature pregnancy loss resulting in miscarriages or preterm deliveries [11].

Pre-pregnancy evaluation and counseling of women with pregestational diabetes mellitus (type 1 or type 2) is critical to minimize the risk to the fetus and mother. Women who are in poor glycemic control during the period of fetal organogenesis, which is nearly complete by seven weeks postconception, have a high incidence of spontaneous abortion and fetuses with congenital anomalies [13].

Aims of the Study

This study carried out to evaluate the following:

1. Detection the incidence of *Toxoplasma gondii* parasite and Cytomegalovirus (CMV) antibodies in the sera of women who suffered from abortion in Al-Hindia city.
2. Measurement level of fasting blood sugar (FBS) in order to determine whether the patients had diabetes mellitus which considered as one of the most important cause of abortion.
3. To evaluate the association between reproductive tract anomalies, cervical incompetence and abortion.
4. To study the association between infertility and abortion by interpreting the patients history.

Patient and Methods

In this study eighty seven (87) women who had history of single or recurrent abortions were included; 29 women had single abortion and 58 with recurrent abortion; they were divided into three age groups as follows:

Age group 1: ≥ 15 to 25 years,

Age group 2: 26 to 35 years

Age group 3: 36 to 45 years.

Twenty healthy pregnant women were selected randomly as a control group without any history of abortion. They were almost similar to patients in age ranges, occupation, social and economic status and their residence.

All of these(patients and control) were undergo the following investigations

1. Fasting blood sugar (FBS) using Enzymatic colorimetric method.
2. Anti-Toxoplasma antibodies (IgM and IgG) were detected by using ELISA technique.
3. Anti-Cytomegalovirus antibodies (IgM and IgG) were detected by using ELISA technique.

The data were analyzed by using computerized SPSS (Statistical Package of Social Science) program; the analysis of variance (ANOVA) and χ^2 test were used to determine the differences between the three groups and within groups. A p value < 0.05 is considered

to be statistically significant (Daniel, 1999).

Results

Toxoplasma infection and it's relation to abortion

Out of 87 cases, 27 (31%) sera were positive for anti-Toxoplasma antibodies, 7 (25.9%) cases were with single abortion and 20 (74%) cases were with recurrent abortions, and the highest number of the positive cases (18) was related to the age group ≥ 15 to 25 years. Also we observed that the higher incidence of abortion was in the first trimester (62.9%) and the most common type of anti-Toxoplasma antibody was the IgM antibody which was found in 22 (81.4%) cases, while the IgG type was present in 5(18.5%) patients. There were significant relationship ($p < 0.05$) between Toxoplasma infection and abortion.

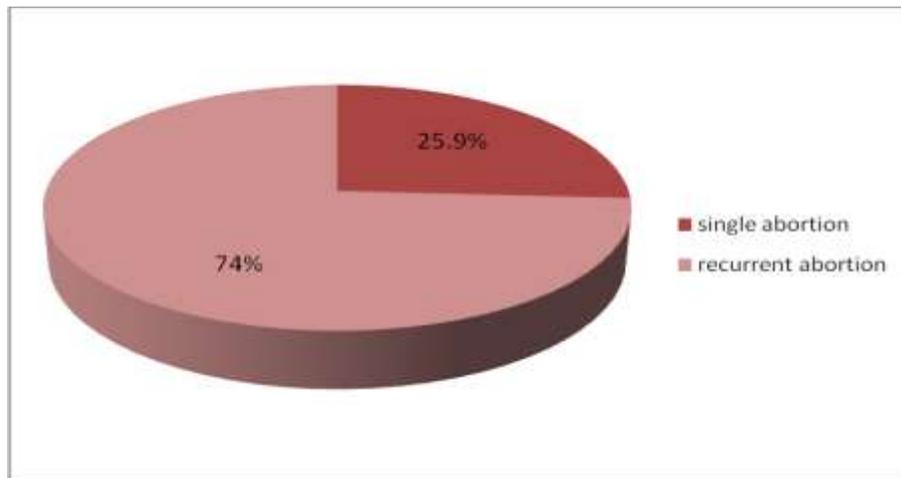


Figure 1 The distribution of the toxoplasma infection in patients with single and recurrent abortion.

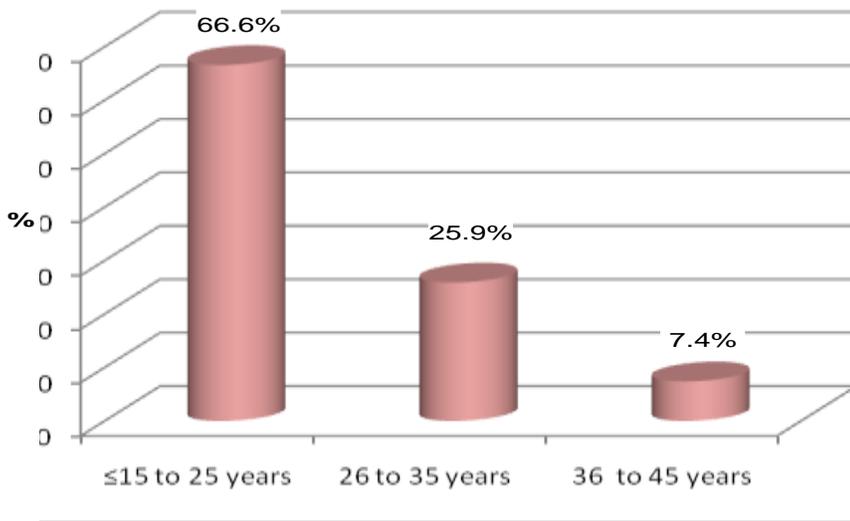


Figure 2 The distribution of Toxoplasma gondii infection according to the ages of the patients.

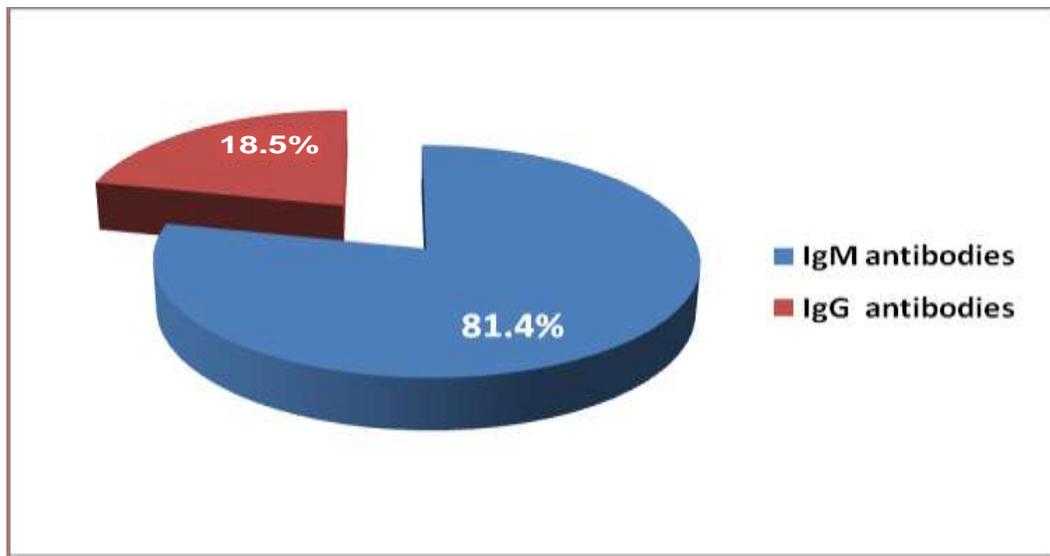


Figure 3 The distribution of Toxoplasma IgM and IgG antibodies in seropositive cases

Cytomegalovirus (CMV) infection and it's relation to abortion

Regarding CMV infections, it had been detected that 15 (17.2%) sera out of 87 were positive for CMV antibodies, 12 (80%) out of 15 seropositive cases developed recurrent abortions, while in the single abortion the number of seropositive cases was

3(20%) cases. Also it found that higher incidence of CMV infections was related to the age group ≤15 to 25 years which was 9.1%, also we found that 66.6% of these cases develop first trimester abortion and the most common type of anti CMV antibodies in seropositive cases was the IgG antibody which was found in 9 out of 15 seropositive cases.

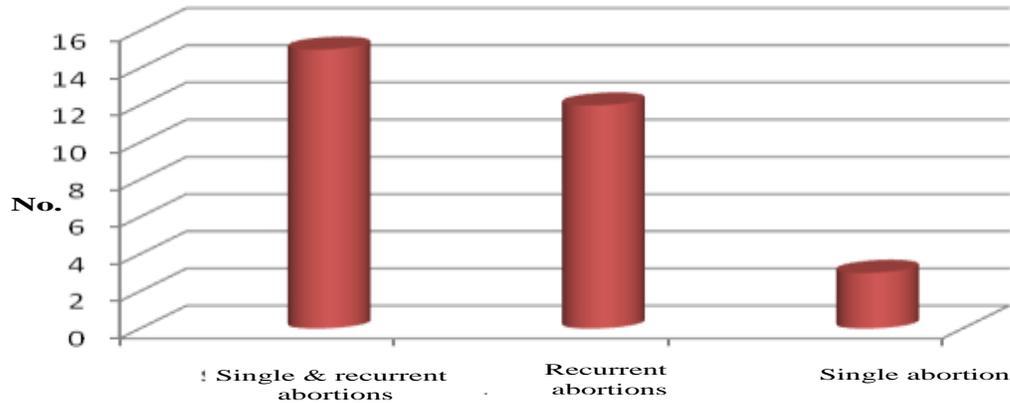


Figure 4 The distribution of CMV infection in patients with single, recurrent and single and recurrent abortions.

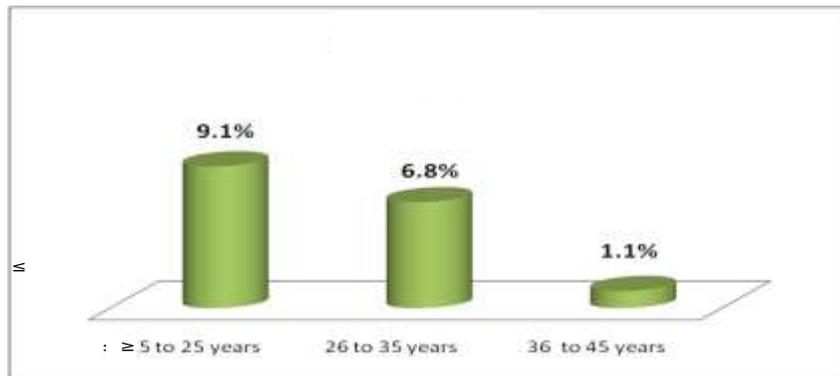


Figure 5 The distribution of CMV infection according to the ages of the patients.

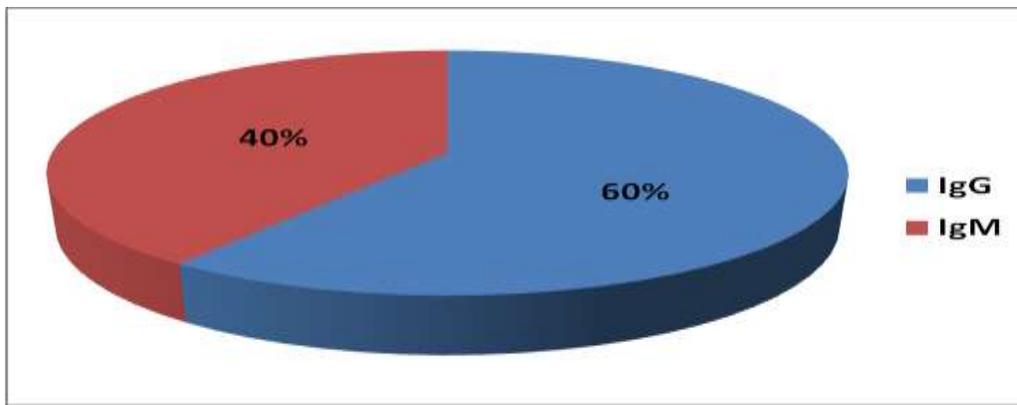


Figure 6 The distribution of anti-CMV (IgM and IgG) antibodies in seropositive cases of abortion.

Abortion and infertility

According to the history of the patients, there were 5 patients with single and recurrent abortions had

primary infertility which constitute 5.7%, 1 of them had single abortion and 4 had recurrent abortions; and also there were 5 patients with single and recurrent

abortions had secondary infertility which constitute 5.7%, 2 of them had single abortion and 3 of them had recurrent abortions. There is significant relationship ($p < 0.05$) between Abortion and infertility

Abortion and diabetes mellitus

Six out of eighty seven aborted women suffered from gestational hyperglycemia, 5(83.3 %) of them related to the recurrent abortion group and 1 (16.6 %) to the single abortion group, and those patients were develop abortion in the first and second trimester of the pregnancy.

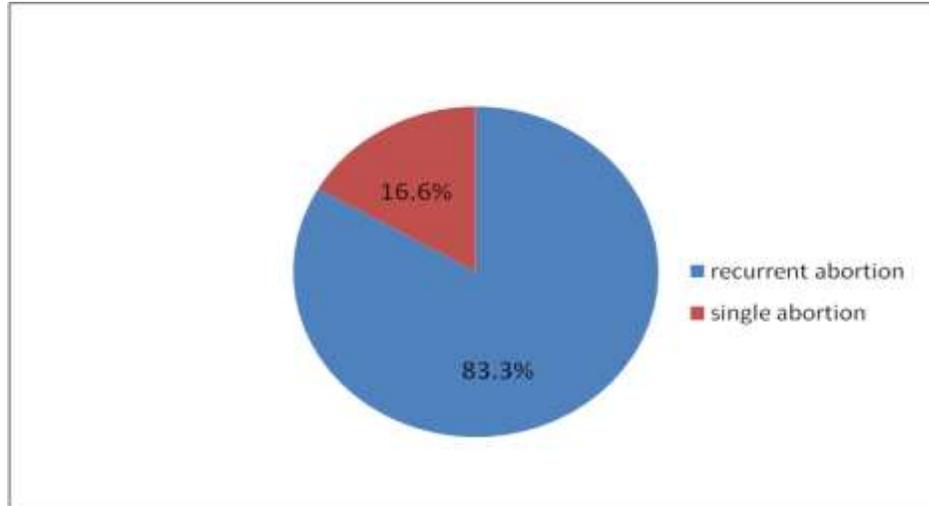


Figure 7 Distribution of diabetes mellitus cases in single and recurrent abortions

Abortion and Anomalies of the female genital tract

By doing abdominal ultrasonography to the patients it had been found that there were 5 out of 87 patients had abnormalities in their uterus, 2(40%) of them had bicornuotated uterus, 1(20 %) had uterine fibroid and the other 2(40%) had septated uterus and all of them developed recurrent abortions, and there is no such abnormalities was recorded in single abortion group. There is a significant differences ($P < 0.05$) between recurrent and single abortion group.

Discussion

As we found in this study the number of positive cases for antitoxoplasma antibodies were 27 (31%) cases ,20 cases was related to

recurrent abortions group and 7 cases with single abortion, so the relationship between abortion and Toxoplasma infection was highly significant ($p < 0.01$). This may be due to the fact that in our society when the woman develop abortion for the first time, she rarely visit the clinic looking for the cause of her abortion, so the parasite remain in latent state and again when the mother become pregnant where her immunity suppressed due to certain physiological changes in the body that occur during pregnancy so the parasite will reactivated again and become the cause of her next abortion in addition to the presence of another factors that act together with T. gondii parasite in killing the developing embryo or fetus.

Regarding the age, the highest number of positive cases for

antitoxoplasma antibody was 18 and related to the ages between ≥ 15 to 25 years. This may explained by that, this age represent the optimum period of fertility and reproduction and because the pregnancy reduce the immunity of the body thus this critical period of woman's life has higher chance for activation of latent infection of T.gondii that can be transmitted vertically to the fetus.

Also this study demonstrated that the most cases of abortion developed in the first trimester of pregnancy which was 62.9% in both single and recurrent abortion groups.

This result consists with Hacker *et al.*, 2010 [14], but not consists with Mohammed (2008) [15] who found that the higher incidence of abortion occurs in the second trimester of pregnancy and the higher incidence of positive cases were related to the single abortion group.

In this study we found that the higher number of CMV infections was related to the recurrent abortions group of the patients which was 12 cases out of 15 seropositive cases . This is can be explain by the fact that the cytomegalovirus is one of the viruses that remain latent in the body and reactivated again when the immunity of the body reduced during pregnancy, so there is vicious cycle that lead to recurrent abortion unless the treatment is received.

Regarding the age, the higher prevalence of CMV infections found in patients whom ages range between ≥ 15 to 25 years where it's incidence was 53.3% .

This may be due to that in the ages between ≥ 15 to 25 years the female in her optimum activity regarding her reproduction and fertility and because that she may had CMV infection which

remained dormant in her body and because that during pregnancy the immunity of the body reduce so the latent cytomegalovirus will reactivated .

This finding is in accordance with Schleiss, 2010 who found that two age groups have higher rates of acquisition of infection: toddlers who attend group daycare and adolescents.

This study demonstrated that 66.6% of the CMV infections occur in the first trimester of pregnancy. This may be due to the fact that first trimester of the pregnancy is considered as a critical period in which the fetus is not well established in the uterus and it is threatened for abortion whenever the mother is expose to any risky factor such as reactivation of latent infection as CMV that result from immunosuppressant concomitant with pregnancy which can lead to placental infection and next placental insufficiency, with subsequent embryonic death.

This result consists with other many studies like Kadhim (2007) [16] and Mohammed (2008) [15].

In this study we found that anti -CMV IgG antibodies had higher incidence, they presented in 10.3% of the sera of aborted women .The presence of both anti-CMV (IgG and IgM) antibodies during pregnancy may be refer to reactivation of a previous latent infection as a result of immune suppression that occur during pregnancy or presence of other infection may also lead to reactivation of latent CMV infection. This result was consisting with that of Kadhim (2007) [16], who found that, 27.8% of the aborted women had anti -CMV IgG antibodies in their sera.

In this study it had been found that there were 10 cases out of 87 aborted women had infertility (5 women

with primary infertility and 5 with secondary infertility so there is significant relationship ($p < 0.05$) between abortion and infertility. This may be due to that most of the pregnancy losses are unrecognized and occur before or during the next expected menses. So the patient considered as infertile because her pregnancy unrecognized clinically. This hypothesis has, in fact, been corroborated by the data collected by Wilcox *et al.*; (1988) [17] they investigated the overall incidence of abortion by measuring daily urinary concentrations of human chorionic gonadotropin (hCG) during menstrual cycles.

With an hCG level above 0.025 ng/mL on 3 consecutive days as a criterion of early pregnancy, they found that 22% of pregnancies ended before pregnancy was clinically detected, and the clinically recognized loss rate was 12%. The finding of this study is in accordance with the study that performed by Dhont (2003)[18].

It had been detected in this study that there was highly significant relationship ($p < 0.01$) between recurrent abortion and diabetes mellitus, in which women with abortions (single and recurrent) had high fasting and postprandial glucose levels.

This may be due to that, poor control of preexisting or gestational diabetes during organogenesis (up to about 10 week's gestation) may lead to increase risk of major congenital malformations and then spontaneous abortion. There are many studies that consist with this study like Dhont (2003) [18], Montvale (2007)[19] and Blackwell (2008) [20].

In this study we found that the higher incidence of the female genital tract anomalies were recorded in the

recurrent abortion group which was 8.6%, and there was a highly significant differences ($p < 0.01$) between single and recurrent abortion groups .

This can be explained by the fact that in our society when the patient get abortion for the first time she do not try to do any investigation until she engaged onto the field of recurrent abortions stat.

This finding in accordance with many studies like Muckle *et al.*(2008) [21] who found that the incidence of abortion due to uterine anomalies were vary from 0.13% to 4.0% ,also Christiansen *et al.*(2005) [11] support this study where he found that uterine anomalies causes 15% of abortion. We conclude that the incidence of the female genital tract anomalies as cause of abortion in our city is double the incidence in other countries.

also we found that cervical incompetence was responsible for 6.8% of abortion's incidence, single and recurrent, but the higher percentage (4.5%), was related to recurrent abortion group of the patients, there is significant differences ($p < 0.05$) between single and recurrent abortion groups. This may be due to that cervical incompetence is one of the causes that required treatment, so if it not treated probably so recurrent abortion will result.

All of those patients develop abortion in the second trimester of their pregnancy. The explanation is that with the progression of the pregnancy, the pressure of the baby on the cervix will increase, and because of the weakness of the cervix, so abortion will take place. This result consists with many studies (Christiansen *et al.*, 2005[11]; *Reprod*, 2006)[22].

Conclusion

1. The most common causes of abortion in this study was *Toxoplasma gondii* infection were the highest number of positive cases was related to recurrent abortion group and the higher incidence of abortion occurred in the first trimester of pregnancy.
2. Cytomegalovirus was the second most common cause of abortion, it was more prevalence in patients whom ages range between ≤ 15 to 25 years, and it was responsible for 66.6% of abortions that occurred in the first trimester of pregnancy.
3. There was highly significant relationship ($p < 0.01$) between recurrent abortion and diabetes mellitus.
4. Cervical incompetence was responsible for 6.8% of abortion's incidence, single and recurrent.

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