

Female Infertility: A Study of Risk Factors

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Summary:

Background: Infertility is a relatively common condition. It can be attributed to factors in a female partner, a male partner, or in both partners. However, certain socio-demographic and life style factors have been linked to female infertility.

Objective: To determine the association between female infertility and selected risk factors.

Patients and Methods: This is a case – control study carried out in Basrah Governorate over a period of ten months, from 1st of January to 31st of October, 2006. Cases were married women who had no pregnancy for at least one year (infertile women), a total of 212 cases were included. The controls were married women who had babies aged less than one year (fertile women); the total number of controls was 213.

Results: the study found that the risk of infertility increases steadily with the increase in age. The risk of female infertility also increased in women with menstrual cycle disturbances (like irregular menstrual cycle length and scanty or heavy menstrual blood loss), women with previous history of abortion, women with previous caesarean section, and in women with previous history of ectopic pregnancy. Infertility was also found to be associated with obesity and with daily caffeine consumption.

Conclusion: the independent risk factors for female infertility were history of previous CS, menstrual cycle disturbance, regular daily caffeine intake and obesity.

Key words: Female infertility, risk factors, Basrah.

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Introduction:

Infertility is a disease or a condition of the reproductive system that interferes with the ability to conceive. It is typically defined as not being able to get pregnant after having regular unprotected sex for one year (1). It is estimated that between one in six and one in seven couples around the world have difficulty to conceive at some point in their lives(2). Infertility can be attributed to factors in a female partner, a male partner, or infertility is caused by problems in both partners. In some cases, the causes are never discovered. Approximately 30% to 40% of all infertility is due to a “male” factor, and 40% to 50% is due to a “female” factor. The remaining 10% to 30% may be caused by contributing factors from both partners, or by no cause that can be identified (3). However certain socio-demographic factors (like woman’s age and occupation) and life style factors (like cigarette smoking and caffeine consumption) were found to be associated with increased risk of female infertility (4, 5). Therefore the present study was carried out to study the association between selected risk factors and female infertility in Basrah.

Patients and Methods:

A case – control study was carried out to study the association between female infertility and selected risk factors. The study was conducted in Basrah Governorate over a period of ten

months, from 1st of January to 31st of October, 2006. Cases were married women who had no pregnancy for at least one year (infertile women) and were attending the infertility centre at Basrah Maternity and Child Hospital during the study period. Both women with primary infertility (had no previous pregnancy) and those with secondary infertility (had at least one previous pregnancy but failed to achieve another one), were included. Women with Infertility due to male factors were excluded. A total of 212 cases were included. The controls were married women who had babies aged less than one year (fertile women). Women who were attending a primary health center adjacent to the infertility center (Al-Razi primary health care centre) and women who were admitted with their infants to the paediatric wards of the same hospital on selected days during the study period (1-2 days / week) and fulfilling the criteria of inclusion were included (213 women). Both cases and controls were interviewed by one of the authors using a special questionnaire form designed for the purpose of the study. The questionnaire was designed to obtain information on socio-demographic characteristics, type of infertility, duration of infertility, obstetric history for cases with secondary infertility and for controls, menstrual history, history of gynaecological operation, medical and surgical history, history of smoking, dietary history, history of physical activity, history of occupational exposure to radiation, certain chemicals and drug history. In addition Body Mass Index (BMI) was measured for each case and control. Verbal consent for participation was obtained from cases and controls. Statistical analysis of the data was conducted using SPSS program (Statistical Package for Social Science) version 11.

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X² test and logistic regression analysis were used to determine the association between selected risk factors and infertility, P value less than 0.05 was considered significant. The odds ratio and confidence interval of the odds ratio for the risk factors under study were estimated.

Results:

The majority of the studied cases (61.8%) had primary infertility, while the remaining 38.2% had secondary infertility. Duration of infertility ranged between 1- 11 years; in 39.2% the duration was between 1-2 years, 34.9% with duration between 3-4 years, and 25.9% with duration of infertility of 5 years or more. The study showed a significant association between woman's age and risk of infertility. The percentage of women aged 30 years or above was higher in cases than in controls, 41.0% and 30.5% for the cases and controls

respectively. While no significant difference between cases and controls with respect to their occupation. The majority of cases and controls were housewives, 85.8% and 85.4% for cases and controls respectively. None of both cases and controls reported history of occupational exposure to radiation and chemicals. Age at menarche, irregular menstrual cycle, and the amount of menstrual blood loss were found to be significantly associated with risk of infertility. A higher percentage of cases than controls had an early (≤ 11 years) or late (14 years or above) age at menarche. Two thirds of cases (63.7%) had irregular menstrual cycle compared to only 3.8% of controls and a higher percentage of cases than controls had scanty or heavy blood loss (22.2% and 0.5% respectively). On the other hand no significant association between duration of menstrual period or history of dysmenorrhea and infertility was found. (Table 1).

Table 1. Distribution of cases and controls according to variables related to their menstrual history

Variables	Cases No	%	Controls No	%	Odds Ratio(OR)	95% C.I. OR
a. Age at menarche						
≤ 11	27	12.7	16	7.5	2.09	1.14 - 3.8
12 – 13	117	55.2	145	68.1	1*	
14+	68	32.1	52	24.4	1.62	1.08 - 2.42
X ² = 7.937 df = 2 P < 0.05						
b. Menstrual cycle						
Irregular	135	63.7	8	3.8	44.927	21.015-96.045
Regular	77	36.3	205	96.2	1*	
X ² = 170.888 df = 1 P < 0.01						
c. Amount of blood loss						
Scantly or heavy loss	47	22.2	1	0.5	60.388	8.245-442.268
Average loss	165	77.8	212	99.5	1*	
Fissure exact test = 0.000 df = 1 P < 0.01						
d. Duration of menses(days)						
9+	4	1.9	0	0.0	2.024	1.838 - 2.229
2 – 8	208	98.1	213	100.0	1*	
Fissure exact test= 0.06 df = 1 P > 0.05						
Total	212	100.0	213	100.0		

Previous abortion, previous caesarean section, and previous history of ectopic pregnancy were found to be

associated with an increased risk of secondary infertility (Table 2).

Table 2. Distribution of cases and controls according to their past obstetric history

Variables	Cases No	%	Controls No	%	Odds Ratio(OR)	95% C.I. OR
a. Abortion						
positive	44	54.3	52	24.4	3.682	2.151 - 6.302
Negative	37	45.7	161	75.6	1*	
X ² = 23.870 df = 1 P < 0.01						
b. Caesarean Section						
Positive	21	25.9	27	12.7	2.411	1.271 - 4.574
Negative	60	74.1	186	87.3	1*	
X ² = 6.308 df = 1 P < 0.05						
c. Ectopic pregnancy						
positive	2	2.5	0	0.0	3.696	3.062 - 4.462
Negative	79	97.5	213	100.0	1*	
Fissure exact test= 0.075 df = 1 P > 0.05						
Total	81	100.0	213	100.0		

Furthermore, a significantly higher percentage of cases than controls gave history of surgical operation (other than caesarean section), 7.5% of cases and 1.9% of controls. While no significant association between medical conditions and infertility was found. With respect to the association between obesity and the risk of infertility, a clear significant association between BMI and infertility was found in the present study. The percentage of cases with BMI of 25 or above (73.5%)

was significantly higher than that for controls (31.5%), ($p < 0.001$). The risk of infertility among women with body mass index exceeding 25 was 6 folds higher than that for women with lower BMI, (odd's ratio=6.1). The study also showed that life style factors like caffeine intake significantly associated with the risk of infertility. Higher percentages of cases than controls reported that they regularly and daily drink tea, drink soft drinks or eat chocolate (Table 3).

Table 3. Distribution of cases and controls according to caffeine intake

Variables	Cases No	%	Controls No	%	Odds Ratio (OR)	95% C.I OR
a. Tea intake						
Regular(daily)	104	49.1	84	39.4	1.479 1*	1.007-2.173
Irregular	108	50.9	129	60.6		
Total	212	100.0	213	100.0		
$X^2 = 3.986$	$df = 1$	$P < 0.05$				
b. Soft drink intake						
Regular(daily)	53	25.0	27	12.7	2.296 1*	1.380-3.822
Irregular	159	75.0	186	87.3		
Total	212	100.0	213	100.0		
$X^2 = 10.561$	$df = 1$	$P < 0.05$				
c. Chocolate						
Regular(daily)	68	32.1	30	14.1	2.881 1*	1.779-4.664
Irregular	144	67.9	183	85.9		
Total	212	100.0	213	100.0		
$X^2 = 19.384$	$df = 1$	$P < 0.01$				

* Reference group

On the other hand, no significant association was found between physical activity and the risk of infertility. In addition, none of both cases and controls reported history of cigarette smoking. Finally, in order to determine the independent effect of different variables on female infertility, a logistic regression analysis was carried out. The results indicated that female infertility was significantly and independently affected by previous history of caesarean section, irregularity of menses, abnormal amount of menstrual blood loss, caffeine intake and BMI (Table 4).

Table (4) Logistic regression for risk factors of female infertility

Independent variables	B	P. Value
A. Significant predictors		
History CS	0.3234	0.0115
Length of menstrual cycle	1.5696	0.0000
Abnormal Menstrual blood loss	-2.2139	0.0030
Caffeine intake which include		
a. Tea	0.5823	0.0192
b. Soft drinks	0.6587	0.0203
c. Chocolate	1.2374	0.0001
BMI	0.3675	0.0000
B. Non significant predictors		
1. Age	0.0523	
2. History of Abortion	0.5934	NS
3. Age at Menarche	-0.2090	

Discussion

It is generally well known that advancing age is one of the risk factors for impaired fertility in women (6). With the increase in age, the chances for fertility decline. Woman's fertility starts to decrease in her 30s and takes a big drop after age 35. Analysis of pregnancy rates based on conception on the day of ovulation suggested that women in the age group 19- 26 years have twice the pregnancy rates as those in the age group 35-39 (5). In the present study, the risk of infertility increased steadily with the increase in age which is in agreement with other studies. A study in Spain showed that the over all pregnancy rate in women aged over 35 years was 37% compared to 45% for women aged less than 35 years (7). Infertility in older women appears to be mostly due to a higher risk for chromosomal abnormalities that occur in their eggs as they age. The results of the present study suggest that some variables related to menstrual cycle are associated with an increase in the risk of infertility. They include age at menarche (early and late age at menarche), irregularity of the menses, and abnormal amount of menstrual blood loss. Regarding menarche, a study was carried out in Copenhagen to study the relationship between menarche and infertility found that menarche was not associated with fertility or fecundity (8). Regarding menstrual cycle patterns, epidemiologist often use menstrual cycle patterns as indicators of endocrine function in environmental and occupational studies, yet few studies have considered whether menstrual

cycle characteristics are associated with fertility or pregnancy outcome. However, a study was carried out in USA about the menstrual cycle characteristics in association with fertility and spontaneous abortion. The results of the study showed that cycles with length 30-31 days preceded cycles with highest fecundity. Shorter cycles were less likely to be followed by conception compared with 30-31 day cycles. Cycles with average loss of 5 days menstrual bleeding had the highest fecundity (9). A similar study in Denmark was carried out to characterize how the menstrual cycle pattern relates to fertility. The researchers suggested that female functional disturbance in ovulation, conception, implantation, or sustained pregnancy linked with variable menstrual cycle length. Thus, identification of medical and environmental causes of abnormal menstrual cycle patterns may provide clue to causes of infertility (10). The present study had also shown that women who had history of previous abortion or previous caesarean section were more likely to become infertile than those without such history. These results agree with many other studies in many countries. In UK a study was carried out to study the association between previous reproductive outcome and subsequently reduced fecundity. The study found that after miscarriage, time to pregnancy was longer than before miscarriage also sub-fecundity after miscarriage increased and the effect was more evident in older and obese women (11). With respect to previous caesarean section, a study was carried out in Sub-Saharan Africa to determine the impact of previous caesarean section on fertility. The study showed that the natural fertility rate subsequent to delivery by caesarean section was 17% lower than the natural fertility rate subsequent to vaginal delivery (12). Another study was carried out in UK to determine whether caesarean section is associated with later sub-fertility. The study found that operative vaginal delivery (forceps and vacuum extraction) and all types of caesarian delivery were associated with longer inter-pregnancy intervals (13). Regarding ectopic pregnancy, several studies reported its effect on subsequent pregnancy. One of these studies was carried out to measure statistically how soon pregnancy can occur after ectopic pregnancy. The study suggested that age and prior ectopic pregnancy are important determinants of pregnancy rates after ectopic pregnancy (14). In France a study had shown that factors associated with lower fertility after ectopic pregnancy were age over 30 years, low educational level, history of infertility and prior tubal damage (15). In addition, many studies in different countries were carried out to study the association between pelvic surgeries and infertility. One study suggested that pelvic surgery was the most important risk factor for tubal infertility; therefore all precautions must be taken to avoid infection and adhesion formation when pelvic surgery is performed (16). Obesity is another factor which has been suggested to be a risk factor for infertility. In the present study, the risk of infertility increased steadily with the increase

of body mass index which is in agreement with other studies (17- 19). A study carried out at seven infertility clinics in the United States and Canada showed that obese women had a relative risk of ovulatory infertility of 3.1 compared with women of lower body weight (BMI 20-24.9) (17). Another study in the United States observed a U shape association between BMI and relative risk of ovulatory infertility (18). Finally the results of the present study indicate that the risk of infertility for women with history of daily caffeine consumption is significantly higher than that for women with no such history. The effect of caffeine consumption on delayed conception was evaluated in a European multicenter study on risk factors of infertility involving randomly selected sample from five European countries (Denmark, Germany, Italy, Poland and Spain). The results of study found that a significantly increased odds ratio of sub fecundity in the first pregnancy was observed for women drinking more than 500 mg of caffeine per day, the effect being relatively stronger in the smokers than in non smokers and the women in the highest level of consumption had an increase in the time leading to first pregnancy of 11% (20). Another study in USA had shown that caffeine consumption is one of the modifiable risk factors in the development of impaired fertility (6).

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