

## ORIGINAL ARTICLE

## RISK FACTORS OF INFERTILITY IN A WOMAN: A CASE-CONTROL STUDY

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## ABSTRACT

The purpose of this study is to identify the risk factors for infertility women compared with fertility women in Sakaka Saudi Arabia. We conducted a case-control study at the Obstetrics and Gynecology department of Maternity and Children Hospital (MCH) in Sakaka from December 2020 to December 2021. A total of one hundred women among fifty infertile (case group) and fifty fertility women (control group) who had normal menstrual cycles (range 28- 30 days) and having children, were enrolled in this study. Data were collected by the method of a pre-structured questionnaire and laboratory reports. Data were also included age, body weight, and details history of menstrual, ovarian, and hormonal disorders. All collected data were entered into a datasheet for analysis of risk factors by using of SPSS 20.00 version with a chi-square test for data comparison and association using Odds ratio and logistic regression. The present study reveals the significant risk factors for primary infertility in a woman including duration of menstrual cycles, Hyperprolactinemia 26%, obesity 48%, ovarian dysfunctions 44%, and thyroid disorders 28%. Early detection of associated risk factors may reduce the rate of infertility and improve fertility by prevention and appropriate treatment.

**Keywords:** Primary infertility, Fertility women, Ovary dysfunctions, Hyperprolactinemia, Thyroid disorder

## INTRODUCTION

Currently, infertility considers a major public health issue. Infertility means being incapable to conceive after 12 months of regular unprotected sexual intercourse <sup>1</sup>. Approximately 70 million couple has been suffering infertility in the world among the most common in developing country <sup>2</sup>. Some studies reviewed and estimated that 18.93% to 78.99% had suffered infertility in Saudi Arabia. while another study reported nearly similar data 65% available<sup>3</sup>. Additionally, the survey of 70 infertility patients in Riyadh Military Hospital, detected that 58.6% and 41.4% were primary and secondary infertility respectively<sup>4</sup>

The etiology of infertility may be male or female causes, while the female issue of infertility is a recent problem around the world due to their stress life, emotion, and as well as late age marriage. Conversely, genetic factors, food habits, environmental factors, and as well as the reproductive disease may lead to infertility <sup>5</sup>. Several factors responsible for female infertility

which included utero-tubular factor 20% and ovarian factor 30% factors were reported respectively <sup>6</sup>. Previously reported that obesity has a positive impact on female infertility due to impaired the normal function of the hypothalamic-pituitary-ovarian (HPO) axis while obesity provokes excessive insulin in circulation which stimulates the ovary to excess secretion of androgen that hence infertility <sup>7</sup>. Besides, increased insulin may cause polycystic ovary syndrome (PCOS) and it considers a major and common cause of infertility at around 90%, while there was a direct link between PCOS and obesity <sup>8,9</sup>. Another study documented hyperprolactinemia in women leading to an abnormal luteal phase that is responsible for infertility <sup>10,11</sup>. However, some risk factors of female infertility may be reversible and some are challenging, early knowledge of risk factors may help to prevent and treatment of infertility. Currently, in Saudi Arabia, has been reported that infertility problems are nearly similar in different regions and consequently affect their individual

physiological affected, meanwhile, psychological illnesses are estimated among approximately 30% and 36.9% of male and female patients respectively<sup>12</sup>. There was little research on the field of infertile with deficiency data. Therefore, the present study investigates the risk factors and comparison between infertility and fertility women in Sakaka, Saudi Arabia.

## METHODS

This case-control study was conducted at the Obstetrics and Gynecology department of Maternity and Children Hospital (MCH) Sakaka, from December 2020 to December 2021. We enrolled a consenting one hundred women were attaining in this study and divided them into two groups, the case group (n=50) as diagnosed infertility women who were married more or less 5 years and unable to conceive after the marriage of free coitus and visited for treatment of infertility and the control group (n=50) as a fertility woman who has a history of a having normal menstrual cycle (range 28- 30 days) the duration of the marriage, more or less 5 years with having 2-4 children. The age range was 20-30 years and similar in both groups. The inclusion criteria included a detailed history of age, body weight, marriage, menstrual pattern, ovary, and hormonal disorder, and all related laboratory reports. We excluded other causes of infertility like secondary infertility, history of ectopic pregnancy, abortion, and pregnancy after infertility treatment and malefactor. Data were collected from investigation reports that were entered into Microsoft excel 2013 by two separate researchers to avoid errors and with direct face-to-face interviews by the questionnaire method. The ethical approval was provided by the ethical committee of Jofu university.

### Statistical analysis

Data were entered into an excel sheet and analyzed to identify the risk factors and their relationship by using Odds ratio, chi-square, and logistic regression. data were a comparison of risk factors between primary infertility and pregnant women. Statistical significance was considered at a p-value <0.05.

## RESULTS

### Characteristics of participants

Table 1 represents the demographic clinical characteristic of study groups, a total of one hundred women participants among fifty primary infertility women (case) and fifty fertile women (control) groups with an age range of 20-30 years. The present study found there was no age

significance in infertility women. From the study, it was found that the primary education 28%, 20%, and secondary education 72% and 80% shows in primary infertility and pregnant woman respectively, therefore it indicates the relationship between educational level and found insignificant in infertility women.

The present study also determined that the age of menarche has insignificant between the two groups. The menstrual pattern was found irregular at 32%, 22%, and regular at 68% and 78% respectively, and suggested that insignificant in infertility woman. However, the duration of the menstrual cycle >35 days and <35 days shows that the correlation between infertility and the duration of the menstrual cycle considered is significant in the menstrual cycle >35 days have a 3.633 times higher risk of becoming infertile than others (table6).

### Imaging study of all participants

Imaging study is essential for the diagnostic evaluation of infertility women, in the present study the pelvic ultrasound shows polycystic ovarian syndrome caused as ovarian dysfunction in 44% of cases and 18% in control groups which typically required further characterization with pelvic magnetic resonance (MRI) imaging.

### Analysis of hormonal assay in a case and control groups

The present study was designed to know the differencing values of the hormonal levels including the follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol, progesterone, thyroid-stimulating hormone (TSH), and prolactin hormone (PRL). We also estimated the values of serum TSH & Prolactin between infertile and fertile females as well as correlated TSH & Prolactin levels in infertile females which are represented in table 3. We noticed Serum FSH, LH, estradiol, and progesterone levels were lower significant in the cases group compared to the control group, meanwhile, the serum prolactin and TSH levels were higher significant in cases than the control group.

The present study also suggested that the Correlation between TSH and PRL has a positive correlation with female infertility which is significant.

### Factors associated with female infertility

The present study estimate, that hyperprolactinemia is considered a significant risk factor presenting to infertility women, and women with hyperprolactinemia have 7.578 times increased risk of infertility than others (Table 6).

Table1: Demographic characteristics of all participants (n=100).

Factors	Case (n=50) %	Control (n=50) %	P -value
<b>Age (years)</b>			
20-25	20 (28.3)	31 (51.6)	0.82
26-30	30(71.6)	29(48.3)	
<b>Education levels</b>			
Primary	14 (28)	10 (20)	0.604
Secondary	36 (72)	40 (80)	
<b>Age of menarche [years]</b>			
<15	3 (6)	2 (4)	1
>15	47 (94)	48(96)	
<b>Menstrual pattern</b>			
Irregular	16 (32)	11 (22)	0.246
Regular	34 (68)	39 (78)	
<b>Duration of the menstrual cycle</b>			
>35 days	13(26)	5(10)	0.02
<35days	37(74)	45(90)	
<b>Duration of marriage (years)</b>			
<5 years	14	7	0.02
>5 years	36	43	
<b>Number of children</b>			
2	-	7	-
3	-	20	
4	-	23	

Table 2: An imaging study of all participants (n=100).

Variables	Infertility(n=50) %	Finding	Fertility (=50) %	Finding
<b>MRI in brain</b>	50(100)	No abnormality	50(100)	No abnormality
<b>Pelvic ultrasound</b>	22(44) %	polycystic syndrome	9(18) %	Polycystic syndrome
<b>Pelvic MRI</b>	22(44) %	polycystic syndrome	9(18) %	Polycystic syndrome
<b>Uterine ultrasound</b>	50(100) %	No abnormality	50(100) %	No abnormality

Table 3: Hormonal study of all participants(n-100).

Variables	Control (n=50)	Case (n=50)	P-value
	Mean ± S.D.	Mean ± S.D.	
FSH(IU/L)	5.61 ± 2.21	3.66 ± 1.34	0.000
LH(IU/L)	4.85 ± 1.64	3.16 ± 1.48	0.000
Estradiol(pg/mL)	0.44 ± 0.11	0.33 ± 0.27	0.005
Progesterone(ng/mL)	34.41 ± 12.2	13.02 ± 9.46	0.00
TSH (µIU/mL)	02.42 ± 1.41	05.14 ± 4.73	0.00
PRL (ng/mL)	08.06 ± 4.62	15.42 ± 9.94	0.00

Table 4: Relationship between serum Prolactin and TSH in cases of infertility women(n-50)

Variables	Mean ± S. D	Correlation of Coefficient (R-value)	p-value
TSH (µIU/mL)	05.14 ± 4.73		0.00
PRL (ng/mL)	15.41 ± 9.94	0.6 8	

Table 5: Risk factors among participants (n=100).

Factors	Case (n=50) %	Control (n=50) %	P -value
Hyperprolactinemia	13 (26)	4 (8)	0.003
Thyroid disorder	14 (28)	3 (6)	0.001
Ovary dysfunction	22 (44)	9 (18)	0.00
Obesity	24 (48)	15 (30)	0.003
Dysmenorrhea	10(20)	23(46)	0.008

The present study shows that thyroid disorder was found in 28% of infertility women compared to 6% control group. thus, thyroid disorder is considered a significant risk factor for infertility in women who have a 10.286 times higher risk of becoming infertile than others (table6). The number of participants who are recognized with ovarian dysfunctions is more found in infertility women (44%) as compared to controls (18%). Therefore, it is considering the presence of a link between ovarian dysfunctions and female infertility is significant 23.059 times the higher risk of ovarian dysfunctions becoming infertile than others (Table 6). The present study reveals that obesity is 48% higher in infertility women compared to 30 % of the control group considered a significant risk factor for the infertility group with a 3.801 times higher risk

for becoming infertile (table 6). Our results show that dysmenorrhea presents 20 % in the cases and 46% in the control group and found a significant correlation between fertility and dysmenorrhea.it has been reported that dysmenorrhea indicates the ovulatory cycle which is an essential requirement for fertilization.

#### Binary logistic regression

The present study estimates the odds ratio obtained from the data analysis, all the risk factors with their p-value  $\leq 0.05$  were taken for binary logistic regression. The related factors such as dysmenorrhea, hyperprolactinemia, ovarian dysfunctions, obesity, duration of menstrual cycles, and thyroid disorders.

Table 6: Crude and adjusted p values and odds ratios

Risk factors	Odds ratio	P-value	Adjusted odds ratio	Adjusted P-value
Hyperprolactinemia	7.578	0.003	8.305	0.003
Thyroid disorder	10.286	0.001	11.977	0.001
Ovary dysfunction	23.059	0.00	15.946	0.000
Obesity	3.801	0.003	8.207	0.003
Dysmenorrhea	0.302	0.008	6.0856	0.008
Duration of menstrual cycles	3.633	0.02	4.762	0.028

## DISCUSSION

We conducted a case-control study that aimed at identifying the risk factors associated with infertility in women at the Maternity and Children Hospital (MCH) Sakaka, Saudi Arabia. To our knowledge, the present study is the first to reveal the risk factors for infertility in women compared to fertility women. The age ranges of all participants were 20-30 years and divided into 20 to 25 and 26 to 30 years. The present study shows that there was no significant relationship between the age in between cases and the control group. Although the pick time of fertility is around age 18-24 years old, the decline of the fertility age begins from age 27 years to more after 35 years<sup>9</sup>. However, our result suggested that marriages should be appropriate age may prevent or reduce the rate of infertility. Besides, it has been reported that advanced maternal age and delayed menarche age are potentially a risk for infertility, especially primary infertility<sup>13</sup>.

Our study also focuses on the duration of the marriage, all participants have different duration of the marriage, thus present study demarked 5 years more or less, and according to the duration period, all participants were included in this section. While the duration of marriages may indicate one of the criteria for diagnosis of infertility. In the present study, we also included the age of menarche and it was divided between below the age of 15 and more than 15, our results showed <15 6%, 4%, and >15 94%, 96% respectively case and control groups. The present study shows that significantly 46 % of dysmenorrhea was found in pregnant women compared to infertility women, thus it is linked to the ovulatory cycle and requires fertilization. The present study also focuses on the educational levels of all participants but the results showed insignificant between the two groups. However, education is very important for knowledge about fertility and infertility. The present study also found associated risk factors between infertility and fertility such as ovary dysfunctions 44% in infertility women and 18% in fertility women. Therefore, it was considered that ovary dysfunction act as one of the most common causes of infertility in the present

study which is similar to another study<sup>14,15</sup>. On the other hand, the present study found thyroid disorder present in 28% of infertility women compared to in 6% of fertility women and suggested strongly significant. Nevertheless, the gonadal axis and thyroid are essential for normal reproductive function, while thyroid hormone also maintains the ovular cycle<sup>16</sup>.

As far, as thyroid dysfunction may lead to ovary dysfunction, irregular menstruation, and as well as infertility<sup>17</sup>. Consequently, above this statement present study found irregular menstruation which was significantly increased in the case group compared to the control group. Besides, hyperprolactinemia occurs in 26% of infertility women compared to 8% of fertility women. Though, another study documented around 46% of hyperprolactinemia found in infertility women<sup>15,18</sup>. As well as most of the infertility cases had shown the relation of hyperprolactinemia with hypothyroidism, which represents 41% in infertility women and 15% in fertility women<sup>19</sup>. It has been well known that obesity responsible for irregular menstruation and ovary dysfunction that lead to infertility<sup>20</sup>. The previous study evaluated 61.7% of infertility woman who has a history of obesity<sup>21</sup>. However, it has been reported that infertility correlated with male, female, mixed, or unidentified causes which are mostly divided one third, another third, and, remaining respectively<sup>21</sup>. The present study found obesity at 48% and 30% in infertility and fertility women respectively and considered significant.

### Study strengths

This is the first study in Aljouf, Sakaka, Saudi Arabia to reveal the risk factors of female infertility in Saudi women. Case and control groups were conducted in the same hospital and evaluated their data from hospital data files. We identified the risk factors and their relationship by using Odds ratio, chi-square, and logistic regression.

### Study limitations

The present study has faced some limitations, first, there was a small patient sample, and second, the patients were only from one hospital. In the Aljouf

region, there is only one government hospital like Maternity and Children Hospital (MCH) located in Sakaka, all infertility, obstetrical, and gynecological patients are referred from primary health care centers in different cities of Aljouf province. We excluded many infertility patients due to missing related data in hospital patients' files.

## CONCLUSION

The present study identified the associated risk factors that comparison between infertility and fertility women. hyperprolactinemia, thyroid disorder, ovary dysfunction, obesity impaired fertility, and subsequent development of infertility. Therefore, early detection of risk factors may help to appropriate treatment hence reducing infertility and improving fertility in women.

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