COMMON RISK FACTORS AMONG FEMALES SEEKING TREATMENT FOR INFERTILITY IN MUSCAT

Fathiya AL-Hassani¹, Eman Al Azawi² and Havagiray R. Chitme* ¹

¹Premedicine and Pharmacy Campus, Oman Medical College, Muscat – Sultanate of Oman
²Al Bushra Medical Specialty Complex, PO Box: 1735, Postal Code: 133, Al Azaiba, Muscat – Sultanate of Oman

ABSTRACT

Female infertility in married couples is considered to be a social and familial stigma. The diagnostic tests and treatments are more expensive, uncomfortable and complicated due to series of tests and trial periods extending over several months and years posing a financial burden on patient and family. Therefore, identification of causes and risk factors plays an important role in early prevention of avoidable factors and improve outcomes. Present study was carried out to understand causative and risk factors underlying in infertile Omani females who sought treatment in two infertility centres located in Muscat. This study was a prospective and retrospective involving patients from both infertility centres. Prospectively study was carried out by using standard questionnaire. Retrospectively the data was collected from case files. Results of our study indicate that there is a significant relation between 26-30 age group and female infertility. The risk of infertility is more after 2 years of marriage; also, it increases after second attempt to pregnancy. It has also revealed that irregular periods in females increase the risk of infertility. Family history of infertility, miscarriage and thyroid disease are significantly associated with infertility. Patients having the past surgical history for fibroids, ovarian cystectomy and early treatment of vaginal infection have significantly lesser risk for infertility. Based on the results we conclude from this study that there is a need to consider identified global causative and risk factors along with local factors for successful prevention and treatment of female infertility.

KEY WORDS: Infertility; Female infertility; Risk factors; Prevalence; Oman; Causes.
INTRODUCTION

International Committee for Monitoring Assisted Reproductive Technology and the WHO defined infertility as a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.\textsuperscript{[1]} There are two major types of infertility and these include; Primary infertility which occurs when a couple indulges in unprotected sex for 1 year or more without conceiving. Whereas, Secondary infertility refers to couples who have conceived in the past but they are not able to get another pregnancy.\textsuperscript{[1]} Global infertility prevalence rates are difficult to determine, due to the presence of both male and female factors. Recent study indicates that globally 10–15\% of couples accounting nearly 72.4 million couples experience fertility problems. \textsuperscript{[2-3]} In Canada it is 10\%, Africa 30-40\%, for example in Nigeria and some parts of sub-Saharan Africa including the Republic of Sudan and Cameroon it is 30\%, Mexico 10\%, USA 10\%, UK 6\%, Denmark 16\%. \textsuperscript{[4-9]}

The statistics calculated among GCC countries based on USA prevalence infertility rate indicates that Dubai is registered with 27,276 infertility cases of which 13,638 are associated with women. In UAE, number of infertility cases are 100,446 are due to 50,223 women. In Kuwait 30,554 infertile women are blamed for 61,108 infertile cases. Similarly, Bahrain, Saudi Arabia and Qatar are estimated with 17179, 552063, 28,691 infertile cases respectively and 8,590, 276,032 and 14,346 infertile women in respective countries. In Oman, 62,392 infertile cases are estimated out of which 31,120 are expected to be due to infertile women. \textsuperscript{[10]}

Many factors are identified as risk and causative factors for female infertility including aging \textsuperscript{[11]} blockage or damage of the fallopian tubes \textsuperscript{[1]} , endometriosis \textsuperscript{[12]} , ovarian insufficiency \textsuperscript{[3]} , pelvic adhesions \textsuperscript{[1]} , thyroid problems \textsuperscript{[14]} , cancer \textsuperscript{[15]} , chemotherapy \textsuperscript{[15]} , caesarian sections \textsuperscript{[16]} , delayed puberty \textsuperscript{[17]} , obesity \textsuperscript{[18]} , amenorhea \textsuperscript{[19]} , tobacco and alcohol use \textsuperscript{[20]} , genetic abnormalities \textsuperscript{[21]} , vitamin D deficiency \textsuperscript{[14]} , and unidentified factors \textsuperscript{[22]} can make conception and pregnancy less likely.

A meeting convened by the World Health Organization in 2001 recommended that infertility be considered as a global health problem and called for innovative approaches in its treatment. \textsuperscript{[23]} This can be achieved through investigation of the leading causes and factors. Although assisted reproduction technology (ART) provides the possibility of achieving
pregnancy, almost 60% of people undergoing ART still cannot conceive. The reasons for infertility can involve one or both partners.

Treatment of infertility depends on the cause, how long they have been infertile, age and partner's age, and many personal preferences. To our knowledge no extensive study has been carried out in Omani patients to know risk and causative factors for female infertility. This study was designed to know whether the prevalence of risk factors and causes of female infertility in Oman is in line with GCC countries and world statistics. Main purpose of the study was to find out the prevalence of risk factors and causes of female infertility in infertile female patients visiting selected two infertility centres located in Muscat.

METHODS

Study location and population

Study was carried out at Al-Bushra Medical Specialty Complex and Advanced Fertility & Genetics Center (L.L.C.) located in Muscat. Present study includes 135 Omani females diagnosed with infertility and equal number of fertile Omani female as matching control. Control groups were selected from the fertile Omani females visiting local polyclinics for other reasons. Data was collected retrospectively by visiting the patients files and prospectively interviewing the patients and filling the standardized questionnaire. Interviews were conducted in both Arabic and English by research person or staff from respective hospitals in private rooms within the clinic lasted about 1 h, although they ranged in length from 0.5 to 1.5 hour.

Biomedical Ethics

Study was conducted according to the guidelines and ethics of selected fertility centres after the official permission. Accordingly, the identity of the patient and their related information will not be disclosed. Verbal consent from each female involved in the study was taken after specifying objectives, assurance of privacy, anonymity and confidentiality, and giving assurance that nonparticipation would not affect their care. They will have the liberty to withdraw from study at any point of time.

The Questionnaire

In this study we aim to explore all aspects of female infertility. Therefore, we developed a questionnaire able to study the personal, dietary, social, psychological and sexological features of infertile female, comprising closed questions and items with answers.
Questionnaire is subdivided into five areas: (i) demography (ii) social (iii) medical diagnosis (iv) sexual health (v) surgical history (vi) medication history and (vi) history of infertility.

Statistical Analysis
Each case was given a case number and the information collected in this study was entered directly into SPSS version 19 and analyzed using descriptive statistics such as mean and standard deviation for continuous numerical data, and for categorical data percentage-frequency distribution was used. Comparison group for the infertile persons included all respondents with no experiences of infertility matching + 2 years of marriage history. Relative risks and the confidence intervals (CI) of infertility were obtained by fitting a linear association model. Any difference in variables of control and case group were analysed by Chi square test. A p-value of less than 0.05 was considered statistically significant.

RESULTS
Frequency and Relative Risk of Female Infertility and Age Group
As depicted in figure 1 maximum number of patients with infertility who sought treatment from selected infertility centres were from 21-35 years age group. In which relative risk was significantly (p<0.05) higher in age group 21-25 but the incidence of infertility was significantly (p<0.05) higher in age group 26-30 years age group.

Regional Distribution and Relative Risk of Female Infertility
In this study, highest number of patients were from Muscat it might be due to location of study centres in Muscat. Al Batinah, Ad-Dakhliay and Al Sharqia followed it. Figure 2 shows that there is a significant (p<0.05) association between the place of origin and female infertility. Risk of infertility was more in patients from Al-Dhabira followed by Muscat, Al-Dakliya and Dhofar. Although the incidence was more in Muscat because most patient participants were lived in it and the lowest were in Al-Wasta.

Marriage Factors Increasing the Risk of Female Infertility
Delayed in treatment and aging has significant impact on female fertility and its outcome. As shown in figure 3 both of these factors reduced the rate of success of infertility treatment. The risk of infertility was more after 2 years and 11 years of marriage. Also it increases after 2nd, 3rd and 6th attempt to pregnancy. These could be reason for previous unsuccessful marriages.
Fertility Factors Increasing the Risk of Female Infertility

Following figure 4 shows that the fertility factors play an important role in female infertility. In this we found that the irregular periods in females increase the risk of infertility by 1.7 times. Also menarche at age 13 years has higher risk of infertility compared to fertile women but the reason unkown. It was also noted that endometriosis and ectopic pregnancy will also increase the risk of infertility in females compared to control group of patients.

Family Factors Associated with Female infertility

As shown in figure 5, family history of infertility, miscarriage and thyroid disease either hyperthyrodism or hypothyrodism are significantly (p<0.05) associated with infertility in females who sought treatment in selected study centres.

Surgical Factors Associated with Female infertility

Results obtained in our study as presented in figure 6 indicates that surgical treatment for fibroids, ovarian cystectomy and early treatment of vaginal infection have significantly (p<0.01) reduced the risk for infertility in females.
Fig. 2

Regional Distribution and Relative Risk of Female Infertility (p<0.05)

<table>
<thead>
<tr>
<th>Number of patients and relative risk</th>
<th>Muscat</th>
<th>Al-Batinah</th>
<th>Al-Dakhya</th>
<th>Al-Sharqia</th>
<th>Al-Wusta</th>
<th>Ad-Dhbira</th>
<th>Dhofar</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1.4</td>
<td>0.5</td>
<td>1.3</td>
<td>1.1</td>
<td>4</td>
<td>1.7</td>
<td>1.2</td>
</tr>
<tr>
<td>Regions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Fig. 3

Marriage Factors Increasing the Risk of Female Infertility

<table>
<thead>
<tr>
<th>Marital Factors</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 Yrs of current marriage</td>
<td>3</td>
</tr>
<tr>
<td>11 yrs of current marriage</td>
<td>2.1</td>
</tr>
<tr>
<td>2nd attempt to pregnancy</td>
<td>4.1</td>
</tr>
<tr>
<td>3rd attempt to pregnancy</td>
<td>7.1</td>
</tr>
<tr>
<td>6th attempt to pregnancy</td>
<td>8</td>
</tr>
<tr>
<td>7th attempt to pregnancy</td>
<td>2</td>
</tr>
<tr>
<td>History of previous...</td>
<td>3.5</td>
</tr>
</tbody>
</table>
Fig. 4:

Fertility Factors Increasing the Risk of Female Infertility

- Irregular periods: 1.7
- Menarche at 13 years: 1.4
- Endometriosis: 1.04
- Ectopic pregnancy: 2

Fig. 5:

Family Factors Significantly (p<0.05) Associated with Female Infertility

- Infertility
- Miscarriage
- Thyroid Diseases
DISCUSSION

As women are born with a finite number of eggs. Thus, as the reproductive years progress, the number and quality of the eggs diminish. The chances of having a baby decrease by 3% to 5% per year after the age of 30.[25] This reduction in fertility is noted to a much greater extent after age 40. The effect of age differed for parous and nulliparous women, with the latter experiencing much stronger age-related declines relative to fecundability at age 20 years.[26] A retrospective population-based study in Norway from two cross-sectional surveys conducted in the mid-1990s and 2000 reported that 87.8% of the women in Cohort 1940 were fertile compared with 84.2% of the women in Cohort 1950. The prevalence of infertility increased over time due to an increase in subfertility from 7.8 to 10.6%. The decline in fertility was related to changes in subfertility.[27] The National Reproductive Health Survey 2008 which was carried out in Oman by Ministry Of Health indicates that the woman in
Oman tend to have most of her children in the middle of her reproductive age span, 25-39. At the current age-span Omani woman will give 2.5 births between age 25 and age 39: more than three-quarters of her life-time fertility. Irrespective of urban/rural residence, fertility peaks in the age group 30-34 at 190.1 per thousand for all Omani women. Results of our study are in line with previous reports as age turned out to be one of the main risk factors where relative risk was more in age group (21-25) and maximum number of patients were from the age group 21-35 years. It is also noted that delay in seeking treatment for infertility and repeated attempts for pregnancy will lead to aging ultimately leading to failure of treatment. One of the reason for decreased fertility in Omani females given in Ministry of Health, Oman is that women are generally married at older ages due to higher level of education and economic prosperity of the country.

A study conducted with an objective to know the distribution of causes of infertility in Israel reported that there is regional difference in common causes of infertility ranging between 21% and 50%. It is also reported from Scotland that there is a lifetime prevalence of infertility is between 6.6% and 32.6% due to population-based differences are commonly due to varied number of miscarriages, ectopic pregnancies, obesity, a history of long-term health problems, chemotherapy, pelvic problems, and sexually transmitted infection. Results of our study also reflects variation in number of infertile women seeking treatment at infertility centres probably due to above causes. However, we have not tried to explore the causes for infertility with respect to region. In our study risk of infertility was higher in patients from Al-Dhahira followed by Muscat, Al-Dakhlyia and Dhofar. Earlier report submitted to MOH indicated that fertility rate ranges from 2.8 births in Muscat to 4.6 in AL Wusta. At the same time, the mean children ever born among women aged 45-49 is lowest in Muscat (7.8) and highest in South Al Batinah (9.4), supporting data of our study. It should be pointed out here that the sample sizes for most regions are inadequate to provide precise fertility estimates at the region level. This could be due to regions differ greatly with regard to the level of desire for more children. The percent of currently married non-pregnant women having a desire for more children ranges from 27.4 percent in South Ash Sharqiyyah to 52.1 percent in Muscat. Regions vary substantially with regard to the prevalence of both mistimed and unintended pregnancies: the prevalence of mistimed pregnancies ranges from 8.8 percent in South Ash Sharqiyyah to 31.6 percent in Dhofar, while the prevalence of unintended pregnancies ranges from 4.2 percent in Adh Dhahirah to 13.8 percent in Muscat.
Family history of infertility, miscarriage and thyroid disease are significantly associated with infertility. The study in Oman shows that for each 100 pregnancies, there are about 10.8 cases end in a pregnancy loss (miscarriage, abortion or still birth) instead of a live birth. This means that life time fertility in Oman is reduced by 10.8 percent only because of the impact of pregnancy loss. The incidence of pregnancy loss is generally higher among younger women. The percent of pregnancies that end in a pregnancy loss is about 24.8 percent among women in the 15-19 age group and declines rapidly over age until it reaches 8.7, 11.1 and 9.9 percent for women in the age groups 35-39, 40-44 and 45-49 respectively. [25] Definitely, an older woman learns, from her past experience, how to look after her successive pregnancies until they end in live births. This may explain why the incidence of accumulated pregnancy losses is lower for older women.

Endometriosis is defined as overgrowth of endometrial tissue outside the uterine cavity associated with dysmenorrheal symptoms, dyspareunia, pelvic pain, abnormal uterine bleeding and infertility. [30] Increasing evidence suggests that 40% of women with endometriosis are infertile. [31] Results of our study also revealed that the risk of developing infertility in women is relatively higher than the control group of population thereby supporting the results of previous studies. We also found that there is an association between risk of female infertility and age of menarche supporting the data of recently reported retrospective cohort study where a significant impact of age at menarche is related to diminished functional ovarian reserve. [32] We also found that the recurrent pregnancy loss and miscarriage will increase the risk of infertility in women. Supporting the study carried out in India. [14, 33] In line with previous study an abnormal bleeding in women, pelvic pain, and ectopic pregnancy were also noted to increase the risk of infertility in female. [34]

Treatment of pelvic inflammatory, infectious, and sexually transmitted diseases either by surgery or medication significantly reduces the risk of female infertility compared to control group of population. These results are in line with matanalysis report on bacterial vaginosis. [35] Pelvic adhesion, tubal umbrella adhesions and atresia are commonly known for infertility in women. Correcting these underlying causes by surgical means not only increases the chances of fertility in women but also reduce risk of infertility. [36] Results of our study supports the statement.

Present study was carried out as a part of graduation research project for a period of six months. This is the first preliminary attempt to generate knowledge about the risk factors and
causes specifically in Omani women diagnosed with infertility essential to health professionals, health policy-makers and government in terms of a healthcare services. To improve reliability of data we carried out individual item analyses. Present study involves only limited number of patients therefore it is very important to calculate practical implications of the findings, and also in interpreting study findings. Due to small sample size it was difficult to assess influence of each factor and also their additive and synergistic effects on women fertility.

Future prospective and retrospective research is advised to investigate how and to what extent infertility causes and risk factors have an individual and cumulative impact on fertility in Omani women. These studies should incorporate both qualitative and quantitative methods involving more patients over a longer period of time to establish a better understanding of these factors and their influence on fertility incidence.

CONCLUSION
We conclude from this study that the aging is associated with the risk of infertility along with variation in regional distribution. We also found that marital factors, fertility factors and family factors have significantly increased the risk of infertility in omani females. However, early treatment for vaginal infections and surgical interventions in fibroids and ovarian cystectomY will significantly reduce the risk of female infertility.

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REFERENCES


