CHARACTERISTICS OF FEMALE PATIENTS VISITING FOR ASSISTED REPRODUCTIVE TECHNOLOGY IN A PRIVATE CLINIC IN LAHORE, PAKISTAN

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ABSTRACT

Background: Infertility has social, psychological and physical effect on couples. **Objective:** To describe the characteristics of women attending a private clinic for assisted reproductive technology. **Subjects & Methods:** The infertile couples who came to Lahore Institute of Fertility and Endocrinology (LIFE) from 1st January to 31st December, 2013 for infertility work up, were included in the study. The sampling technique used in this study was non probability, convenient, and time based, as the study design was cross sectional. Sample size was 534 patients of assisted reproductive technology.(ART). A questionnaire was used for the data collection. This questionnaire included information on woman's demographics, obstetric and infertility history, radiology and hormone investigation. SPSS version 20 was used for the data analysis. **Results:** Patients with age less than 35 years were 398 (74%), between 36-39 were 103 (19%) and more than 40 years were 33(6%). Follicle stimulating hormone (FSH) was less than 9 l U/ ml in 418 (78%) between 9-11 l U/ ml in 83(15%) and greater than 11 l U/ ml in 33(6%). Patients having regular menstrual cycle were 498 (93%). Patients having parity were 118 (22%) who had delivered a child. Body mass index (BMI) was less than 25 in 163(30%), between 25-30 in 219(41%), greater than 30 in 152 (28%).As with the female factors, no causes were found in 254 (47%), tubal cause in 120 (22%), PCO in 68 (12%), endometriosis in 13(2%), un-explained causes were found in 79(5%). Count of antral follicles was 6-8 per ovary in 369 (69%), 3-5 per ovary was 129 (24%), 0-2 per ovary was 36(7%). Primary infertility was seen in 350 (65%) patients, secondary infertility in 178 (33%), unexplained infertility in 6(1%). Regarding duration of infertility, in 113(21%) patients it was 2 or less than 2 years, 118 (22%) was 4 years, in 49 (9%) was 5 years, in 87 (16%) was 7 years, in 82 (15%) was 10 years, in 85 (16%) was greater than 10 years. **Conclusion:** Importance of recognition of infertility as a health issue will not only remove treatment barriers but also improve the health seeking behaviors of the infertile couple. Health education about fertility will ease the social taboos and improve the delivery of health services to infertile couples. Age, FSH, menstrual regularity, parity, BMI, female factor, antral follicles, type of infertility, duration of infertility may have a predictive value forecasting the success of the outcome of IVF. Further research is needed on these lines.

Key words: Female factors Fertility Clinic, Infertility, ART

JSZMC 2014;5(4):715-720

INTRODUCTION

Infertility is a condition characterized by inability to conceive and become pregnant despite regular unprotected sexual activity for whole one year.[1] It is primary when there is no history of conception and secondary when there is a history of pregnancy, followed by infertility.[2] Over the whole world, 10-15% of couples may be infertile: secondary infertility is more common than primary infertility.

There is an estimate of between 60 million and 168 million affected by infertility in the whole world. This tells us that one in every four women who are in their reproductive age and are married may be infertile. In Pakistan, secondary infertility is more common (18%) than primary (4%), the overall prevalence being 22 %. Men and women suffer from infertility equally.[3]

Ignorance and myths prevail in the society about infertility and lack of knowledge about treatments lead to delay in the treatment of infertility.[3,4,5] Self-blame, anxiety, depression, social dysfunction and suicidal ideas sometimes occur in infertile women in higher proportions.[4,6,7,8]

Development of a full-blown psychiatric disorder occurs in a percentage of infertile women before consulting an infertility advisory centre.[9]

An infertile couple becomes the centre of attention and mockery and personal failure, especially for the woman, who endures the most of the blame and stigma.[1,4,8] They become the victims of verbal and physical abuse and sometime have to face a divorce or the husband may bring a second wife or send the

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Received:17-09-2014 **Accepted:** 29-11-2014

first wife to her parent's home.[7,10]

The causes of infertility differ in the developed and developing world. Late marriage, arbitrarily delayed pregnancy, and primary infertility are common in countries of the developed world. STDs and inadequate healthcare may lead to secondary infertility in developing countries along with primary infertility.[11]

PC Steptoe, a gynaecologist retrieved an oocyte laproscopically during a non- stimulated ovulatory cycle and RG Edwards, a British physiologist, fertilized the retrieved ovum in his lab by using the husband's sperm. He placed an 8-cell embryo inside the mother's womb. On July 25th 1978, J Webster performed an elective caesarean and brought the first test-tube baby, Louise Brown into this world.[12,13] This was the beginning of the IVF era. RG Edwards won the Nobel Prize in 2010 for his pioneering work.[14]

The wrong perception has prevailed since the early days of ART that this treatment is only for affluent countries and developing countries do not have the advanced technology to practice IVF.[15,16] However, the situation has changed when countries like Pakistan, Egypt, Middle East and India have managed to practice ART and provide treatment facilities to infertile couples locally with good success.[6,17] Infertility does not harm physical health but may affect the emotional, psychological and social health of the couple.[4,18]

When a doctor examines a female for infertility, a detailed medical history is mandatory. As ART is an expensive treatment, the investigations of the female have to be detail and methodical.[18, 19] Age of the female is the single most important factor in the outcome of any treatment.[20,21] Ovulatory dysfunction, history of systemic disorders and treatment along with the possible use of any recreational drugs like tobacco, marijuana or cocaine are important factors.[22]

Infertility may be unexplained when history, examination and investigations are unable to detect a cause i.e male factors and female factors along with ovulation dysfunction and tubal causes. Investigations need to find out cervical, uterine, ovarian, tubal and peritoneal causes. A high BMI may have an effect on ovulation but does not affect the results of super-ovulation and IVF.[23]

The intention of this study was to look into the female factors in the couples visiting a private ART clinic, for assessment of infertility and choice of treatment. The objective was to analyze the clinical and laboratory characteristics of the Pakistani females presenting themselves for in vitro fertilization in private setting.

SUBJECTS METHODS

The infertile couples who came to Lahore Institute of Fertility and Endocrinology (LIFE) from 1st January to 31st December, 2013 for infertility work up were included in the study. The sampling technique used in this study was non-probability, convenient, purposive and time based, as the study design was cross sectional. Sample size was 534 patients of ART. A questionnaire was used for the data collection. This questionnaire included information on woman's demographics, obstetric and infertility history, radiology and hormone investigation. SPSS version 20 was used for the data analysis.

The females were asked about age, parity, menstrual cycle, duration of infertility. Previous investigations were also checked to assess tubal patency. Then females were examined by gynaecologists and investigated to ascertain the condition of pelvic adnexa and uterine cervix. Level of FSH was checked and ultrasound was performed (TVS) to look for antral follicles. Systemic and local physical examinations were done of both partners. It was followed by semen analysis including both morphological and functional tests. Age, FSH, BMI, menstrual cycle, parity antral follicle, stimulation, duration of infertility, previous investigation, type of infertility, pelvic adnexa, uterine cervix were the variables for the females.

RESULTS

Patients age less than 35 were 398 (74.5%) aged between 36 and 39, 103 (19.3%), aged over 40 were 33 (6.2%). Those with follicle stimulating hormone (FSH) less than 9 IU/ ml were 418 (78.3%), between 9-11 IU/ ml were 83 (15.5%), greater than 11 IU/ ml were 33(6.2%). Patients with regular menstrual cycle were 498 (93.3%) and those with irregular menstrual cycle were 36 (6.7 %). Patients having parity were 118 (22.1%) who had delivered a child, 55 (10.3%) had an abortion, 17 (3.2%) patients had ectopic pregnancies, 344 (64.4%) were nulliparous.

Those with a Body Mass index (BMI) less than 25 were 163 (30.5%), between 25-30 were 219 (41.0%), those over 30 were 152 (28.5%). As with the female factor, no cause was found in 254 (47.6%), tubal

cause in 120 (22.5%), PCO in 68 (12.7%), endometriosis was in 13 (2.4%), un-explained was in 79 (4.8%). Count of Antral follicles of 6-8 per ovary was in 369 (69.1%), 3-5 per ovary was in 129 (24.2%), 0-2 per ovary was 36 (6.7%). Primary infertility was seen in 350 (65.5%) patients, secondary infertility in 178 (33.3%), unexplained infertility in 6 (1.1%). Regarding duration of infertility, in 113 (21.2%) patients it was 2 or less than 2 years, in118 (22.2%) was 4 years, in 49 (9.2%) was 5 years, in 87(16.3%) was 7 years, in 82 (15.4%) was 10 years, and in 85 (15.9%) was greater than 10 years.

Table I: Descriptive analysis of characteristics of women

Variables	Category	Frequency	Percentage
Age	Less than 35 years	398	74.5
	35-40	103	19.3
	Greater than 40	33	6.2
FSH	<9 iu/ml	418	78.3
	9-11 iu/ ml	83	15.5
	>11 iu/ml	33	6.2
Parity	delivered	118	22.1
	abortion	55	10.3
	ectopic	17	3.2
	Nulliparous	344	64.4
BMI	<25	163	30.5
	25-30	219	41.0
	>30	152	28.5
Antral follicles	6-8/ ovary	369	69.1
	3-4/ovary	129	24.2
	0-2/ovary	36	6.7
Duration of infertility	2 and less than 2 years	113	21.2
	4 years	118	22.1
	5 years	49	9.2
	7 years	87	16.3
	10 years	82	15.4
	Greater than 10 years	85	15.9

DISCUSSION

The social and environmental characteristics a woman in the western countries is different as compare to eastern countries. The research data available is mainly about the western woman that is applied to the eastern woman without giving a heed to its implications. Our aim was to study women from Pakistan who may be biologically similar but have a different sociological, demographic, geographic and environmental background.

Females are investigated for infertility with the aim to find the cause, choose treatment with best results. Tests for ovulation and tubal patency are done along with semen analysis. Studies done in the past showed male factor infertility is seen in 25-35 % of the couples, 14-22 % tubal factor, 10-27 %, ovulation problem 5-6 % endometriosis and 10-17 % unexplained infertility.[24]

In a study done by Maheshwari et al, in 2008 younger women presented with different causes of infertility as compared to older women. Primary infertility was found in 51 % and 26.9 % women had age more than 35 years. Unexplained fertility was a common cause after 35 years of age.[24]

When the age increases females become less fertile and sometimes ART fails to compensate.[25,26] Age of the female is one of the most important factor determining fertility and as the age increases obstetric as well as perinatal risks increase.[24, 27] Both ovary and uterus are affected by aging. If we understand ovarian aging we may help our patients in treatments with optimal results.[28]

Lower fecundity is associated with high BMI and appears in all groups of women. A decrease in weight may increase the chance of pregnancy regardless of parity, regular menstruation, age etc.[29,30] Polycystic ovary syndrome (PCOS) is more apparent in women of reproductive age and high BMI. The majority of these women have ovulatory infertility. Ovulatory dysfunction causes infertility and is on the rise as obesity is increasing. Obesity is one of the causes of ovulatory dysfunction.[31, 32] Women with ovulatory infertility and irregular menstruation should lose weight.[33]

It is a known fact that being overweight markedly reduces success in assisted reproductive technology (ART).[34] Lifestyle changes may help in reducing weight, and this helps in restoring the regularity of menstrual cycle and increasing chances of conception.[32,35,36]

Fertility decreases as age advances and it is expected that ovulation may become to an end many years before menopause because of decrease in the number of eggs in the ovaries which is age related.[37] Women's age reflects ovarian aging. When the number of follicles decreases, menstrual cycle becomes irregular, which may culminate as cessation of menses. Oocyte quality is also affected as age increases.[38]

Number of oocytes diminishes when folliculogenesis decreases with decrease in the ovarian primordial follicles as female age increases

with increase in basal FSH.[26,39,40,41]

Lentonstudied the hormonal changes before and after the menopause and compared them with the hormonal changes in the women in control group. They showed that level of FSH increased many years before the menopause. This increase in FSH was related to chronological age as well as to the onset of menopause.[41]

Syrop et al, undertook a study to look into the factors which were considered to be important in the success if assisted reproduction. They concluded that oocyte retrieval was associated with age along with ovarian volume. Less number of oocytes are retrieved with advancing age and small ovarian volume.[42]

With the increasing age folliculogenesis is diminished and FSH levels become significantly higher. So as the age increases there are higher levels of FSH and decreased number of oocytes are collected.[39] There was a significant association of number of oocytes and basal level of follicle stimulating hormone and this association was not dependent on the age. Basal FSH was a better predictor of number of oocytes retrieved.[43]

Menstrual cycle has 2 phases, Follicular and Luteal phase. Luteal phase varies less as compared to follicular phase; follicular phase becomes shorter with age.[44] Length of follicular phase showed a visible decrease with age; women aged 18-24 it was 14.2 days long and women aged 40-44 it was 10.4.[41] Host factors such as ethnicity which is not modifiable and modifiable environmental factors such as smoking, physical exercise and obesity may have influence on the menstrual characteristics of the women[45] Cycles stimulation responses are predicted by Antral follicle count. It also significantly predicts success in clinical pregnancy as well as delivered pregnancy.[46]

Fecundity decreases with age; irrespective of natural or stimulated ovarian induction. Age remains to be of immense importance in predicting potential pregnancies in women with regular menstrual cycles. But research has shown that only chronological age is unable to predict response of the ovaries.[47] Follicles are progressively depleted as age of the female advances and response of the set of follicles to stimulation by gonadotropin is also lessened.[48] Though ovarian reserve tests are able to predict the response of follicles to the ovarian stimulation but may not be of any help towards prediction of IVF success in the form of pregnancy or outcome.[49]

CONCLUSION

Importance of recognition of infertility as a health issue will not only remove treatment barriers but also improving the health seeking behaviors of the infertile couple. Health education about fertility will ease the social taboos and improve the delivery of health services to infertile couples. Age, FSH, menstrual regularity, parity, BMI, female factor, antral follicles, type of infertility, duration of infertility may have a predictive value forecasting the success of the outcome of IVF. Further research is needed on these lines.

Acknowledgment

We would like to acknowledge Biostatisticians Saba at LIFE Sardar and Rameen Nisar for entering and analyzing the data.

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