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Original Article

A Study on Management of An ovulatory Infertility in Urban Nepalese Population

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ABSTRACT

The objective of this study is to investigate the causes of an ovulatory infertility, its management and outcome in an urban Nepalese population. An observational study conducted was among 58 couples visiting the department of Infertility Centre Pvt. Ltd. from November 2010 to May 2011. Infertile patients were mostly of middle reproductive stage ages from 24-39 years .The major contributing factors for female infertility were menstrual disorders due to hormonal disorders, premature ovarian failure and polycystic ovarian syndrome. The main menstrual disorders were amenorrhea (15.5%), oligomenorrhea (10.3%) and menorrhagia (3.4%). The various types of female infertility observed were PCOS (75.9%), premature ovarian failure (3.40%) and poor ovarian reserve (20.70%). Male causes of infertility were mainly oligospermia (10.7%), azoospermia (13.8%), asthenospermia (3.4%) and teratospermia (10.4%). The different types of infertility observed were primary infertility (48.3%) and secondary infertility (27.6%). For the management of anovulatory infertility, female patients with hormonal disorders were prescribed hormonal replacement therapy (48.3%) and those who failed to ovulate were prescribed Clomiphene Citrate (27.6%) for medical ovulation induction. Letrozole (17.2%) prescribed as an aromatase inhibitor used in whom ovulation induction with Clomiphene Citrate had failed. Hyponid, a herbal formulation was given as insulin sensitizing agents. M2 tone was given in managing functional menstrual disorders of adolescents. Vitamin B complex along with Clomiphene Citrate and folic acid prescribed for prevention of fetus neural tube defect. Calcium was prescribed for treating the disturbances with premenstrual symptoms .The majority of the patients who have undergone ovulation induction with Clomiphene Citrate were conceiving mainly by Intrauterine Insemination technique. Infertility is considered as a disgraceful condition, and something that is not discussed freely in developing countries like Nepal. With timely detection and proper therapeutic management an ovulatory infertility can be avoided.

Key Words: Anovulation, Clomiphene citrate, Premenstrual Syndrome, Semen Analysis

INTRODUCTION

Infertility is one of the major health problems in the society. It has been avoided or reduced in many developed countries. However, it is still a severe problem in many developing countries like Nepal. There are several reasons behind it. Before describing the causes it is worthwhile to understand some of the important biological mechanisms of the human body. Ovulation is the result of a maturation process that occurs in the hypothalamic-pituitary-ovarian (HPO) axis and is orchestrated by a neuroendocrine cascade terminating in the ovaries. Any alteration results in a failure to release a mature ovum, leading to an ovulatory cycles. Anovulation may manifest in a variety of clinical presentations, from luteal insufficiency to oligomenorrhea. Anovulation is a not a disease but a sign, in much the same way that polycystic ovaries are the manifestation of a much larger disease process [1]. Infertility is a condition characterized by a reduction in the ability to reproduce or achieve conception [2, 3]. It surprises most people to learn that infertility is a female problem in 35% of the cases, a male problem in 35% of the cases, a combined problem of the couple in 20% of cases, and unexplained in 10% of cases. It is essential that both the man and the woman should be evaluated during an infertility work-up [4].

This study aspires to explore the causes of an ovulatory infertility, its management and outcome in an urban Nepalese population.

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METHOD

Sampling frame and sample size: It is an observational study that consists of all the infertile couples visiting the Infertility Centre Pvt. Ltd., Bijulibazar, Kathmandu, Nepal from November 2010 to May 2011.The written consent was taken from the Infertility Center to conduct the data collection as well as informed consent was taken from the patients, ensuring them not to disclose their privacy. Only fifty eight couples were encountered during the study period.

Selection of patients (Recruitment Method): The couples were selected on the basis of the following inclusion criteria:

- Couples with either primary infertility or secondary infertility or recurrent miscarriage.
- Patients with high Follicle Stimulating Hormone (FSH) or very low FSH & Luteinizing Hormone (LH) levels.
- Patients with abnormal thyroid function.
- Patients with hyperprolactemia.
- The patients admitted in the inpatients department were excluded from the study.

Investigations (Sample size calculations): Semen analysis was carried out for males. Hormonal assay, ultrasonography for ovarian morphology and urine test were performed on female patients. Hormonal investigations such as Follicle Stimulating Hormone (FSH), Luteinising Hormone (LH), Serum Prolactin, and Thyroid Stimulating Hormone (TSH) were carried out. The hormonal assay was performed in the two or three days of the cycle. It was ensured among women with amenorrhea care that they had not taken any hormones or suffered with withdrawal bleeding for at least six weeks before the assay. The hormone assay was performed by Enzyme Linked Immunosorbent Assay (ELISA). Semen analysis investigation was done by microscopy at the laboratory of Infertility Centre Pvt. Ltd.

Data Collection and analysis: The investigation results were entered into a proforma. The additional information about the couples such as age previous medical history, primary fertility, secondary fertility, recurrent miscarriage, trying years, gynecological history, physical examination and concurrent use of other drugs were also recorded. The collected data were compiled into Microsoft Excel and then transferred to Statistical Package for Social Sciences (SPSS 17) to complete the necessary analysis. Beyond basic frequency tables, diagrams, means and medians, correlation analysis was used for assessing relationship between numeric variables and Chi-square test was used for assessing association between categorical variables.

RESULTS

The age range of the female patients was 20-40 years with a mean 28.14 and a standard deviation of 3.78 years. The males had age range of 23-46 years with mean 32.74 years and a standard deviation of 4.74 years. The higher percentage of the females (55.2%) was in age group of 25-29 years and 43% of male patients were in the age group of 30-34 years (Figure 1). Higher percent of patients (96.6%) were of middle reproductive stage i.e. patients in age group 24-39 years, as classified by STRAW stages of reproductive aging. The major menstrual disorders were amenorrhea (15.5%), oligomenorrhea (10.3%) and menorrhagia (3.4%). Higher percentage of females had average menstrual bleeding (61.2%) followed by scanty (28.6%) and heavy (10.2%). Premenstrual tension was seen in 93.1% of patients. Similarly, mastodynia and pruritis vulva were observed in 41.4% and 15.5% of females respectively. About 10% of male had medical history of surgery, 6.9% had tuberculosis and 5.2% had mumps.

Hysterosalpingography discovered tubal occlusion in 7%, salpingectomy in 1.8% and filling defects in 1.8% of cases. Various types of male pattern of infertility was observed in semen analysis mainly oligospermia (10.7%), azoospermia (13.8%), asthenospermia (3.4%) and teratospermia (10.7%). Pus cells were observed in 13.4% cases (Figure 2). Nearly 2 % of male patients had $\leq$30 % sperm motility. The different types of infertility such as primary infertility (48.3%) and secondary infertility (27.6%) were observed (Figure 3). The various types of female infertility observed were PCOS (75.9%), premature ovarian failure (3.40%) and poor ovarian reserve (20.70%) (Figure 4).

Abnormal female hormonal assay revealed LH: FSH (>2) 9%, PRL (20-100) 48%, TSH (>5) 10% estradiol (30-200) 11 % and estradiol (<30) 22% (Figure 5). Thyroxin was prescribed for 72.4% patients suffering from hypothyroidism whilst anti-thyroid hormones (19%) were prescribed for treating hyperthyroidism. Insulin sensitising agents (51.7%) and hormone replacement therapy (48.3%) were mostly prescribed for treating infertility (Figure 6). The total number of patients conceived by using CC with the IUI technique was 11 whilst using CC without IUI technique was 5. Therefore, majority of patients who had undergone ovulation induction with CC were conceiving mainly by IUI technique (Table 1).

DISCUSSION

The treatment of disorders of ovulation depends upon the underlying cause. The prevalence of infertility is more in middle reproductive stage [5, 6]. The mean years trying to conceive was found to be more than three years [7]. Age range of female suffering from infertility was 20-40 years whereas that of male was 23-46 years. Fertility peaks when women are in her late teens and early twenties. It begins to decline at age thirty and drops more rapidly after age 35 years. It plummets after age 40 and pregnancy after age 45 is rare. The effect of maternal age on fertility is an effect of a larger proportion of abnormal embryos with increasing maternal age [8]. Major contributing factors of female infertility were found to be amenorrhoea, oligomenorrhea and menorrhagia [9, 10].The common features seen in patients with infertility were premenstrual tension, mastodynia and pruiritis [11]. Frequently unaddressed, is the effect of the male age. In several studies conducted it was found that the semen quality drops with age [9-12]. Semen analysis of male patients showed the higher percentage of azoospermia, asthenospermia and teratospermia [12-19].

Hysterosalpingography is important to identify whether the uterus and fallopian tubes are normal or not [20, 21]. About 3% had POF also known as hypergonadotropic hypogonadism that occurs when oocytes and surrounding cells are lost prior to 40 years of age [22]. Nearly 76% female patients found to have PCOS. Poor ovarian reserve was found in 20.70%. LH: FSH (>2) MIU/ml was seen in 9%, PRL (20-100) ng/ml in 48%, TSH (>5) MIU/ml 10%, estradiol (30-200) in 11% and estradiol (<30) in 22% patients. For the management of anovulatory infertility, 27.6% were prescribed CC for medical ovulation induction. Hyperprolactemia was treated with bromocriptine, hypothyroidism with thyroxin and hyperthyroidism treated with anti-thyroid hormones [10, 23]. About 7% of the female patients who visited the clinics had suffered from recurrent miscarriage and were treated with the uterine relaxing agents [24]. Around 48% were prescribed hormone replacement therapy such as progesterone, norethidrone acetate, ethinyl estradiol and testosterone [25, 26]. Letrozole was used as aromatase inhibitor to those patients in whom the ovulation induction with CC had failed [27]. Hyponid, an herbal formulation was given as insulin sensitising drug [28]. M2 tone was also used as an alternative to conventional hormonal therapy in managing the functional menstrual disorders of the adolescents [29]. Addyzoa capsules were prescribed for male to improve the semen quality by increasing the sperm count and sperm motility [30]. Vitamin B complex along with the CC was prescribed for neural induction. Calcium was prescribed for treating the disturbances associated with the PMS [31]. The urine test showed chlamydia spots in one patient, repeated UTI in three patients and rubella positive in four patients. Antibiotics such as doxycycline, amoxicillin and clavulanic acid, azithromicin, norfloxacin, rovamycin and clotrimazole were prescribed to treat various encountered infections of the patients [32]. Here, 11 female patients conceived by IUI after undergoing ovulation induction with CC, whilst 5 female patients conceived by ovulation induction only without IUI [33-36].

Although the study provides significant results it has some limitations. The study was monocentered involving limited sample sizes and follow up of patients was also difficult. However, this study definitely provides various important issues related to manage the anovulatory infertility not only in urban Nepalese population but also in other countries of similar backgrounds.

Conclusion: Pregnancy is direct result of ovulation. Patients who do not ovulate cannot conceive without induction and often may need assisted reproductive technology. In this study contributing factors of anovulation due to female infertility were hyperprolactemia, hypothyroidism and hyperthyroidism whereas male infertility were mainly oligospermia, azospermia, asthenospermia and teratospermia. This study shows variety of disorders of ovulation were successfully resulted ovulation by simple CC induction in majority of cases. In addition, patients who have undergone ovulation induction with CC were conceiving mainly by IUI technique. Hence, this study may serve as a reference to the medical community to understand and reduce the infertility in urban Nepalese population.

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Table 1: Comparative Result of IUI & Non IUI

Ovulation induction with CC	IUI	Non IUI
	11	5

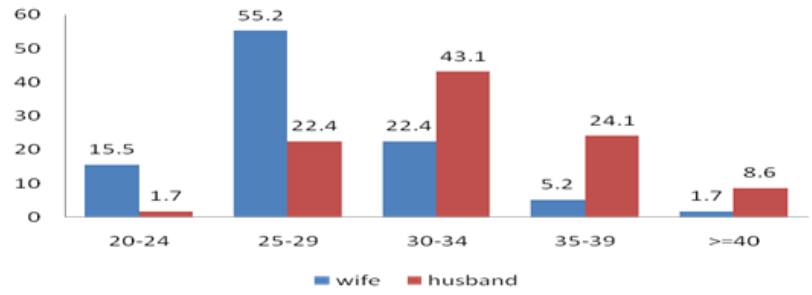

Figure1: Percentage of patients as per their age group

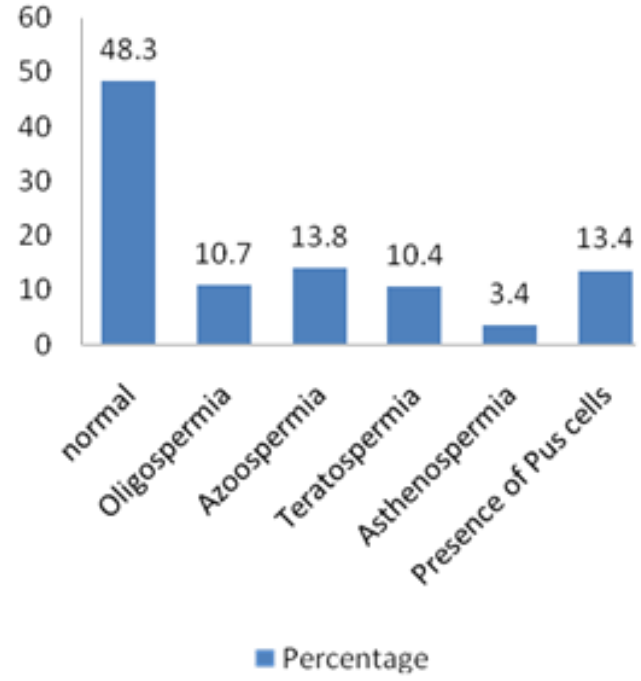

Figure 2: Percentage of male semen analysis

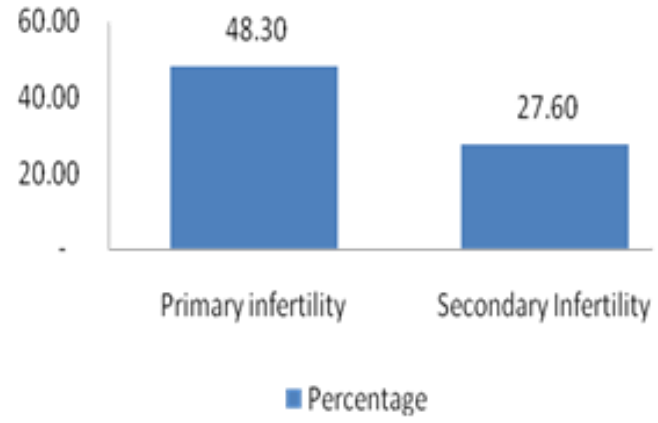

Figure 3: Types of infertility

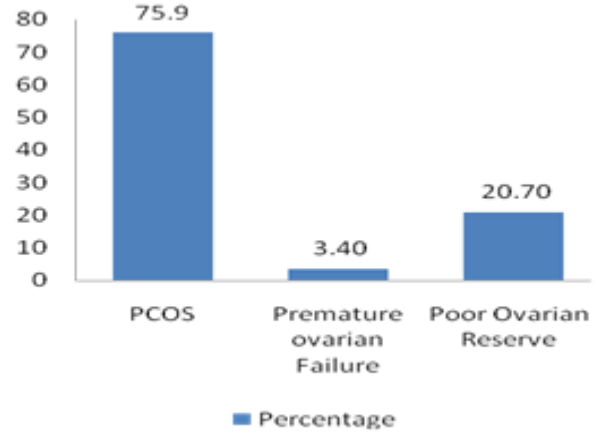

Figure 4: Types of female infertility

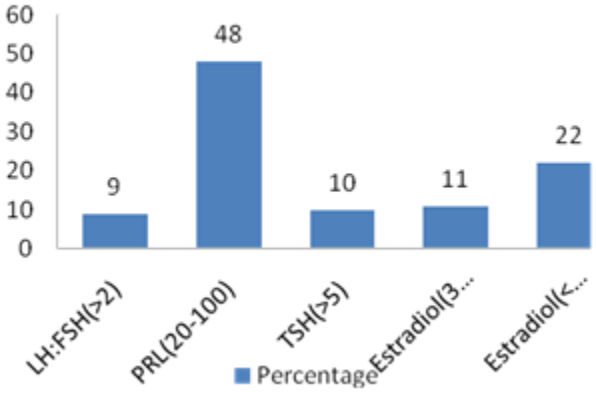

Figure 5: Abnormal Female Hormonal Assay

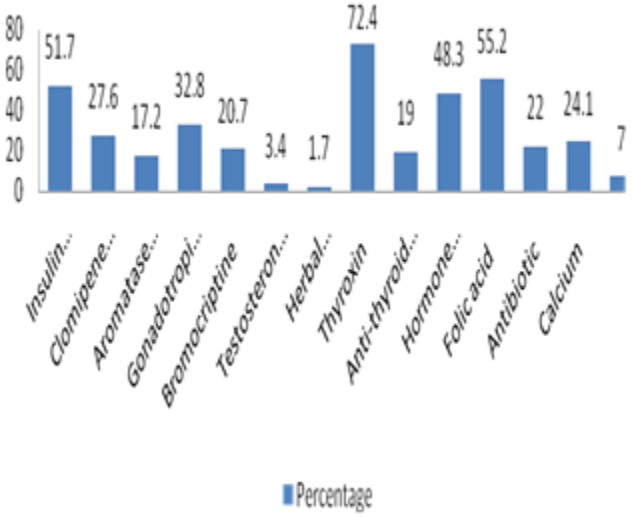

Figure 6: Treatment of infertile patients

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