



A prospective study of Prescribing Pattern of drugs in female infertility cases with Pharmacoeconomics at a tertiary care center in India

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ABSTRACT

The global health community has had great success in improving maternal and child health in the past decade, partly through a focus on reproductive health. Infertility is a critical component of reproductive health which is a global public health challenge. The objectives of the study is to evaluate the prescribing pattern and criteria for selection of drugs for infertility at Basaveshwar Hospital, Gulbarga, India. To analyze the rationality among the prescriptions analysis of pharmacoeconomics. After approval by the Institutional Ethics Committee, 100 consenting female patients aged 18-44 years having diagnosed of infertility, were included in this prospective, observational study. In our study, 49% of the patients belonged to age group 26-30. Twenty six percent were newly diagnosed patients. Eighty seven percent had primary infertility. Polycystic ovaries were the most common cause of infertility (29%). The patients were treated with drugs alone, or with drugs and Intra Uterine Insemination, or with drugs and In Vitro Fertilization depending on their age and cause of infertility. Clomiphene citrate (58%) was the most common drug prescribed for ovulation induction. Twenty two percent of the patients conceived in our study and the average cost of drugs per prescription was 89.55 USD. Women with reproductive dysfunction who fail to achieve pregnancy need assisted reproductive technology. Providing an affordable reproductive therapy is a necessity in the developing world. Modifications of the traditional protocols and monitoring systems will help in reducing costs.

INTRODUCTION

The ability to reproduce and to perpetuate the species is one of the most remarkable features of the living organisms. Fertility and infertility have been a major concern to mankind since time immemorial. Infertility is seldom, if ever, a physically debilitating disease. It may, however, severely affect the couple's psychological harmony, married life and also the healthcare services along with the social environment [1]. The clinical definition of infertility used by the World Health Organization (WHO) is "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" [2]. Infertility can be subdivided into primary infertility, that is, no prior pregnancies, and secondary infertility, referring to infertility following at least one prior conception [3]. Globally, most infertile couples suffer from primary infertility [4]. The demand for overcoming infertility is increasing year by year. Hence there is a

quantum jump in the technology used in the diagnosis and therapy of infertility. There is also a tremendous escalation of cost in management of infertility cases. This fact is an important cause of concern in the economic development of a country. Therefore the following study is an attempt made to see the rationality among the prescriptions with principle aim to study the efficacy, tolerability, safety and cost-effectiveness of the drugs used in infertility cases.

MATERIALS AND METHODS

This prospective, cross-sectional observational study was conducted in the department of Obstetrics and Gynecology at Basaveshwar Teaching and General Hospital, Gulbarga, Karnataka, India. The duration of the study was 15 month period from April 2013 to June 2014 on 100 consenting female infertility patients. Study was approved by institutional ethics committee and written informed consent was obtained from each patient before enrolment. Demographic details, necessary clinical data,

and medication details were collected in a specially designed proforma. Data on utilization of different classes as well as individual drugs were subjected to descriptive analysis.

Inclusion criteria:

Female patients presenting with infertility in the outpatient department of the hospital within the reproductive age group (18-44 years) consenting for the study.

Exclusion criteria:

1. Cancer patients, at terminal stage.
2. Females before and after reproductive age

Drug use indicators were determined as follows:

1. WHO Core Indicators
 - i. Prescribing indicator
 - ii. Patient care indicator
 - iii. Facility indicator
2. Complimentary indicator

RESULTS

In our study, 49% of the patients belonged to age group 26-30. Twenty six percent(26%) were the newly diagnosed patients.

Eighty seven percent (87%) had primary infertility. Table 1 shows that polycystic ovaries were the most common cause of infertility (29%). Table 2 - The patients were treated with drugs alone, or with drugs and Intra Uterine Insemination (IUI), or with drugs and *In Vitro* Fertilization (IVF) depending on their age and cause of infertility. Table 3 - Folic acid was given to all the patients. Clomiphene citrate (58%) was the most common drug prescribed for ovulation induction followed by Human Menopausal Gonadotropin (HMG) (53%). Figure 1 depicts the drugs used for induction of ovulation. Table 4 shows that 22% of the patients conceived in our study. Table-5 depicts the World Health Organization (WHO) drug use indicators. The average cost of drugs per prescription was 89.55 USD.

DISCUSSION

In today's world, medical science has various new and advanced technologies like ART (assisted reproductive technology) and IVF to help those numerous childless couples, who are seeking treatment for infertility. But, it would be nice if we had some test to provide the outcome prognosis for assisted reproductive technology [5]. In the present study, the pattern of drugs used to treat infertility has been studied along with the evaluation of the outcome of therapy and cost of drugs in 100 study subjects who fulfilled the inclusion and exclusion criteria.

Table 1, shows the various causes of infertility. In our study,

Table 1 : Distribution of patients according to the cause of infertility

Cause of infertility	Percentage of patients(n=100)
Polycystic ovaries	29
Polycystic ovarian syndrome	8
Subclinical hypothyroidism	19
Endometriosis	16
Age related ovulatory dysfunction	13
Hostile mucus	4
Unexplained	11

Table 1 : Distribution of patients according to modality of treatment

Mode of treatment	Percentage of patients (n=100)
Drugs alone	52
Drugs + Intrauterine insemination	19
Drugs +Invitro fertilization	29

Table 3 : Distribution of patients according to the drugs administered

Drugs	Percentage of patients (n=100)
Folic acid	100
Progesterone	62
Clomiphene citrate	58
HMG	53
Estrogen	41
HCG	40
FSH	39
Thyroxin	19
Multivitamin	17
Aspirin	16
Coamoxiclav	14
Metronidazole	14
Ranitidine	14
Ibuprofen	14
Cetrorelix	13
Enoxaparin	13
Antioxidants	12
Metformin	8
Tamoxifen	6
Prednisolone	4
Filgrastim	3
Pantoprazole	2
Domperidone	2

HMG : Human Menopausal Gonadotropin
 HCG : Human Chorionic Gonadotropin
 FSH : Follicle Stimulating Hormone

Drugs for ovulation induction

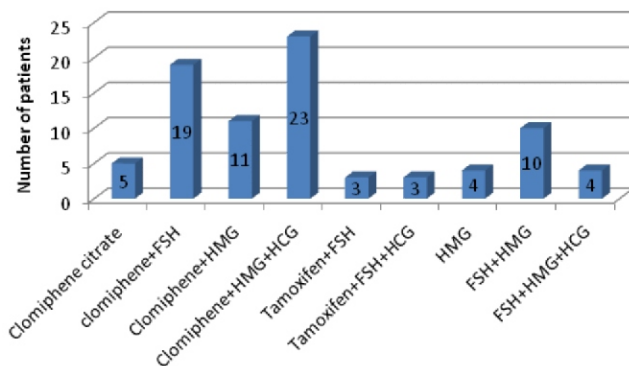


Figure 1: Drugs Used for Induction of Ovulation

Table 4 : Distribution of patients according to outcome of therapy

Outcome of therapy	Percentage of patients (n=100)
Conceived	22
Not conceived	62
Left against medical advice	16

Table 5 : WHO Drug Use Indicators

Prescribing Indicators	Data
Average number of drugs per prescription	5.75
Percentage of drugs prescribed by generic name	11%
Percentage of prescriptions with an antibiotic prescribed	14%
Percentage of prescriptions with an injection prescribed	96%
Percentage of drugs prescribed from essential drug list	64.7%
Patient care indicators	Data
Average consultation time	18minutes
Average dispensing time	4 minutes
Percentage of drugs dispensed in hospital attached pharmacy	64.7%
Percentage of drugs adequately labeled	100%
Patient's knowledge of correct dosage	67%
Facility indicators	Data
Availability of copy of essential drug list	Yes
Availability of key drugs	64.7%
Complimentary drug use indicators	Data
Average drug cost per prescription	89.55 USD
Percentage of drug cost spent on injection	84.74%

29% of patients had polycystic ovaries whereas only 8% had polycystic ovarian syndrome. PCOS was diagnosed by the presence of oligomenorrhea, clinical and biochemical signs of hyperandrogenism, polycystic ovaries (PCO) and follicle stimulating hormone (FSH)/luteinizing hormone (LH) ratio $\geq 2:1$ [6]. In our study, 19% of patients had subclinical hypothyroidism. Hashimoto's thyroiditis is the most common endocrinopathy in premenopausal women, and is associated with various gynecological problems, including recurrent miscarriage and unexplained infertility. Strict thyroid hormone supplementation regimen is beneficial in order to achieve lower TSH levels [7].

Table 2, shows the modality of management of patients. Based

on the age of patient, diagnosis, duration of infertility the patients were treated with drugs followed by either intrauterine insemination or *in vitro* fertilization. Table 3, shows the distribution of patients according to various drugs administered. In our study, 100% of the study subjects (n=100), have received folic acid, as it is essential to prevent neural tube defects in the fetus. Progesterone preparations were given in 62% of our patients either through oral or parenteral route and in some through both the routes. It is well established that luteal function is compromised in *in vitro* fertilization (IVF) [8]. Thus progesterone supplementation is essential for luteal phase support in cases of luteal phase defect. Gleicher et al have further demonstrated that combined estradiol and progesterone substitution of the luteal phase of ovulation induction cycles increases the overall pregnancy rate, especially in women below the age of 38 years and in nulliparous females [9]. Metformin along with clomiphene citrate was used in patients having polycystic ovaries. In a high percentage of clomiphene resistant patients with PCOS, treatment with metformin is followed by regularization of menstrual cycles, reduction in hyperandrogenism, and improvement in rates of ovulation and conception. [10] Figure 1, shows the distribution of patients according to the drugs used for ovulation induction. Clomiphene citrate (selective estrogen receptor modulator), alone was used in 5% patients. Clomiphene citrate has antiestrogenic action, which induces gonadotropin secretion by blocking estrogenic feedback inhibition of pituitary [11]. Nineteen percent (19%) of patients received clomiphene with FSH (follicle stimulating hormone). FSH induces follicular growth, development of ovum and secretion of estrogens [12].

Table 4, shows the outcome of therapy. Twenty two percent (22%) of patients conceived, 62% did not conceive whereas 16% of patients left against medical advice. This shows the low success rate of infertility management despite advanced treatment.

Limitations

1. The sample size may not be adequate to reflect the exact picture of prescribing patterns of infertility.
2. The pharmaco-economic study in the context of cost benefit analysis could not be done because of limited number of cases and short duration of follow up of the cases.
3. Further studies in different hospitals are required which broadens the knowledge about the management of infertility along with its pharmaco-economics.

CONCLUSION

Women with reproductive dysfunction who fail to achieve pregnancy need assisted reproductive technology (ART). The use of pharmaco-epidemiological data can aid the design, delivery & evaluation of interventions to improve the use of fertility drugs and health outcomes of the patients. Infertility is a global health issue. The cost-effective management of such an enigmatic condition is the need of the hour. In our study, clomiphene citrate was used most commonly for ovulation induction. The rate of conception was poor being 22%. The average cost per prescription was 89.55 USD, which is highly unaffordable for people of all the sectors.

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