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A RETROSPECTIVE STUDY ON PRESCRIBING PATTERN OF DRUGS IN FEMALE INFERTILITY AT A TERTIARY CARE CENTRE IN SOUTH INDIA

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ABSTRACT

Introduction: 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. 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. **Aim/ Objective:** To observe the rationality among the prescriptions with principle aim to study the efficacy, tolerability, safety and cost-effectiveness of the drugs used in infertility cases and to evaluate the prescribing pattern and criteria for selection of drugs for infertility. **Methodology:** A retrospective, observational study was conducted in the department of Obstetrics and Gynecology at Owaisi Hospital and Research Centre, Hyderabad, India. The duration of the study was 15 month period from September 2015 to Dec 2016 on 300 consenting female infertility patients. **Results:** In our study 43% of patients belonged to age group 26-30. 45% were newly diagnosed patients, 65.3 % of patients had primary infertility and whereas 34.6% had secondary infertility. Menstrual irregularity were the most common cause of infertility (36%). The patients were treated with drug alone depending on their age and cause of infertility. Clomiphene Citrate (12.76%) was the most common drug prescribed for ovulation induction. 55.3 % of patients conceived during our study, women who failed to achieve pregnancy needed Assisted Reproductive Technology. The PDD and DDD was calculated to achieve rationality of prescriptions. **Conclusion:** Infertility is a critical component of reproductive health which is a global public health challenge. The use of pharmacoepidemiological data can help in designing, delivering and evaluating many interventions to improve the use of fertility drugs and outcome of patients as Infertility is a global health issue.

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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 and to evaluate the prescribing pattern and criteria for selection of drugs for infertility.

MATERIALS AND METHODS

This Retrospective, observational study was conducted in the department of Obstetrics and Gynecology at Owaisi Hospital and Research Centre, Hyderabad, India. The duration of the study was 15 month period from September 2015 to Dec 2016 on 300 consenting female infertility patients. No Institutional ethics committee approval was required as it is a retrospective observational study 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 (20-40 years) consenting for the study.

Exclusion criteria:

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

The data analysis was done as follows

1. Assessment of prescription pattern as per WHO drug use indicator.
2. The prescribed drugs were classified according to the Anatomical Therapeutic classification (ATC)-Defined Daily Dose (DDD) Classification.[5]
3. The prescribed Daily Dose (PDD) was calculated by taking the average of the daily doses of psychotropic drugs as PDD. The PDD to DDD Ratio was then calculated.[5]

RESULTS

Table 1 Based on Age.

Age	No. of Patients (%)
20-25	122(40.6)
26-30	129(43)
31-35	33(11)
36-40	16(5.3)

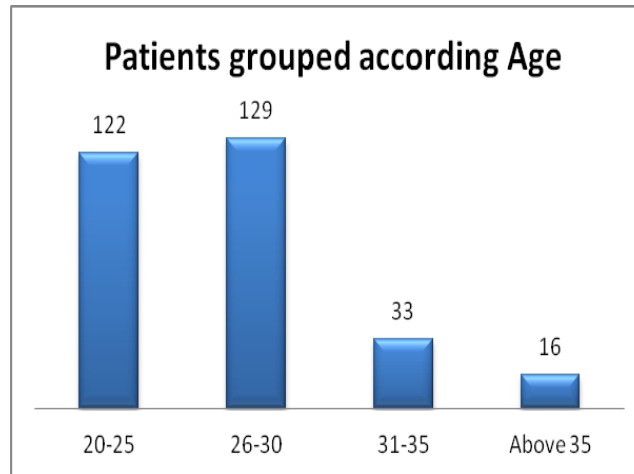


Figure 1: Based on Age.

Table 2 Grade of Infertility.

Grade of Infertility	No. of Patients (%)
Primary	196(65.3)
Secondary	104(34.6)

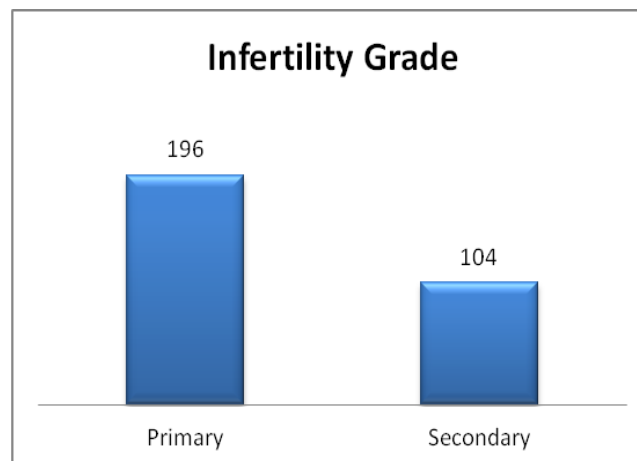


Fig 2: Grade of Infertility.

Table 3 Based on Associated Co- morbid Conditions/ Cause of Infertility.

Cause of Infertility	No. of Patients (%)
Polycystic Ovaries	31(10.3)
Polycystic Ovarian Syndrome	47(15.66)
Subclinical Hypothyroidism	16(5.3)
Endometriosis	14(4.6)
Age related Ovulatory dysfunction	12(4)
Hostile Mucus	7(2.3)
Increase level of Prolactin	24(8)
Menstrual irregularities	108(36)
Genital Kochs	14(4.6)
Unexplained	27(9)

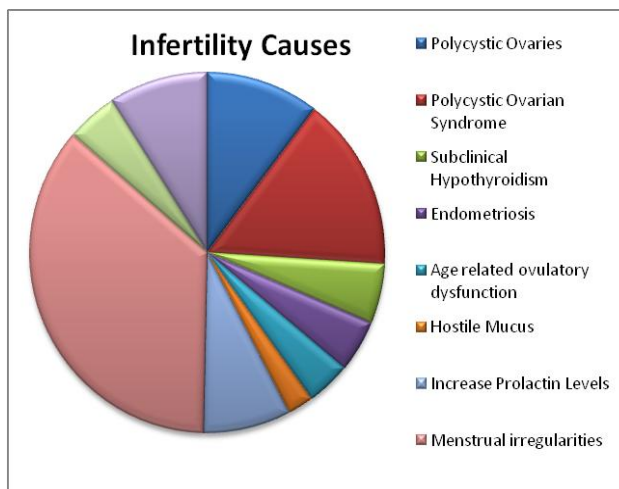


Fig 3: Based on Associated Co- morbid Conditions/ Cause of Infertility.

Table 4. Distribution of Drugs prescribed in patients (N=300).

Name of the Drugs	% of Prescribed drugs
Siphene (Clomiphene Citrate)	12.76
Duphaston (Dydrogesterone)	12.56
Progynova(Estradiol Valerate)	16.27
Regesterone (Norethindrone acetate)	8.70
HCG (Human Chorionic Gonadotropin)	1.18
Positive(Pioglitazone)	4.49
Glyciphage(Metformin)	2.03
Tamoxifen(Tamoxifen Citrate)	3.89
Geocyst (Metformin+Myoinositol)	0.92
Cabergoline(Cabergoline)	0.35
Folvite(Folic Acid)	86.9
Oflox(Ofloxacin)	5.7
Clindamycin(Clindamycin)	0.46
Norflox(Norfloxacin)	0.79
Anti Tubercular	0.18
Taxim (Cefixime)	0.31
Azwin(Azithromycin)	0.26
Monocef (Cefpodoxime)	0.56
Metrogyl IV(Metronidazole)	0.05
Augpen (Amoxicillin+ Potassium Clavunate)	0.27
Diclomol(Diclofenac+ Paracetamol)	4.24
Chymoral Forte(Chymotrypsin+Trypsin)	0.39
Voveran(Diclofenac Sodium)	1.91
Pyridoxine	7.42
Eltroxin(Levothyroxine)	0.21
Ebexid	0.13
Hydrocort(Hydrocortisone)	0.10
Zofer(Ondansetron)	0.36
Rabion(Rabeprazole)	4.49
Pantop(Pantoprazole)	1.69

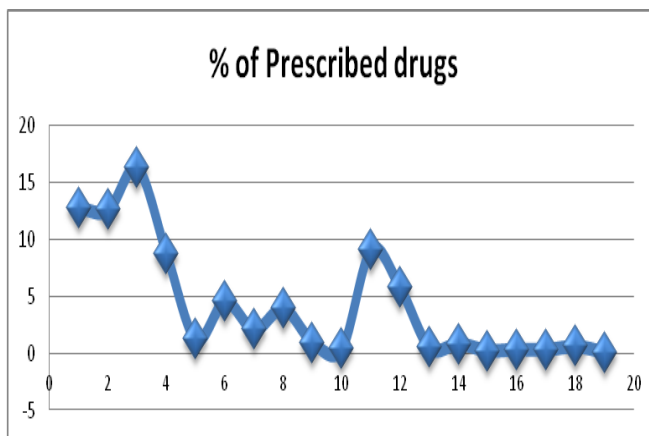


Figure 4. Distribution of Drugs prescribed in patients (N=300).

Table 5: Distribution of Patients according to outcome of therapy.

Outcome of Therapy	No. of Patients (%)
Conceived	166(55.3)
Not conceived	73(24.3)
Missed Abortions	12(4)
Ectopic Pregnancy	4(1.33)
Left Against Medical Advice	45(15)

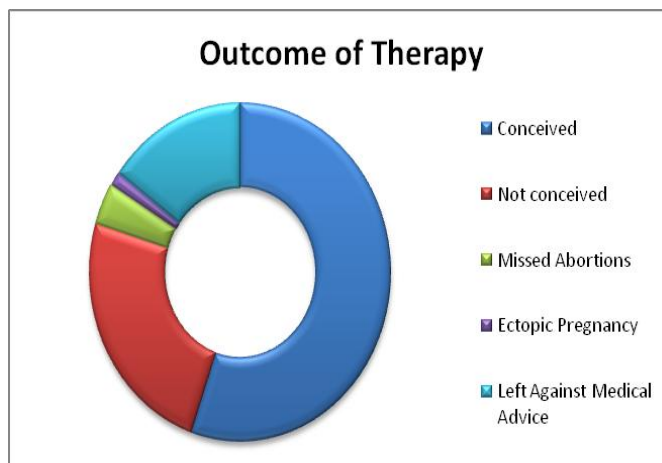


Figure 5: Distribution of Patients according to outcome of therapy.

Table 6: WHO Drug Used Indicators:

Prescribing Indicators	Data
Availability of copy of Essential Drug list & Hospital Formulary	Yes
Total no. of Drugs in 300 Patients during the study period	7569
Average no. of drugs per patient during the study period	25
Total no. of Ovulatory Drugs in 300 Patients during the study period	5328
Percentage of Ovulatory drugs per patient during the study period	70.3%
Percentage of Other drugs per patient during the study period	21%
Percentage of Drugs prescribed by generic Name	58%
Percentage of Prescriptions with an antibiotic prescribed	8.62%
Percentage of Prescriptions with an Injection Prescribed	1.34%
Percentage of Drugs prescribed from Essential Drug List / Hospital Formulary	80%

Table 7: PDD Values & PDD/DDD Ratios of Ovulation Drugs prescribed in a sample of 300 Patients attending Infertility Unit.

DRUG	ATC CODE	ROA	DDD (mg)	PDD (mg)	PDD/DDD
Siphene	G03GB02	Oral	50	161	3.22
Duphaston	G03DB01	Oral	10	31.7	3.17
Progynova	G03DC02	Oral	2	8.2	4.10
Regesterone	G03DC02	Oral	5	10.983	2.19
Cabergoline	G02CB03	Oral	0.5	0.045	0.09
Glyciphage	A10BA02	Oral	250	128.33	0.513
Positive	A10BG03	Oral	15	17	1.13
Tamoxifen	L02BA02	Oral	20	19.66	0.98
Geocyst	A10BA02	Oral	500	116	0.23
HCG-5000IU	G03GA01	IM	500	150	0.3
Folvite	B03BB01	Oral	5	9.06	1.81

$$\text{PDD} = \frac{\text{Quantity of drug dispensed} \times \text{Strength of drug}}{\text{No. of Patients}}$$

Table 8: DDD Values of Ovulation Drugs prescribed in a sample of 300 Patients attending Infertility Unit.

Drugs	No. of Prescribed Doses	Strength	DDD	WHO-DDD	DDD/300 Patients		PDD
		mg	mg	gm	mg	gm	
Siphene	966	50	50	0.05	0.166	0.0016	161
Duphaston	951	10	10	0.01	0.03	0.000033	31.7
Progynova	1232	2	2	0.002	0.007	0.0000066	8.21
Regesterone	659	5	5	0.005	0.016	0.000016	10.98
Cabergoline	27	0.5	0.5	0.0005	0.0016	0.0000016	0.045
Glyciphage	154	250	250	0.25	0.83	0.000833	128
Positive	340	15	15	0.015	0.05	0.00005	17
Tamoxifen	295	20	20	0.02	0.06	0.00006	19.66
Geocyst	70	500	500	0.5	1.66	0.001666	116.6
HCG-5000IU	90	500	500	0.5	1.66	0.0016	150
Folvite	544	5	5	0.005	0.0166	0.000016	9.06

DISCUSSION

In our study of 300 patients, 43% belonged to age group of 26-30 as shown in Table and Figure 1. 45% were newly diagnosed patients. 65.3% had primary infertility as depicted in Table and Figure 2. Causes of infertility are shown in Table and Figure 3 where menstrual irregularities (36%) were noticed as a common cause for infertility. Sub clinical hypothyroidism was observed in 5.3% of patients. Hashimoto's thyroiditis is the most common endocrinopathy in premenopausal women, and is associated with various gynecological problems, including recurrent miscarriages and unexplained infertility. Strict thyroid hormone supplementation regimen was followed to achieve desirable TSH levels.[6] The distribution of drugs prescribed in 300 patients during study period are depicted in Table and Figure 4 among which Clomiphene Citrate (12.76%) was commonly prescribed as ovulation induction drug as it has antiestrogenic action, which induces gonadotropin secretion by blocking estrogenic action, which induces gonadotropin secretion by blocking estrogenic feedback inhibition of pituitary[7] along with supportive therapy with Progynova (16.27%) as a study conducted by Gleicher et al have demonstrated the combined effect of estradiol and progesterone substitution of the luteal phase of ovulation induction cycles increases the overall pregnancy rate, especially in women below 38 years of age and nulliparous women[8], progesterone supplementations were advised in patients as it is essential for luteal phase support in patients with luteal phase defect.[9] and Folic Acid supplementation (86.9%) as it is a well-established fact that folic acid supplementation reduces neural tube defects of fetus.[9] In patients with PCOS showing Clomiphene resistance, metformin was prescribed followed by regular menstrual cycles, reduction in hyperandrogenism and improvement in rates of ovulation and conception.[10]

The outcome of therapy is depicted in Table and Figure 5, Conceived were 166(55.3%) patients. As illustrated in Table 6, Total drugs prescribed in 300 patients during the study period of 15 months were 7569 among which ovulatory drugs were found to be 5328. Percentage of ovulatory drugs per patient contributed to 70.3% whereas other drugs advised were 21%. Average no. of drugs per patient were 25; drugs prescribed with generics were 58%. Antibiotics prescribed were 8.62%, Drugs from EDL and Hospital Formulary were 80%.

PDD- Prescribed Daily Dose of drugs and DDD- Defined Daily Dose was calculated as depicted in Table 7. The ratio of PDD/DDD was calculated for each drug and the prescribing pattern of drugs was found to be rational as well explained in Table 8. In today's modern world, medical science has various new and advanced technologies like ART (Assisted Reproductive Technology) and IVF (In Vitro Fertilization) to help those numerous childless couples, who are seeking treatment of infertility, some tests should be initiated to provide the outcome prognosis for assisted reproductive technology [6] In the present study, the pattern of drugs used to treat infertility has been studied along with the evaluation of outcome of therapy in 300 patients after fulfilling the inclusion criteria.

LIMITATIONS OF THE STUDY:

1. The sample size of the patients was small to calculate prescribing pattern of drugs in infertility cases.
2. Follow up duration is short.
3. Further studies in various hospitals are required which will broaden the knowledge about the management of infertility.

CONCLUSION

Women with reproductive dysfunction who fail to achieve pregnancy need ART/IVF. The use of pharmacoepidemiological data can help in designing, delivering and evaluating many interventions to improve the use of fertility drugs and outcome of patients as Infertility is a global health issue.

CONFLICTS OF INTEREST:

No conflicts of interest to declare.

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