

Anovulatory infertility - management and maternal outcome

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Abstract

Background: Present study intended to evaluate causes of anovulatory infertility and its outcome after treatment.

Methods: This prospective cohort study was conducted in Jk loan hospital, Govt medical college, Kota. 100 females who attended Gyne OPD with infertility due to ovulatory disturbances were enrolled in the study and managed according to cause of anovulation and with ovulation induction. Results: Out of 100 enrolled 66 had polycystic ovarian syndrome, 20 had hyperprolactinemia, 10 had hypothyroidism and 4 had pituitary fossa tumour. We found that 65.15%, 65% and 90% conceived in polycystic ovarian syndrome, hyperprolactinemia and hypothyroidism group respectively. Pituitary fossa tumour group was not followed after surgical reference.

Conclusions: The ideal management lies in identifying root cause of infertility and managing the same before assisted reproductive techniques.

Keywords: Anovulation, Hyper prolactinemia, Hypothyroidism, Infertility, Polycystic ovarian syndrome,

Introduction

Infertility is defined as failure of couple to conceive even after 12 months of frequent unprotected intercourse. Infertility and subfertility affect a significant population. Infertility is a serious health issue worldwide affecting 10-15% of couple. According to a report by WHO one in every four couples in developing country is affected by infertility.

Factors that affect fertility are divided into 3 categories

1. Female factors (65%)
2. Male factors (20%)
3. Unexplained (15%)

Causes of female infertility

1. Ovarian (30-40%)
2. Tubal and peritoneal factors (25-35%)
3. Endometriosis (1-10%)

WHO classifies ovulatory disorders into 3 broad categories as follows:

Group 1 Hypogonadotropic hypogonadal anovulation (5-10% of anovulatory women): it includes low FSH and low Estradiol due to absent or abnormal hypothalamic GnRH secretion or pituitary insensitivity to GnRH.it

includes women with hypothalamic amenorrhea related to physical, nutritional or emotional stress, weight loss, excessive exercise and anorexia nervosa. Women in this group require hypothalamic-pituitary imaging to exclude a mass lesion.

Group 2 EU gonadotropin EU estrogenic anovulation (75-85%): FSH and estradiol levels remain normal and LH concentration may be normal or elevated. Most common example is PCOS, which is the commonest cause (70%) of anovulatory infertility.

Group 3 hypergonadotropic anovulation (10-20%) FSH levels remain elevated. The classical example is premature ovarian failure.

Hyperprolactinemic anovulation: Approx. 5-10% of anovulatory women have hyperprolactinemia, which inhibits gonadotropin secretion, consequently, serum FSH and estradiol also tends to be relatively low. Most of these women have oligomenorrhea or amenorrhea.

When ovulation is the only infertility factor, the prognosis for pregnancy generally is quite good, because modern ovulation induction strategies are highly effective. All anovulatory women deserve at least some preliminary evaluation to exclude important pathology, which may require medical attention before ovulation inducing agents. At least screening for thyroid disorder and hyperprolactinemia should be done because both require further evaluation and specific treatment. Screening semen analysis is prudent, because male factors are an important contributory cause in 20-40% of infertile couples. Preliminary HSG and TVS are recommended when medical history or physical examination raises suspicion for coexisting uterine or tubal infertility factors, for women over age 35, and when ovulation induction requires treatment with exogenous gonadotropins.

Aim and Objective

Aims

To assess the management of a subgroup of anovulatory infertility patients reporting to our institution.

Objective

1. To estimate the prevalence of various common causes of anovulatory infertility.
2. To evaluate the appropriateness of treatment in a patient group based on underlying pathology.
3. Comparing the outcomes of various therapeutic measures.

Material and Methods

This prospective cohort study was carried out in J K Lohia hospital, Govt. Medical College, Kota, Rajasthan, a tertiary health care centre, enrolling subjects who had attended the outpatient department of gynecology with complaints of infertility. Study was conducted over a period of one and a half years. One hundred females were enrolled in the study. Informed consent for the participation in the study was taken from the subjects.

Inclusion criteria

1. Infertile couple reporting to the OPD with a minimum 1 year of unprotected regular intercourse.
2. Women in the age group 25-35 years.
3. Women with ovulatory causes of infertility.

Exclusion criteria

1. Couples with male causes of infertility.
2. Women with causes of infertility other than anovulatory such as tubal block, pelvic inflammatory diseases.

Subjects that were eligible for participation in the study and agreed to participate, were explained about the purpose of the study and after taking informed consent, detailed history of the patient was taken, general physical

examination, per speculum and Pelvic examination was performed.

Levels of TSH, LH, FSH, Prolactin, Estradiol and progesterone were assessed.

USG abdomen and pelvis was used to evaluate status of uterus and adnexa and status of ovulation. HSG, SSG or Hysteroscopy was performed to evaluate uterine cavity and tubal status whenever required.

Management done accordingly with thyroxin in hypothyroid, with cabergoline in hyperprolactinemia, metformin in PCOS, antiestrogens like clomiphene

citrate for ovulation induction and according to individual requirement of patient.

Observations and Results

Total 100 patients with anovulatory infertility were enrolled in the study. Out of them 66 had PCOS, 20 had hyperprolactinemia, 10 had hypothyroidism and 4 had pituitary fossa tumour.

Table 1: Distribution of patients based on cause of anovulatory infertility

Sn.	Group wise distribution of patients	N	%
1	PCOS	66	66%
2	Hyperprolactinemia	20	20%
3	Hypothyroidism	10	10%
4	Pituitary fossa tumor	4	4%

Table 2: Mean age in each group

Sn.	Group	Mean age (years)	SD
1	PCOS	29.02	± 2.78
2	Hyperprolactinemia	28.85	± 2.62
3	Hypothyroidism	29.5	± 3.06
4	Pituitary fossa tumor	28	± 2.94
Total		100	100%

Table 3: Management of subjects

Sn.	Group	Management	Number	Percentage
1	PCOS	OC Pills	21	31.82%
		Metformin	24	36.36%
		OC Pills + Metformin	21	31.82%
2	Hyperprolactinemia	Cabergoline	20	100%
3	Hypothyroidism	Thyroxin	10	100%
4	Pituitary fossa tumor	Surgical Reference	4	100%

Table 4: Treatment added or altered

Group	Clomiphene Citrate		OC pills		Metformin		Total	
	n	%	n	%	n	%	N	%
PCOS	28	59.57%	12	25.53%	7	14.89%	47	71.21%
Hyperprolactinemia	7	53.85%	5	38.46%	1	7.69%	13	65.00%
Hypothyroidism	4	57.14%	2	28.57%	1	14.29%	7	70.00%

Table 5: Proportion of patients that conceived and did not conceive

Conceived/ Not Conceived	PCOS		Hyperprolactinemia		Hypothyroidism		Pituitary fossa tumor	
	n	%	n	%	N	%	N	%
Conceived	43	65.15%	13	65%	9	90%	0	0%
Not Conceived	23	34.85%	7	35%	1	10%	4	100%
Total	66	100%	20	100%	10	100%	4	100%

Table 6: Proportions of the patients in whom the pregnancy carried till term

Sn.	Group	Term		Miscarriage		Total	
		n	%	n	%	N	%
1	PCOS	30	69.77%	13	30.23%	43	100%
2	Hyperprolactinemia	12	92%	1	8%	13	100%
3	Hypothyroidism	7	78%	2	22%	9	100%
4	Pituitary fossa tumor	0	0%	0	0%		
	Total	49		16			

Discussion

In the present study that enrolled 100 patients with anovulatory infertility, prevalence rate of PCOS, hyperprolactinemia, hypothyroidism and pituitary fossa tumour was 66%,20%,10% and 4%, thus we observed that PCOS was the commonest cause of anovulatory infertility.

Melo AS, et al found in his study that PCOS represents 80% of anovulatory infertility cases.

Prevalence of hyperprolactinemia in our study was 20% that was nearly similar to another study (24) done by

nallusanys et al. Prevalence of hyperprolactinemia in our study was very high compared to study done by Agrawal M etal which was 11.5%.

Prevalence of hypothyroidism in our study was 10%, whereas it was 23.9% in infertile women in another study done by Verma etal.

Incidence of pituitary fossa tumour was slightly high (4%) in our study as compared to that seen in another study done by Verma etal where incidence was 0.33%.

Mean age of subjects in our study was 29.02+_{2.78}, 28.85+_{2.62}, 29.5+_{3.06} and 28+_{2.94} y in PCOS,

hyperprolactinemia, hypothyroidism and pituitary fossa tumour respectively which was nearly similar to that seen in another study 30.9+-9.2 done by beats man et al.

In hyperprolactinemia, all subjects were managed using cabergoline while in hypothyroid group all subjects were managed using thyroxin. Patients that presented with pituitary fossa tumour were referred to surgical ward.

Good clinical practice recommendations for management of infertility in patients from India with PCOS were proposed by an author Malik S et al. Author recommended following measures.

1. Counseling in preconception phase.
2. Modification of life style
3. Pharmacological measures
4. Surgical measures
5. Assisted reproductive technologies

In our study, apart from life style changes, subjects with PCOS were pharmacologically treated with either OC pills or metformin alone or a combination of both.

Melo A S et al explained in his study that OC pills reduces hyperandrogenism by promoting direct negative feedback on LH secretion, which results in decreased ovarian synthesis of androgens and thereby normalize LH/FSH ratio. Literature also recommends pretreatment with OC Pills prior to initiation of clomiphene for better results.

Insulin resistance is a concern in majority of PCOS subjects. Metformin has been most widely used drug since long and is recommended to be used either alone initially or in combination with clomiphene.

In a study conducted by Dasai Petal, in 24 women with infertility due to PCOS, a significantly higher rate of ovulation (70%) and pregnancy rate (25%) was observed

with concomitant use of metformin and clomiphene as compared to alone.

In hyperprolactinemia, excessive prolactin secretion decreases pulsatile release of GnRH that impairs the pituitary production of FSH and LH and also directly impairs endocrinal activity of ovarian follicle results in defective leu teal phase, inconsistent ovulation and chronic anovulation in such patients.

In our study in patients with hyperprolactinemia cabergoline, a dopaminergic agonist was initiated and subsequent to normalization of prolactin, clomiphene was subsequently added in 53.85% subjects.

Thyroid disorder can cause infertility and subfertility due to anovulation, leu teal phase defect, hyperprolactinemia and imbalance of sex hormones. Hypothyroidism can be easily corrected using oral preparation of levothyroxine. Target TSH levels are <2.5 mu/l

We did not follow subjects of pituitary fossa tumour after surgical reference.

In study done by Arain F et al 69.01% subjects having PCOS had conceived as compared to 65% in present study.in present study 90% patients conceived after being treated for hypothyroidism. this was higher compared to observed in study by Verma et al wherein 76.6% of infertile women conceived.

In present study 65.15% conceived in hyperprolactinemia group as compared to 31 in 34 patients of hyperprolactinemia in study done by Crosignani PG et al. this high rate may be because of long duration of follow up which was around 2 years as compared to present study in which follow up was done for 3 cycles. In the span of 3 months, we observed high pregnancy rate because with induced ovulation using clomiphene along with control of high prolactin levels using cabergolin.

In present study 30.23% of patients that conceived in PCOS group had miscarriage, while in study done by Palomba S et al, it was 15.4%.

In hypothyroid group observed miscarriage was 22% in our study. Sarkar D et al found in her study that there is strong relationship between presence of thyroid antibodies and infertility and miscarriage.

Conclusion

In a country that needs vigorous control of population growth concerns about infertility may seem odd but if a couple is urged to postpone or widely space pregnancy, it is imperative that they should be helped to achieve pregnancy when they then decide, in the more limited time they will have available. Due to alteration in life style and building up of stress, prevalence of infertility is increasing day by day. Mean age of patients at presentation was on higher side across all the age groups as people tend to wait for spontaneous conception due to which losing important years. Managing infertility involves cost however cost-effective solutions are available before ART, patient should be managed conservatively using counseling, OC pills, ovulation induction agents, metformin for PCOS, cabergoline for hyperprolactinemia and thyroxin for hypothyroidism.

References

1. Crosignani P. G. Management of hyperprolactinemic infertility. Middle East fertility society journal. 2012 (17), 63-69
2. Verma I, et al. Prevalence of hypothyroidism in infertile women and evaluation of response of treatment for hypothyroidism on infertility. Int J Appl Basic Med Res. 2012; 2(1): 17-19
3. Agrawal M et al. Prevalence of hyperprolactinemia in infertile cases and its correlation with TSH in a rural

set up hospital. Int J Reprod Contracept obs gynecol. 2013 Dec; 2(4): 626-630

4. Malik S, et al. Good clinical practice recommendations on management of infertility in patients from India with polycystic ovary syndrome. Fertil Sci Res. 2015; 2: 107-32
5. Melo AS et al. Treatment of infertility in women with PCOS: approach to clinical practice. Clinics. 2015 Nov (11): 765-769
6. Deatsman S, et al. Age and Fertility: A study on patient awareness JBRA Assist Reprod. 2016 Jul - sept; 20(3): 99-106
7. Kafeel G et al. historical background of anovulatory infertility. International journal of current research. 2017 June; 9(6): 52035-8.
8. Nallusamy S, et al. Prevalence of hyperprolactinemia in infertile women and its association with hypothyroidism. Int J Adv Med. 2016 Feb; 3 (1): 33-38.
9. Rui Wang, Wentano Li et al, The first line ovulation induction for polycystic ovary syndrome, human reproduction update, volume 25, issue 6, Nov-Dec 2019; 717-732.