

FOGSI guidelines for the Practising Obstetricians and Gynecologists of India



I take this opportunity to express my deep gratitude to the members of the managing committee of FOGSI for entrusting me the task of preparing the F O G S I GUIDELINES.

My special thanks are to Prof. R.D.Pandit, the Editor of FOGSI Journal for appointing me as the Guest Editor of this publication that is to be released in December, 1998. We are practising obstetrics and gynecology in the most trying period of advanced patient education and information. The newer developments in technology and therapeutics aim at prevention or simplified treatment of various disease processes. Practice of obstetrics and gynecology has become evidenced based, than established on opinions and personal bias.

Under these changed circumstances there is but no option for the practicing obstetricians and gynecologists of our country to change and adapt themselves to the newer trends. Taking into consideration the magnitude of the

changing trends the Federation of Obstetric and Gynecological Societies of India has undertaken the responsibility of preparing a practical guideline which is well balanced between the most conventional approach and the ultra-modern methods.

The chapters have been contributed by the stalwarts of FOGSI who have experience and expertise in their own field. This publication should be useful as a referral book for patient management in accordance to the modern thoughts. The intention is to describe an optimized patient care through proper investigations and treatment options. The authors have also taken care to prepare the text in a manner that at least for the coming next 5 years the concepts described will be valid. I should admit that only certain topics of practical importance has been included.

This is the first time the Federation has attempted to publish a guideline for the benefit of the clinicians. Periodically this book could be edited depending on the changing trends and the requirements of the future. Let me thank all the contributors for their contributions which are of high academic standard and practical value. I am also indebted to them for their kind co-operation.

I, on behalf of the Federation of Obstetric and Gynecological Societies of India, wish our members a successful and safe practice of the art and science of Obstetrics and Gynecology.

With warm regards

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Guest Editor

Guidelines for Practice of Infertility

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The current technological sophistication enjoyed by the reproductive physicians and surgeons immensely benefit the infertile couples by way of more effective therapeutic benefits through much simpler, quicker and least invasive investigative and treatment modalities. By modern concepts the etiology of infertility should be discerned as much as possible by the first visit itself with a recourse to non-invasive diagnostic methods such as vaginal sonography. Decision on a definitive treatment such as male factor management, operative endoscopy or induction of ovulation should be made at the first visit of the couple. The choice of treatment procedure should be one that does not require frequent monitoring and repeated stressful follow-up visits. In effect, unnecessary hospitalization, invasive investigative and treatment protocols, frequent monitoring and repeated follow-up visits and the prohibitive cost involved which are quite frustrating experiences for the infertile couple could be considerably minimised.

Management of Oligospermia

To achieve this goal the infertility evaluation should be couple oriented with both partners interrogated and physically examined by the first clinician who is usually the gynecologist. A fresh sample seminal parameter study evidencing atleast 10 actively motile sperms (purposeful movement of grade II +) per high power field sufficiently excludes a male factor at the first round. In couple with proved male factor such as azoospermia or oligospermia the co-existing female factor is seen only in 12% of female partners.

Oligospermic subjects should be advised a good quality life and refrain from smoking. Any evidence of infection should be sought after by seminal parameter study. If number of pus cells are > 10 per field seminal culture could be considered. Infections should be treated with

appropriate antibiotics. Metabolic diseases such as diabetes should be excluded and if anatomical defects such as varicocele were identified, appropriate surgical consultation will be mandated. However, a course of hCG has been currently advised as medical treatment for varicocele and oligospermia. At clinical and basic seminal parameter study, if no definite cause has been found the condition is considered as idiopathic oligospermia. If the female partner is young, regularly ovulating and proved normal at endovaginal sonography, hCG treatment of idiopathic oligospermia (10,000 i.u. / once a week for 10 injections) provides a pregnancy rate of 38.78%.

If these simpler measures fail to achieve results in a reasonable period of 6 months to 1 year, the couple should consult an andrologist or should resort to Assisted Reproductive procedures.

Investigative strategy for female partner

Subjects with oligomenorrhoea or secondary amenorrhoea are usually anovulatory, and seldom (3.00%) a pelvic factor mandating surgical correction co-exists in these subjects. Hence these subjects should be evaluated endosonographically and endocrinologically for etiology of anovulation. Endoscopy should not be employed as the primary investigative modality.

On the contrary subjects with regular menstrual cycles should be considered to be regularly ovulating. These subjects, in whom a male factor has been excluded, will harbor a pelvic factor to the extent of 35%, particularly if >25 years of age and / or married for more than 2 years. Such subjects should be investigated by endovaginal sonography and endoscopy and hormone estimations of relevance at the outset. Nearly 85% of subjects with pelvic factors detected at scan will be proved correct at

endoscopy. Operative endoscopy should be choice for surgical correction for pelvic factors, except huge abdominal masses that may mandate laparotomy.

Endosonographic classification of female infertility

After excluding male factor the female partners are subjected to endovaginal sonographic evaluation with the proper clinical evaluation and are classified into: 1. those with normal pelvic anatomy; 2. those with altered pelvic anatomy; 3. those with endocrine cause of infertility.

Endovaginal sonography provides for a precise evaluation of the pelvic anatomy. The size, shape and mobility of the uterus and ovaries could be well discerned at endopelvic scan. So much so that any pathological entities causing anatomical alteration should remain easily identified. Uterine myoma, uterine anomalies, endometrial cavity pathologies, ovarian endometrioma, ovarian tumors, functional cysts of ovary, hydrosalpinx, tubo ovarian masses, and pelvic adhesions are diagnosed by endopelvic scan with fair amount of precision.

Since the advent of cross sectional study of ovarian and endometrial morphology, the concept of endocrine infertility evaluation and management has been throughly changed. Hormone estimation which is the biochemical method of evaluation of endocrine infertility has been elegantly replaced by the biological approach of studying the end organ response to hormones rather than quantifying the hormone itself. Bilaterally active ovaries with thecal prominence indicates PCOS, bilaterally inactive but normal looking ovaries with poor endometrial estrogenization indicates secondary gonadal failure (the commonest cause being hyperprolactinemia, usually presenting with amenorrhoea and galactorrhoea). Poor endometrial estrogenization attended with poorly imaged ovaries indicate primary gonadal failure.

In effect the following information could be gathered at the first visit: 1. clinical evaluation of the male and study

of seminal parameters; 2. clinical evaluation of the female partner; 3. endosonographic evaluation of pelvic anatomy; and iv. endosonographic evaluation of ovulatory status. Based on the informations derived by these noninvasive, simple and quick investigations the following strategies could be evolved. The best policy should be to first diagnose the commonest and the most effectively treated conditions which offer the best fertility rate, preferably by the least invasive and simplest approach.

Normally Ovulating Subjects

Normally ovulating subjects will have regular menstrual cycles and asymmetric ovaries, with one ovary harbouring a dominant follicle or a corpus luteum and the other ovary remaining quiescent. Endometrium will reveal either evidence of proliferative or secretary pattern depending on the phase of the cycle. In such subjects the clinician should concentrate on other cause of infertility. In these regularly ovulating subjects there is a 30% incidence of male factor and another 40% incidence of pelvic factor. Hence immediate attention should be focused on sonographic identification of pelvic factors and if necessary a hystero-laparoscopic evaluation.

Anovulatory infertility

Endosonographic evaluation of anovulatory infertility is very easy. In a simplified manner it can be effected by imaging both ovaries. Anovulatory subjects typically have bilaterally symmetrical ovaries, which could be either bilaterally active with antral follicles, or bilaterally devoid of follicles. The latter constitute the primary gonadal failure and are invariably attended with hypoestrogenic endometrium and hypoplastic myometrium.

Those anovulatory subjects with symmetric ovaries imaging antral follicles could be subgrouped into: 1. estrogenized anovulatory subjects; 2. androgenized anovulatory subjects; and 3. hypoestrogenic anovulatory subjects.

Estrogenized Anovulatory Subjects:

These patients essentially have delayed cycles / oligomenorrhoea and normal physique. The ovaries are bilaterally active with heterogeneous follicular enlargement, and are devoid of ovarian stromal hyperplasia. Endometrium is significantly estrogenized. They are best treated employing low dose clomiphene citrate (50 mg for 5 days from the third day of the cycle). Proper selection for CC therapy is more important than follicular monitoring and administration of ovulatory dose of hCG. Since 90% of CC induced subjects have spontaneous and normal LH surge there is no need for hCG administration for follicular rupture. Hence it is suggested that these subjects are treated for 3 to 6 cycles without any form of follicular monitoring and thus avoiding frequent visits. Either during treatment or within the first 3 non-treatment cycles, a conception rate of 67 to 79.41% has been reported in younger subjects who had no prior exposure to CC. Only if this regime fails other treatment modalities like increasing the dose of CC or combination with Brom or DEX or hMG therapy and follicular monitoring (for hCG administration) is to be considered. Alternately ovarian follicular puncture offers 27.59% pregnancy rate for CC failed subjects.

Androgenized Anovulatory Subjects

These subjects are relatively obese and hirsute with bilaterally active ovaries imaging homogenous antral follicles (8 to 10 mm) and thecal hyperplasia. The typical necklace pattern of PCOS is quite often evident in scan. Endometrium could be estrogenized, hyperplastic or even hypoestrogenic due to androgen excess. They may be hyperglycemic in 50% of occasions. Hence weight reduction and if found hyperglycemic, treatment with insulin is appropriate. These subjects are best treated by laparoscopic follicular puncture or low dose gonadotropin therapy. It should be noted that ovarian follicular puncture does not need any follow-up visits. To be least invasive and simple, laparoscopic follicle puncture should be performed employing 4 mm telescope for visual axis at

the intra-umbilical port and Verres needle used for follicle puncture. An average of 5 to 10 punctures per ovary will be performed, and diathermy or laser should be avoided in order to negate the risk of post-operative ovarian adhesions.

If the cycles are reverted to normal it is understood that ovulation is restored and a conception rate of 38.89% is achieved within 6 months. If the cycle control is not restored, CC or low dose hMG should be considered which will add to the therapeutic response of ovarian follicle puncture.

An alternate to ovarian follicle puncture will be ovulation induction with low dose hMG (1 to 2 amps / day for 5 to 7 or 10 days) with strict follicular monitoring and endometrial dating, and optimally timed hCG (3000 to 5000 i.u) or Busereline (500µ gm for 2 doses at 12 hr apart) administration. A pregnancy rate of 33.33% which is comparable to that of operative laparoscopy is achieved. However, with the difference that frequent cycle monitoring is indicated which could be avoided if follicular puncture is preferred.

Hypoestrogenic Anovulatory Subjects

These subjects have normal ovaries with antral follicles which could be heterogeneous and devoid of thecal hyperplasia. The consistent finding is the endometrium is hypoestrogenic measuring less than 5 mm from interface to interface. The etiology for this secondary gonadal failure is either hyperprolactinemia or hypofunction of hypothalamopituitary axis. Serum prolactin estimation will discriminate the two conditions. Of course, the hyperprolactinemic subjects could be galactorrhoeic as well. Bromocriptine in a dose of 2.5mg to 7.5 mg per day (average 5mg) promotes pregnancy in 70%, and there is no need for frequent monitoring or follow-up visits.

Normoprolactinemic secondary gonadal failure is treated with hMG/hCG regime. Since they are hypogonadotropic

average dose of 2 to 3 ampoules of hMG per day will be needed for follicular maturation.

Hormone study

In this approach to evaluation of female infertility the role of hormone study is very much limited. Secondary gonadal failure is ideally investigated with serum prolactin estimation, because hyperprolactinemia is the commonest etiology for secondary gonadal failure. Marginal hyperprolactinemic subjects should have their thyroid function tested. Primary gonadal failures diagnosed at endovaginal sonography are better confirmed by study of FSH levels. One may employ (but not mandatory) LH : FSH ratio in confirming the diagnosis of PCOS, however, serial study will be needed to confirm this diagnosis. If endosonographic study of adrenal or ovary suggests a tumor or there is evidence of severe androgenization there will be a need for study of serum testosterone, DHEA (S) and cortisol.

Estimation of estradiol and progesterone will not be routinely required unless cycle monitoring is difficult at endovaginal sonography or when one employs IVF OR ICSI

Altered Pelvic Anatomy and Infertility

If endopelvic scan suggests distorted pelvic anatomy an immediate endoscopic evaluation is ordered. Altered pelvic anatomy could be involving the adnexal structures or the uterine cavity, and hence depending on sonographic dictates laparoscopy, hysteroscopy or hystero-laparoscopy will be warranted. Special situations demand tubal catheterization and salpingoscopy. The possibility of anovulatory infertility co-existing in these subjects is only 5%, and hence the physician should concentrate exclusively on endoscopies and not lose time on endocrine and other investigations.

The pelvic pathologies could be ovarian endometrioma or other ovarian enlargements, tubo-ovarian mass or

adhesions and uterine myoma, and these conditions are best managed by operative laparoscopy. If uterine cavity pathologies such as submucous myoma, uterine septae or intrauterine adhesions are located operative hysteroscopy is considered. The laparoscopic surgery involves use of 10 mm 0 degree telescope at the intra-umbilical port and two 5 mm accessory operative ports. Tissue retrievals are preferably effected through the umbilical 10 mm port. Hysteroscope (4mm 30 degree fore oblique) and resectoscope will be needed for treatment of cavity lesions.

Endometriosis

Operative laparoscopy is the choice for treatment of pelvic endometriosis and no medical treatment either pre- or post-operative is advised. An average pregnancy rate of 57.89% for moderate endometriosis and 46.43% for severe endometriosis have been reported. Ovarian endometriosis, not involving the fallopian tube, subjected to operative laparoscopy results in 67 to 80% conception rate. Paradoxical adnexal removal or tubectomy (when one adnexum is severely damaged) offers 62.96 to 73.68% conception chances. However, treatment of minimal or mild endometriosis, which does not distort the pelvic anatomy does not offer a higher pregnancy rate (27.27%) than that of diagnostic laparoscopy

Ectopic Gestation

Ectopic gestations are precisely diagnosed at endovaginal sonography and urine β hCG study, and live ectopic gestations of >2 cm sac diameter and big tubal moles are managed by laparoscopic salpingostomy. Tubal rupture is managed by salpingectomy, particularly when the contralateral tube is normal. Intact gestation sac of <2 cm are managed by parenteral methotrexate therapy (75 mg single dose), and regressing smaller ectopic gestations are managed on expectant lines. Overall intrauterine pregnancy rate for treatment of ectopic gestation has been 57.14%.

Other Pelvic Factors

Pelvic inflammatory disease with unilateral hydrosalpinx responds best to paradoxical salpingectomy at laparoscopy, and a pregnancy rate of 66.67% has been reported. Myomectomy, and ovarian cystectomies for benign ovarian tumors, when other pelvic causes have been excluded, are attended with a pregnancy rate of 31.57% and 25.00% respectively.

Pregnancies in infertile subjects.

Corrected Pregnancy Rate: 47.22%

Clomiphene induction in PCO	79.41%
Hyperprolactinemia	70.00%
Paradoxical adnexectomy	66.67%
Sterilization Reversal:	62.50%
Moderate Endometriosis:	57.89%
Treatment of Ectopic Pregnancy	57.14%
Severe endometriosis:	46.43%
Unexplained young infertile	44.07%
Operative Laparoscopy in PCOD	38.89%
hCG for Oligospermia	38.78%
Low dose hMG for PCOD:	33.33%
Diagnostic Endoscopy (Young Unexp)	33.33%
Fibroid: Laparoscopic Myomectomy	31.57%
Ovarian cystectomy(Tumors)	30.00%
Minimal / Mild Endometriosis:	27.27%
Diagnostic Endoscopy (Elderly Unexp)	20.00%

Average pregnancy rate for operative laparoscopy :

39.23%

Unexplained infertility

Those subjects with a normal male factor, regular ovulatory cycles and normal pelvic anatomy at endovaginal sonography including normal endometrial morphology are divided into three groups : (1) those young subjects of less than 25 years, and married less than 2 years, 2) those who are above 25 years and married for more than 2 years; and (3) elderly subject of above 33 years and who probably have exhausted all treatment modalities.

Unexplained infertility in younger age group

The first group of young infertile subjects have the following options of (i) proper counselling and expectant management for 6 to 8 months or (ii) undergoing PCT and minimally invasive tubal function studies such as sono-hysterosalpingography. Uterine cavity, tubal patency and tubal fimbrial floatation could be documented at endovaginal sonography and hystero-sono-salpingography. Nearly 44.07% of young subjects conceive within 6 to 8 month of these simpler nonsurgical measures.

There are two options for those who fail to conceive within 6 to 8 months. Either they could opt to undergo intrauterine insemination (IUI) following controlled ovarian hyperstimulation (COH) employing CC or small dose hMG. Or prefer detailed endoscopic evaluation to unearth correctable pelvic factors. The choice could be given to the couple, or alternatively, IUI could be planned after excluding pelvic factors by hystero-laparoscopy. Moreover, it also should be kept in mind that spontaneous conception following normal hystero-laparoscopy could be expected in 30% of subjects within 6 months.

Unexplained infertility in Subjects > 25 years

Those who are >25 yrs and married > 2 years have 35% chances of harbouring a pelvic pathology even though sonographically normal, which could be confirmed and precisely treated at endoscopy. Hence hystero-laparoscopy is to be immediately considered. Office hysteroscopy and minilaparoscopy should be the choice, employing the same 4 mm 30 degree telescope for both procedures. Intra-umbilical 5 mm incision should be preferred, and suprapubic long Verres needle should be employed for organ manipulation. Minor surgical procedures such as functional cyst aspiration and follicle puncture could be accomplished with Verres' needle. This is the least invasive manner in which hystero-laparoscopy could be performed and can be completed with local anaesthesia and sedation. If minimal adhesiolysis or fulguration are warranted one 5 mm port could be employed. If major pathology is encountered the 4 mm telescope is replaced by 10 mm telescope at

the umbilical port and two 5 mm accessory ports are employed for operative procedures.

If no pelvic pathology is detected at endoscopy these patients have the following three options: (1) await spontaneous conception following diagnostic endoscopy, and usually a pregnancy rate of 20% could be achieved within 6 months; (2) detailed endocrinological study employing cycle monitoring with vaginal ultrasound and hormone estimations. Any subtle endocrine dysfunctions such as abnormal folliculogenesis and luteal phase defect will be diagnosed by serial sonographic evaluation of follicular dynamics and endometrial dating. If any follicular or luteal dysfunction is identified at endovaginal sonography hormone estimations will detect the cause of the dysfunction as hyperprolactinemia, hyperandrogenemia or pituitary insufficiency. The optimal treatment could be instituted for the respective endocrine disorders; (3) Or else sperm function tests such as antibody tests could be conducted to evaluate the sperm transport

An alternate approach which is a short-cut for the above will be to prefer COH and IUI. Controlled ovarian hyperstimulation will correct subtle ovulatory disorders, and IUI will take care of dysfunctions at sperm transportation

ART Procedures such as IVF and ICSI

The third category of elderly infertile subjects who have exhausted all the therapeutic options, and those who have failed to achieve conception within 6 months to one year of definitive therapy should be considered for A.R.T. procedures.

Conclusion

I have summarized the investigative and therapeutic approaches to infertility in the most practical way, taking

into consideration all the available clinical and modern technological advances. This strategy provides for a corrected pregnancy rate of 47.22%. It is quite understandable that a female with altered menstrual pattern should be investigated for endocrine cause of infertility, and there is no role for hysteroscopic or laparoscopic evaluation. Patients with regular menstrual cycles are more often candidates to have pelvic factors, and to be benefited by hystero-laparoscopic evaluation. Particularly those with pelvic findings detected at endosonography should be investigated for tubo-peritoneal cause for infertility. It is also clear that when one definite cause for infertility has been identified other factors do not co-exist that frequently. Younger infertile subjects with no explainable cause for infertility at the noninvasive evaluation could wait for spontaneous conception. Whereas relatively elderly subjects should be hurried through the relevant investigations and treatment.

Endosonography is the pivot of infertility evaluation which is capable of diagnosing pelvic pathologies and endocrine causes almost with same accuracy and precision. Endoscopy is the main therapeutic surgical armamentarium which has practically replaced laparotomy in the management of infertility.

Approach to treatment of infertility should be such that the most common, easily treated and the one that gives highest fertility rate should be searched for at the outset and treated optimally, so much so that more difficult situations could be reserved for ART procedures. Ovulation induction and laparoscopic surgery for endometriosis are the conditions attended with highest success rate. By this strategy the treatment is relatively non-invasive, no time is wasted, and the treatment is more economical and well accepted by the infertile couple. Atleast the couple could realize at the outset their chances for having a baby and could plan accordingly.