Various Factors for Infertility - In Infertility Clinic, Gynae Unit-I, Services Hospital, Lahore

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The prevalence of various infertility factors in 683 case of infertility coming from various parts of country were studied at infertility clinic gynae unit-I Services Hospital, Lahore from June 1999 to December, 2003. Factors like age, type, duration of infertility were assessed of 683 cases, only 90 cases (13.2%) had complete follow up while 222 patients (32.5%) had incomplete follow up and 371 (54.3%) cases had only one booking visit. The various investigations performed to evaluate infertility factors are discussed in detail. The results are grouped into male and female factors and unexplained infertility. The male factor included semen abnormalities and coital problems while the female causes are grouped into ovulatory disorders, tuboperitoneal factors. The study revealed that ovulatory dysfunction was the most common factor and accounted for 40% (274) cases, followed by tuboperitoneal factor 32.7% (223 cases) and male factor was present in 22.3% (141patients). The prevalence of all these factors in our study correlated with prevalence quoted in literature.
Key words: Infertility, infertility factors, ovulation disorders

Infertility is inability of a couple to obtain a clinically recognizable pregnancy, after 12 months of unprotected intercourse[1]. While prevalence of infertility is its occurrence in an unscreened population and may be 15%[2]. Infertility is a world wide problem. In our society due to social implications the stresses on infertile couple are manifold and hence the desire for conception and to give birth is much more intense than other parts of world.

Management of infertility includes evaluation of both partners simultaneously by detailed history, clinical examination, investigations and follow up and treatment according to the causative factor. These women should be evaluated and managed in specialized units for proper management. These centres are very well developed in developed countries. We have started infertility clinic at SHL in gynae unit – I under Supervision of Prof. Rehana Mahmood Malik and patients consulted this centre from various parts of country and some had complete follow up. SHL is tertiary care hospital attached previously to Postgraduate Medical Institute Lahore, and now to SIMS.

The objective of infertility evaluation is to determine the probable causes, to provide accurate information regarding prognosis, to counsel and guide regarding best options of management.

Materials and methods:
All cases were registered at infertility clinic gynae unit – I SHL from June 1999 to December 2003 and were analysed to find the prevalence of various causes of infertility. The clinical features and various investigations carried out were noted on a typed performa paper. Detailed history of couple included age of both partners, duration of marriage and infertility, menstrual history and other relevant complaints like vaginal discharge, dysmenorrhoea, coital history, previous medical or surgical illness while in cases of secondary infertility previous obstetric history and postnatal complications were also noted followed by thorough clinical examination. Then investigations were performed accordingly at 1st visit and at follow up visits and are grouped in table - 1

A) 1st visit investigations

(i) Baseline investigations included haemoglobin, urine analysis, blood sugar random level, hepatitis viral serology.

(ii) Specific investigation included semen analysis and ultrasound scan of female pelvic organs.

B) Subsequent investigations included (i) hormone assays in male and female partner (ii) and tubal patency tests in female. Various investigations performed for evaluation of fertility factors are given below in table 1.

Table 1: Various investigation performed for evaluation of fertility factors

1).	Semen analysis.
2).	Hormone assay in male and female.
3).	Ultrasonography.
4).	Hysterosalpingography (HSG).
5).	Diagnostic Laparoscopy and dye test (Pelviscopy).

Test for male factors:: The semen was evaluated for volume, PH, sperm density, motility and morphology of sperms, using WHO reference value for semen analysis 2000[3].

Routine semen analysis is highly subjective test and grossly azoospermic specimen may contain few sperms after centrifugation (cryptozoospermia)[4]. The specimen of semen is centrifuged at 2000 rpm and resulting specimen (pellet) is examined. The sperm pelleting was performed on all patients with azoospermia irrespective of FSH levels.

Hormone assays in male: Performed if abnormalities of semen e.g. oligozoospermia, azoospermia, aspermia, are

found on routine semen analysis. Serum FSH, LH and testosterone and prolactin was carried out in all clinical cases of hypogonadism, sexual dysfunction and gynaecomastia to screen for pituitary tumour. Patients with gynaecomastia also had serum oestrogen and HCG levels, as these hormone may be produced by adrenals or testicular tumour.

Tests for female factor

Test for ovulation:- Following investigations were carried out to assess ovulation.

Ultrasonography: Both abdominal and vaginal ultrasound scans were performed. Serial vaginal ultrasound scans were carried out for ovarain follicular growth with simultaneous assessment of endometrial thickness. The size and number of developing ovarian follicles were noted. Follicular size of 18-22 mm (mean D) in diameter was considered as an evidence of ovulation and endometrial thickness was also noted simultaneouly. This also helped in interpretation of plasma hormone levels. Ultrasound also helped in detection of gross structural abnormalities of uterus and adnexae like fibroids, adnexal cysts.

Hormone assays on female.

Midluteal phase serum progesterone level: It was performed on day 21 of a 28 day cycle and on day 28 of a 35 day cycle to assess the ovulation and adequacy of luteal phase. Midluteal phase progesterone levels assay (>30 nmol /L) in woman with regular cycles indicates that ovulation has occurred but occasionally unruptured luteinized follicle may give normal progesterone levels. A low progesterone level confirms anovulation in menstrual cycle.

Other hormone assays: Were performed in selected cases i.e those women with infrequent or irregular periods, secondary amenorrhoea, glactorrhoea, suspected polycystic ovarian disease (PCOD) and thyroid disease. These included serum FSH, LH prolactin testosterone and thyroid function tests, i.e. serum TSH, T_3, T_4 levels.

Tests for assessment of tubal disease and pelvic factors

Hysterosalpingography (HSG)

It was carried out in postmenstrual phase within ten days of menstruation. HSG provides an outline of both uterine cavity and fallopian tubes and at the same time assesses any endometrial cavity defects like sub-mucous fibroid, polypi, intrauterine adhesions.

Laparoscopy with dye (pelviscopy): The pelvis was visualized systematically for structural abnormalities like fibroids, adnexal cysts, tubo-ovarian masses, par-ovarian cysts, peritubal and periovarian adhesions, evidence of endometriosis and tubal inflammation. Then methylene blue dye was injected through cervix via Rubin's cannula and looked for spillage of dye through tubal ostia in the peritoneal cavity. On the basis of these investigations the infertility factors were grouped as follows.

Male factors included (a) semen abnormalities (b) coital problems.

Ovulation disorders Included anovulation and infrequent ovulation.

Tubo-peritoneal factors (a) Tubal disease comprised tubal obstruction and pelvic adhesions due to infection, endometriosis and pelvic surgery, while pelvic or peritoneal factors comprised of endometriosis, uterine abnormalities like submucous fibroids or cervical fibroids and intrauterine adhesions, tubo-ovarian masses.

Results:

Six hundred and eighty three cases of infertility were studied. Only 90 patients (13.1%) had complete follow up and investigations and 222 patients (32.5%) had incomplete follow up while 371 patients (54.3%) had only one booking visit (table 2). These are the patients who go from one physician to other physician in the hope that there may be a short cut or any new treatment or approach. But when they find same reply as from previous consultant they do not turn up.

Table 3 shows that primary infertility was found in 58.3% of patients and secondary infertility in 41.7% of cases. While table 4 reveals that majority of women were between age group of 20-30 years, followed by age group 31-35 years in both types of infertility patients i.e; primary and secondary infertility. In case of secondary infertility some of the patients also consulted above the age of 40 years, while only one patient with primary infertility at this age presented for management. Few patients with primary infertility presented at younger age i.e, less than 20 years.

Regarding the duration of infertility, majority of patients (57.7%) presented between 2-5 years. While 34.8% had infertility of more than 5 years. Only 12.5% (86) of patients had duration of infertility of less than 2 years (Table 5).

Prevalence of various factors for infertility is shown in table 6. Ovulation disorders constituted the major factor for infertility 41.1% of patients, followed by tuboperitoneal factor 32.7% while the male factor was found in 22.3% of cases.

Table 7 reveals the distribution of various semen abnormalities and coital problem in male. Majority of the men had low sperm motility 34.8% (49 patients), oligo-aesthenozoospermia was present in 43 (30.5%) patients. 16 patients (11.3%) had azoospermia, 6 patients had severe oligozoospermia, while 2 patient had necrospermia and coital problems were observed in 10 patients (7.1%)

Table 8 shows ovulation disorders, of which anovulation was present in 31% of cases (85 patients) and infrequent ovulation was observed in 69% of cases.

Tuboperitoneal factor was present in 32.7% of total cases of subfertility (Table 9). Chronic pelvic infection was major factor found in 44.8% patients while 33.4% of patients had tubal blockage. Endometriosis was found in 48 patients (21.5%) of tuboperitoneal disease (Table 9) and 7% of subfertile patients.

Uterine factor was present in 6.9% cases of the subfertility and almost all patient had uterine myomas (Table 6). While unexplained infertility was found in only 1.9% of cases (Table 6)

Table 2: Frequency of follow up (n=683)

	=n	%age
Complete follow up	90	13.1
Incomplete follow up	222	32.5
Only one visit	371	54.3

Table 3 Type of infertility.

Type of Infertility	=n	%age
Primary	398	58.3
Secondary	285	41.7

Table 4 Age incidence in infertility patients n: 683

Age (Years)	Primary Infertility	Secondary Infertility
< 20	11	(2.7%)
21-30	291 (73.1%)	191 (67%)
31-35	78 (19.1%)	65 (23%)
36-40	17 (4.2%)	22 (7.7%)
> 40	01	07

Table 5 Duration of infertility

Duration (years)	**=n**	**%age**
< 2	86	12.5
2-5	359	52
> 5	238	34.8

Table 6 Factors for infertility

Factor	=n	%age
Male	141	22.3
Female		
Ovulatory dysfunction	274	40.1
Tuboperitoneal disease	223	32.7
Uterine factor	47	6.9
Unexplained	13	1.9

Table 7: Frequency of various semen abnormalities & coital problems.

Male Factor	141	(22.3%)
Low motility	49	(34.8%)
Oligo-aesthenozoospermia	43	(30.5%)
Azoospermia	16	(11.3%)
Asthenoteratozoospermia	09	(6.4%)
Severe oligozoospermia	06	(4.3%)
Aspermia	06	(4.3%)
Necrospermia	02	(1.4%)
Coital problem	10	(7.1%)

Table 8: Ovulation disturbances n-274(40.1%)

Factor	=n	%age
Anovulation	85	31
Infrequent ovulation	189	69

Table 9: Tuboperitoneal factors n. 223 (32.7%)

Factor	=n	%age
Tubal blockage	75	33.6
Chronic pelvic Infection	100	44.8
Endometriosis	48	21.5

Discussion:

The investigations performed in this study for evaluation of couple were minimum in number, simple, minimally or non-invasive and safe.

In this study assessment of ovulation was based on clinical history of menstrual molimina and regular menstrual cycles in range of 26-36 days are indicative of ovulation[5]. About 8% of regularly cycling women may be anovulatory[2]. Hence women with regular menstrual cycles and more than two years of infertility were offered midluteal phase serum progesterone levels. Midluteal phase S. progesterone levels (> 30 nmol/litre) in women with regular cycles usually indicate that ovulation has occurred. A low progesterone level confirms anovulation in menstrual cycle but a high level does not necessarily confirm ovulation.

We performed midluteal phase S. progesterone assay as it is simple safe and easy for patient to obtain. It retrospectively confirms ovulation and also gives assessment of adequacy of luteal phase. Disadvantage is that progesterone levels may vary and provide no assessment of endometrium. In our study assessment of endometrium was done by transvaginal ultrasound scan while monitoring follicular growth. This is noninvasive and simple test.

Basal Body Temperature charts used previously to indicate ovulation time. Although inexpensive & safe, it requires literate person to check temperature. Also it does not reliably predict ovulation and adequacy of ovulation and is not recommended[6] (level B recommendation). Hence not used in our study.

LH Testing predicts onset of ovulation but does not give information regarding quality of follicular development or luteal phase adequacy. Hence not offered in this study. Serial ultrasound scans on day 12, 14 and 21 are very predictive of follicular growth and documentation of ovulation. It also simultaneously assesses the endometrial thickness. It also identifies the gross abnormalities of upper genital tract like ovarian cysts, fibroids, PCOD and tubo-ovarian mass. But serial scans are costly.

Vaginal cytology was not done because of unreliability and lack of efficient laboratories and experts. Endometrial biopsy in premenstrual phase gives indirect evidence of ovulation and timed endometrial biopsy was considered gold standard for assessment of luteal phase defects. It is costly, painful, invasive and same information can be obtained by non- invasive method e.g, ultrasound scan. Also there is no consensus of opinion about diagnosis or effective treatment of luteal phase defects and its role as a cause of infertility has been questioned[7,8]. The benefit of treatment for luteal phase defect on pregnancy rates has not been established[9,10]. (evidence level 1b-3)

This study reveals that ovulation disorders and tuboperitoneal factors were two major factors responsible for female infertility in our centre (Tables 6). The

prevalence of ovulation disorders was 40% which correlates well with cohort study carried out in Duhock Iraq 2002[11]. While in British literature estimated prevalence for ovulation disturbance is 20-30%[12].

The prevalence of tubo-peritoneal factor in this study was 32.6% (223) cases (Table 9). While in British literature estimated prevalence of tubal factor is 20-35%[12] and correlates well with prevalence quoted in literature. Endometrios accounted for 7% of total subfertility cases, which correlates well with prevalence quoted in British literature 5-15%[12].

We used both HSG and diagnostic laparoscopy with dye insufflation to test the tubal patency. These are two most widely used methods to test tubal patency. Both are invasive but HSG is less so. HSG was used in patients with either no history of pelvic co-morbidities or where diagnostic laparoscopy was contraindicated or prior to myomectomy where there were suspected submucous fibroids or fibroid polypi or to assess the level of tubal blockade prior to tubal recanalization procedures.

Although diagnostic laparoscopy with dye insufflation (pelviscopy) is more invasive compared to HSG but it is gold standard basic investigation to detect tubal and peritoneal factors in women with possible co-morbidity. It also allows systematic visulaziation of pelvis to detect a number of associated uterine and adnexal pathologies as mentioned above under investigation of tubal patency. It identifies , previously unsuspected pathologic conditions in 30-50% of women with unexplained infertility. Among women whose tubes were found patent (unobstructed) using HSG 18% were found to have tubal obstruction or peritoneal adhesions using laparoscopy and further 34% were found to have endometriosis and / or fibroids[13]. Thus pelviscopy should have a primary place for assessment of tubal disease and co-morbidities.

It should also be carried out prior to diagnosis of unexplained infertility despite a normal HSG. However this test does not point the level of tubal occlusion, is expensive and not available at all places.

Hystero-contrast sonography (Hyco-syn) is modern ultrasound based investigation using negative (normal saline) and a positive (Echovist-Contrast) agent to out line the uterine cavity and fallopian tubes. It is simple and safe as it avoids the exposure to x-ray and anaesthesia and yields similar information to HSG. Evaluation studies of HyCo-Sy showed good statistical comparability and concordance with HSG and laparoscopy combined with dye[14]. (evidence level 1-b). Hycosy is well-tolerated and can be suitable screening outpatient procedure and effective alternative to HSG for women who is not known to have co-morbidities. However this is expensive test and not available everywhere and requires expertise. This test was not offered to patients in study as the majority of patient were non-affording.

Fertiloscopy is relatively new procedure defined as combination in one investigation of transvaginal hydropelviscopy, dye test, optional salpingoscopy and hysteroscopy performed under local anaesthesia or neuroleptanalgesia[15].

Falloposcopy is transvaginal microendoscopy of fallopian tubes and direct visualization of entire fallopian tube lumen. While salpingoscopy can be performed by retrograde route through laparoscope. It may be more discriminatory test of tubal pathology because women with normal fallopian tubes at falloposcopy achieve higher spontaneous pregnancy rates (27.6%) than those with mild or severe endotubal disease (11.5% to 0%)[16]

In another study management plan was changed in 90% of women following falloposcopy and 24% concieved naturally[17]. Further diagnostic evaluation studies are required and technical problems with falloposcopy limit their use in routine clinical practice[18,19].

Diagnostic fertiloscopy used to identify tubal pathology as an alternative to laparoscopy. This procedure has risks of bowel and rectal injuries[15]. Moreover diagnostic accuracy of fertiloscopy in comparison to HSG and laparoscopy needs further evaluation.

Other pelvic factors apart from endometriosis are uterine abnormalities such as submucous fibroids or endometrial polypi and intrauterine synechae, all accounted for 6.9% cases of subfertility in the study. While in British literature estimated prevalence is 10-15% of women seeking treatment for infertility problems[20].

The prevalence of male factor in study was 22.3% of cases which correlated well with frequency quoted in literature. Male fertility affects 25% of subfertile couples[12]. In UK low sperm count or quality is found to be only cause of infertility in 20% couples. Idiopathic semen abnormalities occur in 26% of infertile men[21].

In our study evaluation of male was carried out by semen analysis using WHO reference value apart from clinical features. This is simple test, easy to obtain and perform, noninvasive and inexpensive.

Postcoital testing of cervical mucus which aimed at evaluating periovulatory cervical mucus and sperm survival was not used in this study. As the value of post coital testing of cervical mucus for presence of motile sperm is controversial and subject of continuing debate[22, 23] due to poor predictive value of a negative test.

The routine use of post coital testing of cervical mucus in investigations of fertility problem is not recommended because it has no predictive value on pregnancy rates. (NICE guideline). Therefore it was not used routinely in study.

In this study in 1.9% cases has unexplained infertility (table 6). While the quoted prevalence in literature is 8-28%[24] of infertility couples. It is a diagnosis by exclusion when standard investigations have not detected any abnormality.

It is difficult to determine the true cause of infertility because there are numerous factors that bias studies. The cause is only established after investigations and therefore can be affected by resources available and investigations instituted, referral policies, types of couples seeking investigations.

Hence unexplained infertility of a couple in one centre may be explained in another that has facilities for more detailed investigations. Moreover the causes of infertility vary from one geographical area to another. Social factors also have an influence on the cause.

Sepsis plays a significant role in infertile population in our community. As most of the patient consult TBAS and lower paramedics who do not observe asepsis and insert unauthorized medications into vagina which lead to subclinical and clinical ascending pelvic infection resulting in chronic PID and tubal blockage and damage.

Hence this malpractice,by quacks should be banned to prevent this complication in developing countries prior to thinking of sophisticated procedures.

Conclusion:

The investigations must be aimed at individual couples. Simple and safe investigations should be used to investigate the subfertile couples and they may be treated on their basis. Early investigation, treatment and referral to specialist unit should be individualized, if female partner's age is 35 or more, had menstrual irregularities, previous history of abdominal or pelvic surgery, STD or if abnormal findings at examination or husband had semen abnormalities.

Simple cost effective evidence-base treatment should always be considered as the first option.

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