Vol. 8 / May. 2019 - Jul. 2019

NEWS LETTER

Email: kjkhospital@gmail.com | www.kjkhospital.com

KJK HOSPITAL

FERTILITY RESEARCH AND GYNAEC CENTRE

Shawallance Lane, Nalanchira, Trivandrum-15
Phone: 0471-2544080, 2544705, 2544706 Fax: 0471-2543926

From the Editors Desk.....

Core outcome measures' for improving the reliability of fertility trials

Substantial heterogeneity exists in the reporting of outcomes of fertility trials, with inconsistencies in numerators, denominators and definitions making results difficult to interpret, compare and combine in meta-analyses. Jack Wilkinson presented the rationale for a core outcome set of measures for fertility trials on behalf of the Cochrane Gynaecology and Fertility Group and the COMMIT initiative in Vienna.

More than 800 combinations of numerator and denominator were reported as outcomes in 142 IVF randomised controlled trials (RCTs) published in peer-reviewed journals in the space of just one year, according to a statistician from the Cochrane group. Important outcomes such as clinical pregnancy were defined in over 60 different ways or were not defined at all, thus causing methodological frailty in the evidence base. This was the prelude to an important session in Vienna organised by the Cochrane Gynaecology and Fertility group which would ultimately call for outcomes defined by 'core' consistent measures related to birth rate in final reports. IVF treatments, said statistician Jack Wilkinson, include a succession of bottlenecks which would be used incorrectly as denominators when randomisation had occurred earlier. Thus, outcomes such as miscarriage may be reported per clinical pregnancy or per embryo transfer when women were in fact randomised prior to oocyte pick-up. Fewer than half the RCTs reporting live birth actually presented a correct calculation which included all randomised participants or only excluding protocol violators. One of the important consequences of these inaccuracies and inconsistencies in reporting trial outcomes, said Wilkinson, is imprecision. The median width of the 95% confidence intervals calculated for live birth in meta-analyses was 21 percentage points, which, he said, would lead to a failure to detect plausible improvements in live birth rate.

Selective reporting has proved another problem. This occurs when authors selectively reveal or suppress information in order to present the trial findings in a more favourable light. One in five trials provided primary outcomes in their manuscript that were inconsistent with their original trial registry description - and this may be even more worrying in trials which are not even registered.

Wilkinson was thus keen to explain the option of 'registered reports' as one potential solution in which 'trials can be peer reviewed before they happen on the basis of their importance and methodology'. This, he said, would remove 'the incentive for selective reporting of results'. 'Fertility and Sterility should be congratulated for leading on this development, and I look forward to other journals in our field embracing the format,' he added.

Thus, defining a set of core outcome measures to be used by all trials would allow more trials to be included in meta-analyses and consequently increasing their power and precision. This should be supported by the use of statistically sound methods and measurements in fewer, but larger fertility trials.

Dr. K. Jayakrishnan

MAGNETIC ACTIVATED CELL SORTING AND MICROFLUIDIC BASED SPERM SORTING - NOVEL METHODS FOR SPERM SELECTION

Dr Ashwin Jayakrishnan

Basic semen analyses and standard methods for sperm selection, such as density gradient centrifugation (DGC) and swim-up (SU) techniques, have been used with good results. However, there is controversy regarding the role of sperm DNA fragmentation in assisted reproduction techniques because this method detects late apoptosis in sperm, and understanding all of the stages of apoptosis is far more informative.

One of the early markers of apoptosis is the loss of membrane integrity, which leads to phospholipid phosphatidylserine externalization (a molecule with a high affinity for annexin V).Therefore, annexin V (used as an apoptotic sperm marker) conjugated with magnetic microspheres, which are exposed to a magnetic field in an affinity column, can separate apoptotic from non-apoptotic sperm. This procedure is called magnetic activated cell sorting (MACS).

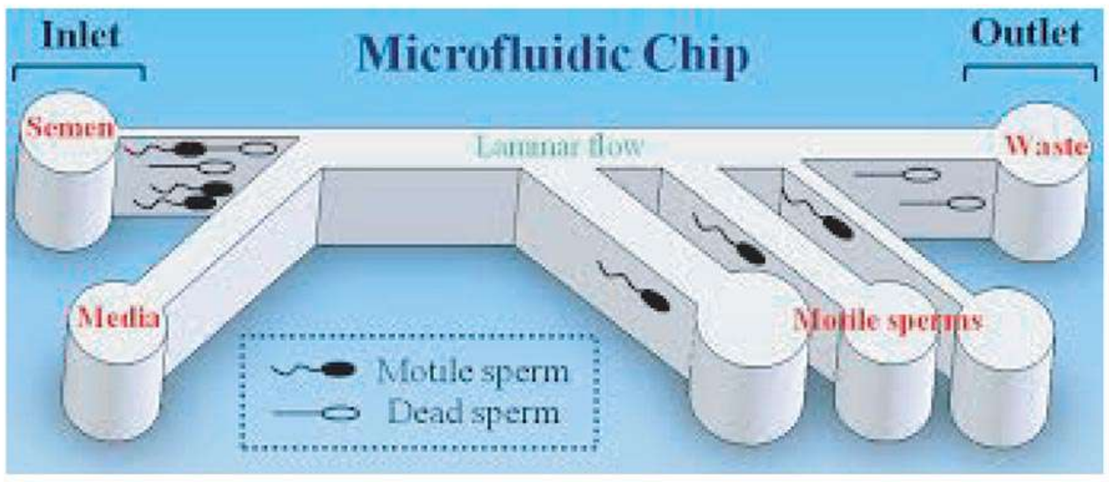
Many studies have recently evaluated the use of MACS as a method to reduce apoptotic sperm and improve sperm and embryo quality. Recent studies have recommended MACS selection regardless of DNA fragmentation results because apoptotic sperm is not exclusively associated with sperm DNA fragmentation

Five studies (prospective randomized trials) that comprised 499 patients were included. Sperm selection using MACS resulted in statistically significant differences in pregnancy rates when compared with density gradient centrifugation and swim-up techniques (RR?=?1.50, 95 % CI 1.14-1.98). (Journal of assisted Reproductive Technology 2016 November).

Another upcoming technique is microfluidic based sperm sorting which is the science and technology of accurate manipulation of small amounts of fluids, which is typically done in micro channels with dimensions of a few hundred micrometers. By relying on these advantages, microfluidic systems have been utilized in the field of assisted reproductive technologies (ART) to assist with sperm sorting.

Microfluidic system based sperm sorting processes can improve recovery of motile sperm from semen, recovery of sperm from highly heterogeneous mixtures, and possibly reduce clinician skill requirements for sperm purification process. Recently, de Wagenaar and coworkers developed a microfluidic device to detect and sort morphologically normal cells. A common sperm defect is the presence of a cytoplasmic droplet attached to the sperm flagellum. Using electrical impedance measurements, droplet presence was detected and the defective sperm cells were flagged. This work is a good example of the concept that microfluidic devices can be used to detect and sort sperm cells with abnormal morphology with considerable precision.

Therefore it can be concluded that MACS appears to be a safe and efficient method to select functional sperm with consistently good results. This technique may improve pregnancy rates when used to complement standard sperm selection methods in ART.



The gynecologic surgeon must be familiar with the basic principles of intestinal surgery and be prepared to deal with problems such as intestinal adhesions. In addition they should be prepared to identify problem areas during the course of these operations and thereby, significantly reduce the likelihood of technical accidents or complications.

Risk category: Patients who have had multiple previous abdominal operations are the group who have at least the potential for intra operative injury or postoperative bowel obstruction. These patients should be regarded at high risk not only for intestinal complications but also for infections and other types of complications.

Incidence: Incidence of bowel injury during laparoscopy cases are reported to be around 0.8 %, During laparotomy hysterectomy 0.8 %. While in LSCS 0.08 %

Pre OP Preparation: Patients for major gynaecologic surgery usually is complemented by the use of a mechanical bowel preparation, such as an enema, to evacuate the colon as much as possible. An MRI pre operatively can act as a guide in expecting the reach of bowel adhesions / ureteric involvement or other complications that are to be anticipated in a difficult surgery especially in a patient with a history of multiple surgeries. Gastro surgeon to be informed in prior to tackle such scenarios.

Dr Abhilash Antony V

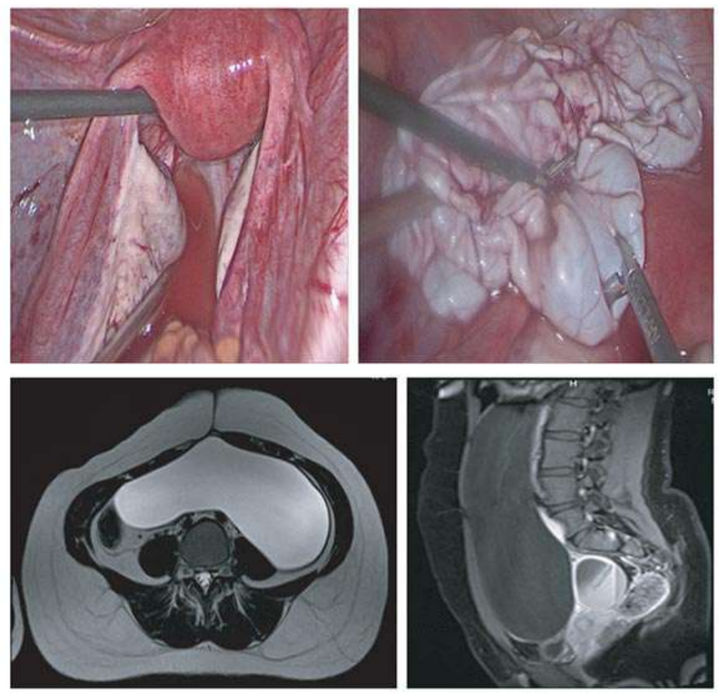
INCIDENTAL DIAGNOSIS OF A MESENTERIC CYST MIMICKING AN OVARIAN/ PARAOVARIAN CYST DURING LAPAROSCOPY

Mesenteric cysts are usually not considered in the differential diagnosis of pelvic cystic masses. The more common considerations for pelvic cystic masses include ovarian cysts such as, endometrioma, dermoid cyst, and other neoplasm. Here we report a case of 20 year-old girl with pelvic cystic mass; it was initially thought to be ovarian/paraovarian cyst, but the operative and histologic findings revealed a mesenteric cyst.

A 20-year-old unmarried girl presented with history of irregular menstruation and an incidental pelvic cystic mass. The patient did not complain of dysmenorrhea and menorhaghia. The past medical history was unremarkable. Laboratory tests including complete blood cell count and renal and liver function tests were all normal. The level of CA-125, CEA, LDH, AFP were 8.09 IU/mL, 6.74 IU/mL, 162 U/L and 0.2 ng/mL, respectively (all were within normal range).

Trans abdominal ultrasound revealed 19 x 22 cm abdominopelvic clear cyst on the left side with septations, with normal vascularity and no solid components. We did an MRI, which shows large clear cyst 19 x 23 cm without any solid components, and origin of lesion thought to be left ovarian or paraovarian. Based on the clinical impression of an ovarian/paraovaian cyst laparoscopic approach was planned to perform left ovarian cystectomy/oophorectomy. During the operation, it was confirmed that the origin of the cystic mass was not ovary, but mesentery. Both ovaries were intact. Histopathological examination confirmed mesenteric cyst.

Mesenteric cysts are rare intra-abdominal disease, identified in about 1 out of 100,000 admissions in adults and 1 out of 20,000 in children. Mesenteric cysts are known to occur in every part of mesentery, and the most common site is small bowel mesentery (ileum in 60%) and next is mesocolon (ascending colon in 40%). Although etiology and classifications are still controversial, mesenteric cysts are clinically divided into 6 groups based on histopathological features: lymphatic origin; mesothelial origin; enteric origin; urogenital origin; mature cystic teratoma; nonpancreatic pseudocysts with traumatic or infectious origin.



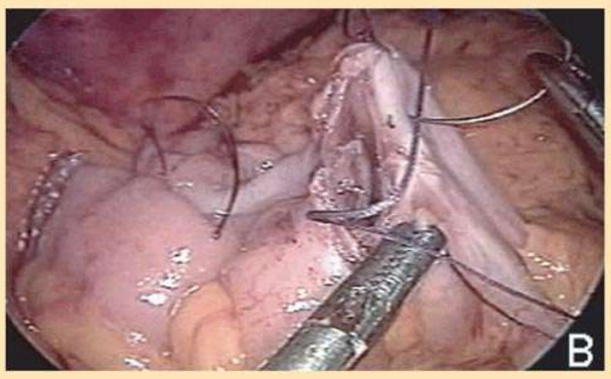
Most mesenteric cysts are asymptomatic; therefore correct diagnosis is difficult and incidentally diagnosed during imaging tests or surgery in many cases. Ultrasonography is the first-line diagnostic method. CT and MRI could be more informative in measuring the exact extension and association with bowels. However, if a mesenteric cyst locates within the pelvic cavity, as like our case, it may be misdiagnosed as an ovarian/paraovarian cyst. It has been recommended that large mesenteric cysts are removed in order to exclude malignant transformation and prevent further complications. The treatment of choice is complete surgical resection, and sometimes it may need bowel resection. A relation of the mesenteric cyst with the major abdominal vessels should be considered, and if needed, careful and accurate dissection should be performed. To conclude, mesenteric cysts should be considered in the differential diagnoses when a pelvic cyst is found in a woman. In addition, we believe that the laparoscopic approach is an appropriate procedure for the management of mesenteric cysts, especially in cases with equivocal preoperative diagnoses. The treatment of choice is the complete surgical excision of the cyst.

Dr Revathy Panicker

"A stitch in time saves nine"

Intra operatively: During surgery the surgeon must be well versed with the anatomy of the operating part. Always consider the technique of sharp dissection close to bladder or while conducting adhesiolysis dissection should be held close to the body of uterus or structures known. Try avoiding usage of electrocautery devices while operating close to bowel obliterated plane. When in doubt call for a GI expert to rule out any possible complications, also to favour a documentation ascertained by the expert to avoid complications in future. Bowel Insufflation technique also helps to rule out any possible bowel injury. Doing a PR can hint if u have messed with the rectum.

How to tackle: The technique of walking the course of bowel is followed by GI surgeon. Here they trace the small bowel loops from the start to rule out any site of perforation or obvious injury. Primary closure is conducted for injuries less than a size of 1 cm, Additonally resection anastomosis to be considered if the damaged segment of the bowel has poor blood supply, Serosal tears can be left alone, However small tear to the serosa and muscularis can be managed with a single layer closure using a 3 x o absorbable or permanent suture (lambert suture) wherein the suture passes though the serosal and muscularis layer in an imbrecating stich. For a full thickness injury a double layer closure is recommened involving the inner layer including mucosa. Thermal injuries and segments with multiple



entrotomies is best repaired with resection and re anastomosis technique. Large bowel injuries: serosa and superficial laceration can be managed with a primary closure. For more extensive injuries resection, colostomy and re anastomosis may be required.

Post Operatively: Use of NG tube, Complete bowel rest and proper antibiotic coverage is required

The magic verse is: Hope for the best, But be prepared for the worst !.

Rules: Be sure of anatomy, Operate close to site you are familiar with. Avoid electrocautery devices while you are unsure about your plane. Most importantly trust your gut and call for help "stat" as it is most easier to diagnose and repair intra op than having it subjected to a 2nd look surgery because a stitch in time save NINE !

A CASE OF VASA PREVIA

Dr Anju K

A 25 yr old, presented to our hospital with primary infertility, married for 5 yrs with Regular cycle, normal BMI (23kg/m2), with no significant past or family history. Patient underwent ICSI+TESE (indication - Malefactor), Patient conceived, and 1 st trimester went uneventful.

At 18 week POG, she presented with bleeding p/s- cervix os closed, bleeding +, USG was done and on ultrasound - SLIUG 18 weeks placenta mainly upper segment distant between lower margin of placenta and internal os 3cm, min fluid collection seen inferior to placenta 15x4mm(SCH), cx 3.7cm, canal and internal os closed. Bleeding stopped by conservative management, and patient was under observation. At 20 weeks ultra sound was repeated in view of spotting p/v, and on ultrasound - SLIUG 20 weeks, placenta left lateral, lower margin is 3 cm from the internal os, prominent marginal vessel seen extending up to the internal os suggestive of Vasa previa, fluid collection so 30x14mm noted near the lower margin of placenta (SCH), cx 3.6cm, canal and internal os closed. Patient was on strict monitoring in view of vasa previa throughout the pregnancy, patient was taken up for elective LSCS at 38 weeks, Intra operative findings - placenta anterior with velamentous insertion of cord with fetal vessel traversing through placental membrane close to internal os.

Discussion : Vasa praevia is uncommon in the general population with a prevalence ranging between 1 in 1200 and 1 in 5000 pregnancies, although the condition may have been under-reported. Vasa praevia occurs when the fetal vessels run through the free placental membranes. Unprotected by placental tissue or Wharton's jelly of the umbilical cord, a vasa praevia is likely to rupture in active labour, or when amniotomy is performed to induce or augment labour, in particular when located near or over the cervix, under the fetal presenting part.

Vasa praevia is classified as type I when the vessel is connected to a velamentous umbilical cord, and type II when it connects the placenta with a succenturiate or accessory lobe. Vasa praevia may be diagnosed during early labour by vaginal examination, detecting the pulsating fetal vessels inside the internal os, or by the presence of dark-red vaginal bleeding and acute fetal compromise after spontaneous or artificial rupture of the placental membranes. The fetal mortality rate in this situation is at least 60% despite urgent caesarean delivery. However, improved survival rates of over 95% have been reported where the diagnosis has been made antenatally by ultrasound followed by planned caesarean section. The classic presentation of unexpected vasa praevia in labour is the presence of painless vaginal bleeding (also known as Benckiser's haemorrhage). This occurs mainly when the cervix is effaced and dilated, and the membranes rupture spontaneously or are ruptured artificially.As the total fetal blood volume at term is approximately 80-100 ml/kg, the loss of what may appear as a relatively small amount of blood can have major implications for the fetus and is rapidly fatal.

A systematic review and meta-analysis of the association among placental implantation abnormalities (including placenta praevia, placenta accreta, vasa praevia, velamentous cord insertion) and preterm delivery in singleton gestations has found a perinatal death rate random effect pooled risk ratio of 4.52 (95% CI 2.77-7.39) for vasa praevia. There is insufficient evidence to support universal screening for vasa praevia at the time of the midpregnancy routine fetal anomaly scan in the general population.

How to manage a patient with vasa previa? In the presence of confirmed vasa praevia in the third trimester, elective caesarean section should ideally be carried out prior to the onset of labour.

A decision for prophylactic hospitalisation from 30-32 weeks of gestation in women with confirmed vasa praevia should be individualised and based on a combination of factors, including multiple pregnancy, antenatal bleeding and threatened premature labour

Because of the speed at which fetal exsanguination can occur and the high perinatal mortality rate associated with ruptured vasa praevia, delivery should not be delayed while trying to confirm the diagnosis, particularly if there is evidence that fetal wellbeing is compromised The ultimate management goal of confirmed vasa praevia should be to deliver before rupture of membranes while minimising the impact of iatrogenic prematurity. Based on available data, planned caesarean delivery for a prenatal diagnosis of vasa praevia at 34-36 weeks of gestation is reasonable in asymptomatic women Administration of corticosteroids for fetal lung maturity should be recommended from 32 weeks of gestation due to the increased risk of preterm delivery.

PRE-CONCEPTIONAL LAPAROSCOPIC CERVICAL ENCERCLAGE AND A CASE OF SUCCESSFUL PREGNANCY:

Dr Sija Chandran L.J.

30 yr old lady, married x 5 years, k/c/o PCO, presented to us with history of 3 previous second trimester abortions at around 20-24 weeks due to cervical incompetence even after placement of vaginal encerclage in the last 2 abortions.

She underwent preconceptional abdominal cerclage placement via laparoscopy at our hospital. Dissection of the vesicouterine space was done. Mersilene tape with curved needle was used as suture material and bite was taken from anterior to posterior at the level of the internal os. The needle was passed between the uterine vessels and the cervicoisthmic junction, coming out through the posterior leaf of the broad ligament, approximately 1 cm above the uterosacral ligament. Knot was tied posteriorly.

Patient conceived after ovulation induction after 2 months of lap encerclage. Patient was antenatally monitored for cervical length. Elective LSCS was done at 37 weeks in v/o mild IUGR and in v/o lap encerclage and delivered a live term male baby of weight 2.43kg.APGAR was 9 at 1'. Cerclage was not removed in v/o wish for future pregnancies.

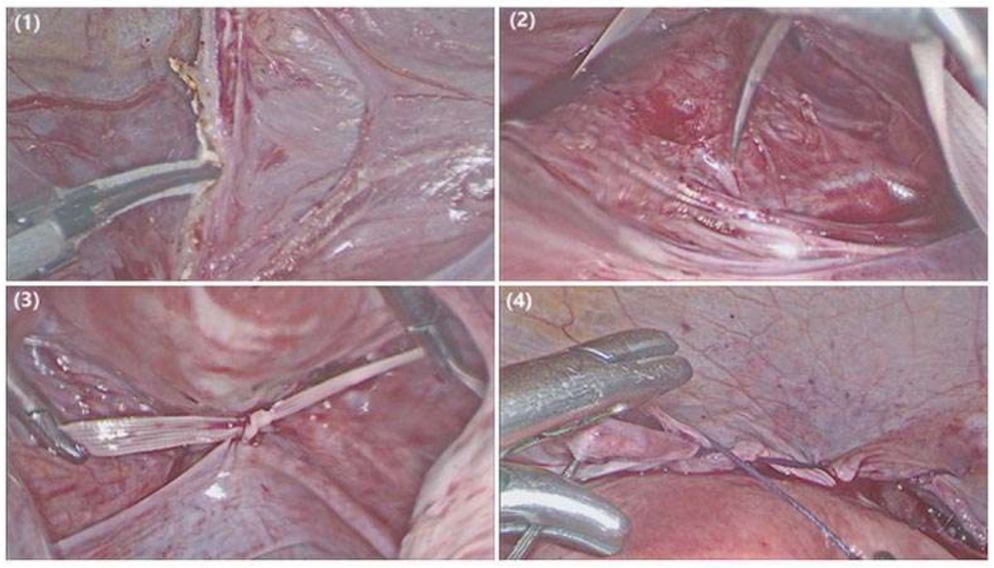


Figure-1: Dissection of vesicouterine space. Figure-2: Mersilene tape bite taken from anteriorly to posterior. Figure-3 : Knot tied posteriorly. Figure-4: UV Fold approximated

DISCUSSION : Cervical incompetence is defined as the inability of the uterine cervix to retain a pregnancy in the second trimester in the absence of clinical contractions labor or both. There are two approaches for cervical cerclage placement- Transvaginal which can be done using the McDonald or Shirodkar technique, or transabdominal placed laparoscopically or via laparotomy.

Currently, the best evidence for history indicated Transvaginal cerclage (performed between 12-14 weeks GA) is in women with a history of >3 Preterm births or second trimester losses. In addition Transvaginal cerclage is also indicated in women found to have short cervix (<25mm) with a history of 1 or more spontaneous preterm birth or second TM losses, in which case it is referred to as ultrasound indicated Trans-vaginal cerclage (performed between 16-23 weeks). The main indications for trans-abdominal suture are a grossly disrupted cervix, an absent vaginal cervix, and previous failed elective vaginal cerclage. The timing of abdominal cerclage placement can occur either pre- or postconception, depending on the patient's presentation. The benefits of laparoscopic surgery include decreased blood loss lower risk of post op DVT, reduced post op pain,and shorter hospital stay. The reported success rate lap cerclage is 85-90%. In complicated cases, for example where membrane rupture or intrauterine death in the midtrimester occurred, then the suture can be removed by posterior colpotomy, thus avoiding the need for a second laparotomy or laparoscopy during pregnancy failure.

In our hospital, a total of 15 lap abdominal cerclages have been done so far, in which 13 were preconceptional cerclages and 2 postconceptional. All cases were done in view of previous second trimester losses and failed vaginal cerclage. Among the 13 preconceptional cerclages, 7 conceived, 5 had successful delivery (71%), 1 was a case of unexplained IUD at 37 weeks, and one is undergoing antenatal check up at our hospital. 4 cases lost follow up and 2 which were done recently are yet to conceive. 2 cases were done post conceptional at around 12 weeks, in which 1 case PPROM occurred at 21 weeks and suture was removed laparoscopically and 1 case had successful delivery at 37 weeks.

Patients who failed to benefit from vaginal cervical cerclage may benefit from the simplified laparoscopic abdominal cervical cerclage. With a known history of cervical incompetency, preconceptional cerclage should be considered for improved perinatal outcomes.

ENDOMETRIAL RECEPTIVITY ARRAY

Dr Danu C

Successful implantation requires the presence of a healthy embryo, a receptive endometrium, a synchronized and successful molecular dialogue between the two and immune protection from the host. The human endometrium is a dynamic tissue; it undergoes changes at multiple levels during the menstrual cycle in response to ovarian hormones and paracrine secretions. The endocrine and paracrine secretions control gene expression of the different endometrial cell types. The postovulatory progesterone rise brings about secretory changes and the endometrium acquires a receptive phenotype permitting implantation of the blastocyst. This period of receptivity is known as the "window of implantation" (WOI). The WOI opens on day 19 or 20 of the cycle and remains open for just 4-5 days at the time when P reaches peak serum concentrations. During the phase of receptivity, the endometrium undergoes morphological, cytoskeletal, biochemical, and genetic changes to become functionally competent. The ability to identify the endometrial WOI in the clinical setting would enhance the outcome of fertility treatments such as IVF.

Histological, biochemical, and ultrasound markers of ER have been proposed for use to improve implantation rates (IRs) in IVF. ER is assessed on the basis of endometrial thickness, character, volume, and blood flow patterns. Endometrial pinopods identified on electron microscopy also generated interest as a marker of ER. Pinopods are cytoplasmic projections of the luminal epithelial cells, abundant during the WOI, thought to promote blastocyst adhesion. The presence of pinopods was demonstrated in post receptive endometrium, and this precluded their use as a useful marker of ER. Mid-secretory phase integrins, leukemia inhibitory factor, homeobox A10, mucin 1, calcitonin, and cyclo-oxygenase 2 have shown significant association with the WOI. Although to date no single, clinically relevant morphologic, molecular, or histologic marker capable of indicating endometrial receptivity status has been identified, global transcriptomic analysis of human endometria performed in the last decade has given us insights into a genomic signature that is capable of identifying endometrial receptivity. The various molecular approaches for the study of biological samples are collectively called the "Omics" and include - genomics (study of genes), epigenomics (study of epigenetic DNA modifications), transcriptomics (study of gene expression), proteomics (quantification of proteins), metabolomics and lipidomics (composition and quantification of metabolites and lipids). Currently, transcriptomics is considered the most established technology available for evaluation of the endometrial factor.

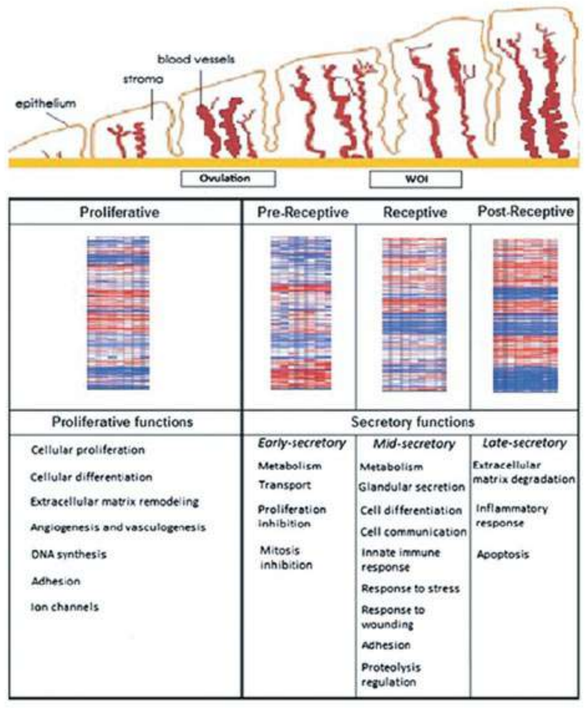
The transcriptome of the endometrium has been defined in all phases of the menstrual cycle; clustering of genes into four groups was identified and these were consistent with histological phenotypes of proliferative (PE), early secretory (ESE), mid-secretory (MSE), and late-secretory (LSE) phases. At a molecular level, the prereceptive/early secretory phase is characterized by increased metabolic activity in preparation for implantation. This leads to a predominance of products related to cell metabolism (fatty acids, lipids, eicosanoids, and amino alcohols), transport, and germ cell migration. There is an inhibition of mitosis during this phase as suggested by the downregulation of several growth factors.

The receptive phase witnesses a "transcriptional awakening" or upregulation of most gene expression. Apart from a high level of metabolic and secretory activity there is also an upregulation of genes involved in the activation of the immune response. During the late-secretory phase, the WOI closes and in this phase genes related to immune response-both cellular and humoral, blood coagulation, steroid bio-synthesis, and prostaglandin metabolism are regulated

Search for an adequate marker of ER, led to the development of a molecular diagnostic test - the endometrial receptivity array (ERA). ERA consists of a customized microarray based on the transcriptomic signature of human ER, specifically when the human endometrium is receptive to blastocyst adhesion.

It has been designed to identify ER by comparing the genetic profile of a test sample with those of luteinizing hormone (LH) + 7 controls in a natural cycle, or on day 5 of progesterone administration (P + 5) after E2 priming in a HRT cycle. The test contains 238 genes that are differentially expressed between these profiles. This array is coupled to a computational predictor that can diagnose the personalized endometrial WOI of a given patient regardless of their endometrial histology.The bioinformatic predictor classifies an endometrial sample as "receptive" or "nonreceptive." The "nonreceptive" ERA is further classified as prereceptive or postreceptive giving an exact status of the endometrium at the time of biopsy. ERA has a sensitivity and specificity of 99.7% and 88.5%, respectively. Garrido-Gómez et al. 2013, in their study demonstrated that the transcriptomic profile of the mid-secretory phase endometrium did not change significantly between cycles or over relatively long periods (3 years).

Embryo-endometrial synchrony is fundamental to successful implantation. It has also been established that many failures in IVF can be attributed to embryo-endometrial asynchrony. Ovarian stimulation given for follicular recruitment advances endometrial development; by the time embryos are transferred the WOI has closed. The transcriptomic signature of the WOI can be used to define an individual's personalized receptive window for use in IVF. It could also help in understanding the effect of different infertility treatments on the endometrial WOI and possibly identify the cause of treatment failure.



Defining a receptive window would avoid embryo wastage and emotional, physical, and financial distress. Its use in patients with adenomyosis, endometriosis, and chronic endometritis can prove beneficial, as these conditions are associated with an altered ER. Persistent thin or thick endometrium is also an indication for carrying out ERA. The invasive nature of the test, the need for embryo vitrification and cost are some of its limitations.

At our institution we investigated patients with RIF who had more than three IVF failures using ERA test. Patients underwent ERA on day P + 5 in an HRT cycle. The results showed that a changed WOI existed (non-receptive endometrium) in 60% of RIF patients whereas 40% had receptive endometrium. This suggests that an endometrial factor exists in more than half of patients with RIF and could contribute to their implantation failure. Among the patients with receptive endometrium 83.3% conceived and among patients with non-receptive endometrium 55.5% conceived after transfer according to ERA result. A total clinical pregnancy rate of 66.7% was achieved after transfer according to ERA result. We could find that correcting the WOI by doing a "personalized embryo transfer" (pET) improved the reproductive outcome.

CONVERSION OF A HIGH RESPONDER IN A OI CYCLE TO IVF

Dr Abirami

HISTORY: A 27-yr old patient, with history of irregular cycles and 3yrs married life presented at our hospital for treatment of primary infertility. Routine investigations were done and were normal. Her husband had a normal semen analysis.

She proved to be clomiphene citrate resistant and therefore an ovulation induction cycle with letrozole and recombinant FSH 50 IU daily in a low-dose step-up protocol was started 3 days after a progesterone induced withdrawal bleeding. The daily dose of r Fsh was given for 5 days and follicular monitoring done As there was no ovarian response, the same dose of FSH was continued for a further 3 days.

The daily dose of r FSH was increased up to 75 IU for 4 days, as there was no ovarian response. Daily dose was again increasedafter 4 days, this time to 150 IU. Four days later, a hormonal profile and a vaginal ultrasound were performed: oestradiol 3134 pg/ml; progesterone 0.8 ng/ml; LH 1.93m IU/ml; and ultrasound 8 follicles between 10 and 14 mm, two follicles between 14 and 15 mm, and 3 follicles between > 18mm.

Subsequently, the patient was counselled about the risks for OHSS, multiple pregnancy and the different treatment options available (including termination of cycle)

The decision was made to perform rescue IVF. The gonadotrophin administration was continued for 2 more days and 0.25 mg of Cetrorelix was started simultaneously. Two days later, an ultrasound report of five follicles between 14 and 15 mm, five follicles between 16 and 17 mm, and six follicles > 18 mm. Because of the rising oestradiol concentrations and the developmental maturity of the follicles, inj decapeptyl 0.2mg (Gn RH agonist) given s/c. Nine oocytes were retrieved 36 h later and decision taken to freeze all oocytes and to do a frozen embryo transfer after 2 months.

DISCUSSION: Ovulation induction with aromatase inhibitors or recombinant FSH or both together combined are frequently used as an effective treatment for infertility. However, this treatment is associated with a significant risk of multiple gestation and OHSS. Rarely, there is development of supernumery follicles and a rise in level of estradiol in the cycle leading to cancellation of the said cycle

However, canceling a cycle is frustrating to both patients and physicians, wastes money and resources, and destroys the hope of a pregnancy occurring in that cycle. As a result, clinicians have searched for an alternative to canceling cycles that offers protection from the complications of OHSS and multiple gestations.

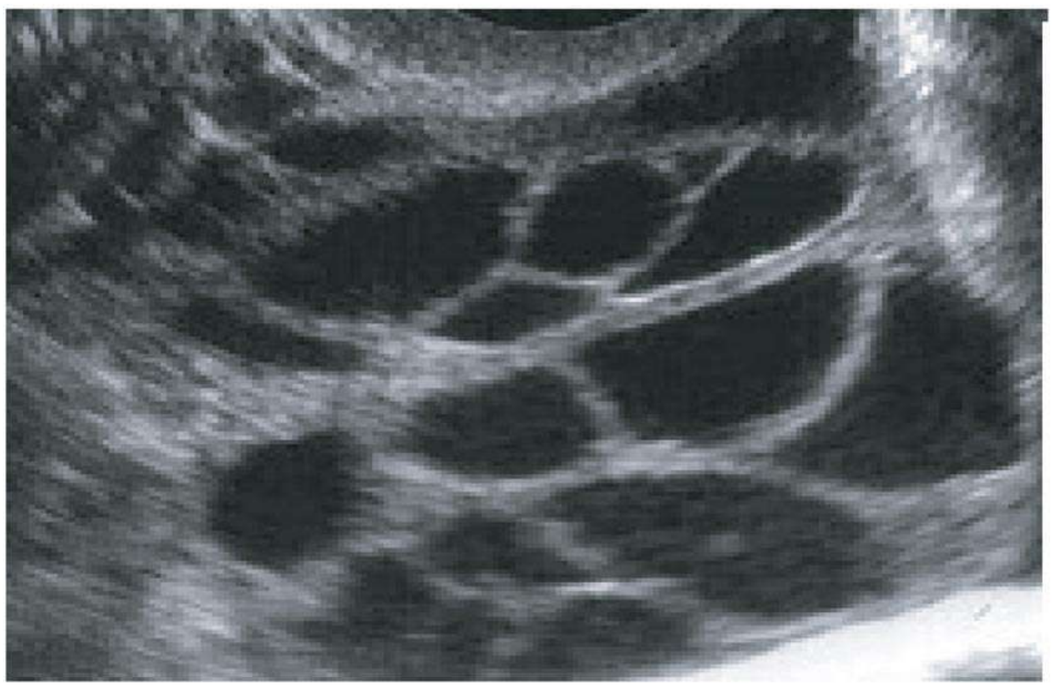
A safe alternative to cancellation may be to convert an OI cycle to IVF, thereby giving clinicians control over how many embryos are introduced into the uterus. Conversion also prevents the complete financial loss and frustration of a canceled cycle by maintaining a pathway toward possible pregnancy, although the added costs of IVF are incurred.

It should also be noted that the risk of ovarian hyperstimulation can further be decreased by inducing final oocyte maturation with a GnRH agonist and not with HCG. Further, in our case, we had opted to freeze all oocytes and to continue Cetrolix for 5 more days after ovum pickup along with Cabgolin to prevent OHSS.

It may be significant in this context to emphasize that the absence of GnRH downregulation in this cycle may entail a premature leutinizing hormone surge and luteinization. But the administration of Cetrolix causes the immediate LH suppression without a negative effect on the developing follicles.

It also demonstrates that GnRH antagonists, due to their immediate action, can offer an extra tool to convert 'explosive' ovulation induction into controlled rescue IVF cycles, something that was not possible before their advent

When a decision is made to convert to IVF, the FSH stimulation with injectable gonadotrophins is to be continued even if GnRH antagonist is started until the follicles are mature.



The combination of GnRH antagonist and the discontinuation of FSH stimulation results in a dramatic fall in oestradiol concentrations and a developmental arrest of ovarian follicles. It can be speculated that the administration of 0.25 mg of GnRH antagonist and a slight reduction of exogenous FSH might be sufficient to achieve this purpose.

Amy M. Antman et all studied 77 patients conversion of gonadotropin/IUI cycles at high risk of high-order multiple pregnancies to IVF. They reported high delivery rates: 45.5% as compared with 39% for E2 and age matched IVF controls and 32.5% in age- and attempt-matched controls Even though fewer embryos were transferred in the study group than in the two control groups, a high implantation rate (30.5%) was seen. Further, they also reported that there were no pregnancies when patients were converted to IVF with E2 levels < 1,000 pg/mL, despite the fact that these patients had higher numbers of follicles.

Some authors also advocate the use of coasting along with conversion to IVF to prevent OHSS, but there has been no added benefit as demonstrated in several studies

This case report suggests that rescue IVF, with or without coasting, should be considered as an extra option for patients at risk for multiple pregnancy and/or hyperstimulation after ovulation induction.

Dr Aishwarya

CASES OF SUBMUCOUS FIBROID UTERUS (TYPE II) DEALT BY LAPAROSCOPY

Usually, submucous fibroids are best dealt by hysteroscopy. However, here are two cases where in they were dealt by laparoscopy, due to their size and location.

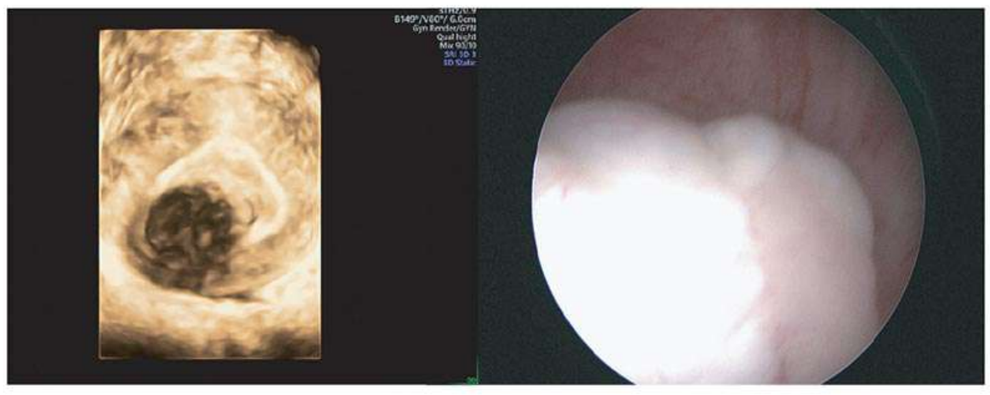
CASE 1 : Mrs X, aged 42 years. P1 L1, reported to our OPD with complaints of heavy menstrual bleeding since one year. She complained of heavy flow during the first three days of menses, with passage of clots.

USG pelvis revealed an intramural fibroid with submucous extension measuring 2.5 x 2.3 cm. After routine investigations and pre anesthetic clearance, she was posted for hysteroscopic myomectomy. On hysteroscopy, only a part of the fibroid was seen, which was resected using resectoscope. Remaining fibroid was dealt with laparoscopically, and the entire fibroid was removed and sent for histopathology. HPE report came as leiomyoma.

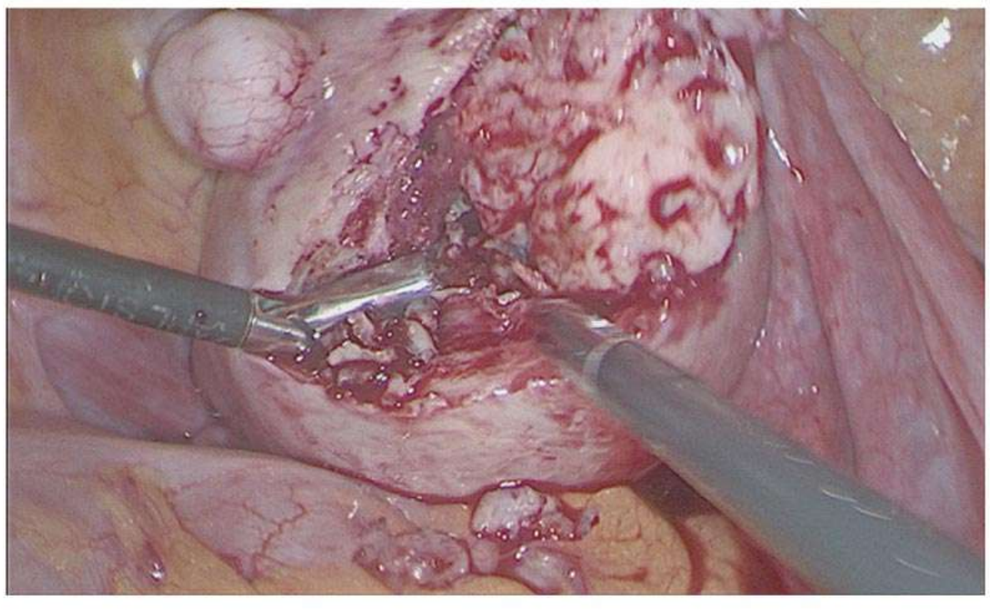
CASE 2 : A 42 year old lady, P2L2, both LSCS, came to our OPD with complaints of heavy menstrual bleeding since 1.5 years. She gave history of passage of clots too. The menstrual cycles were regular, at intervals of 28 days. On per abdomen examination - a mass of about 14 weeks size was felt. On per speculum examination- cervix and vagina were normal. On per vaginal examination- uterus was about 14 weeks size, mobile, posterior fornix was obliterated.

USG pelvis- showed a submucous fibroid with intramural extension- 7 x 6 cm. 3 units of blood transfusion was done to correct anemia.

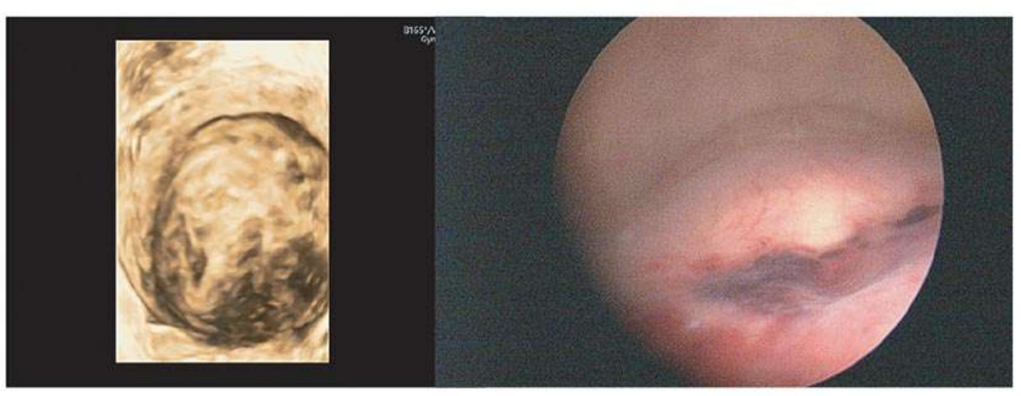
She was planned for laparoscopic myomectomy and operative hysteroscopy. On hysteroscopy, the myoma was seen indenting the posterior wall. Laparoscopic myomectomy was done and specimen was sent for HPE.



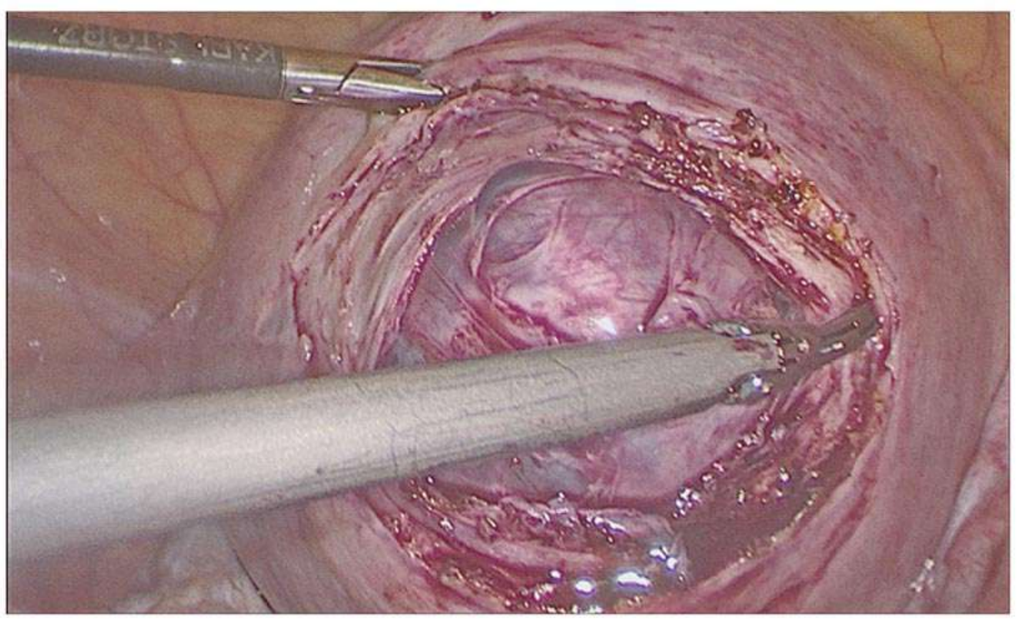
Sub mucous fibroid on hysteroscopy



SMF with intramural extension, on laparoscopy



Fibroid seen indenting the cavity



Laparoscopic myomectomy done.

DISCUSSION : Myoma of uterus is one of the most common benign tumours of the reproductive system in women, the incidence rate is about 50-60%, and it occurs frequently in the female in the reproductive age group. The incidence of submucous myoma of the uterus is about 10-15 %.

Submucous myomas with a diameter of 4 cm and less should be dealt with hysteroscopically. Like in the cases mentioned above, where in the fibroids are of larger size, pre treatment with GnRH analogues may prove to be beneficial in reducing the size of the fibroid, thus considerably reducing the intraoperative blood loss. Also, SMF having an intramural extension need to be dealt with laparoscopically too since only a part of the fibroid can be removed through hysteroscopy.

For multiple myomas, patients should be counselled about an increased recurrence risk and the need for doing the surgery in two sittings to avoid the risk of pulmonary edema due to prolonged surgery. When a hypotonic distension medium is used for myoma removal, careful watch on the inflow and outflow should be kept, aiming at the fluid deficit upto a maximum of 1500 ml. Possible additional measures to be taken in case of an increasing deficit of distension medium include the use of mannitol, physiological saline solution or diuretics.

Data from our hospital from the last 3 years (2015-2018) shows that a total of 42 infertile patients underwent hysteroscopic SMF resection, out of which 11 patients have conceived (26.1%).

STATISTICS

APRIL - JULY 2019

LAPAROSCOPY	**86**
TLH +BILATERAL SALPINGECTOMY	9
TLH+BSO	10
PCO PUNCTURING	17
LAPAROSCOPIC MYOMECTOMY	19
LAPAROSCOPIC RECANALISATION	2
ENDOMETRIOTIC CYSTECTOMY	16
LAPAROSCOPIC SACROCOLPOPEY	1
STERILISATION	1
DERMOID CYSTECTOMY	3
ADENOMYOMECTOMY	2
ECTOPIC -SALPINGECTOMY	9
SALPINGOSTOMY	2
LAVH+PFR	1
HYSTEROSCOPY	**80**
PRE IVF HYSTEROSCOPY	67
SMF RESECTION	5
SEPTAL RESECTION	1
TUBAL CANNULATION	1
HYSTEROSCOPIC POLYPECTOMY	5
HYSTEROSCOPIC INTRA UTERINE ADHESION RELEASE	1
OBSTETRIC CASES	**128**
LSCS	80
FTND	38
VACUUM DELIVERY	9
HYSTEROTOMY	1
MINOR CASES	**89**
SUCTION EVACUATION	13
FC	1
PIPELLE SAMPLING	8
MIRENA INSERTION	2
ERA TESTING	5
EUA	2
PPS	2
CERVICAL CERCLAGE	55
AMNIOCENTESIS	1
MALE SURGERY	**12**
TESA	3
TESE	4
PESA	4
VARICOCELECTOMY	1
OPEN CASES	**3**
TAH + BSO	1
VH + PFR	1
MYOMECTOMY	1
CONCEPTION +IUI STATISTICS	
TOTAL CONCEPTION	108
SPONTANEOUS	9
POST LAPAROSCOPY	13
ART	44
IVF/ ICSI STATISTICS	
TOTAL	109
POSITIVE	44 (42.3%)
FET (TOTAL)	51
POSITIVE	24 (47%)
IUI STATISTICS	
TOTAL	221
POSITIVE	29 (13.12%)

Published quarterly by KJK Hospital for private circulation only ■ Edited by Dr. K. Jayakrishnan Co- Editor Dr. Deepti B.