THE ART OF MULTIPLES

There was a time when we welcomed the super MOM's (moms of multiples) in assisted reproduction as an accepted side effect of ovulation induction with medications and protocols for embryo transfers. Now we seem to be wary of numbers, as the fraternity marches towards single embryo transfers, declaring the once popular MOM's as an extreme high risk group.

Pregnancies are always categorized as low risk or high risk and never as "no risk". Multifetal gestations raise that risk factor. There is an increased risk of intra-uterine growth restriction, premature births and its sequelae and increased possibility of pregnancy induced hypertension and diabetes. However, in current practice most of these are overcome with anticipation, timely detection and early interventional therapy. In addition, adequate screening procedures are implemented to rule out anomalies in the first trimester well before the level 2 scan in the second trimester.

The preconception assessment of high risk patients provide sufficient insight into severity of disease and hence optimum control can be achieved of a diabetic or hypertensive state before attempting to conceive. Given all these measures and foresight, it would not be perilous to transfer more than one good grade embryo (either Day 3 cleavage or blastocyst) in order to achieve pregnancy with the risk of a multiple one. Good quality embryos can be transferred prudently but in the event of moderate to poor quality, one does not have a choice but to transfer extra, in case the opportunity to grow into a blastocyst is a remote possibility. Single blast transfers can work well, if the initial cohort of embryos were of good grades and the numbers adequate (at least 3 or 4).

WHY DO WE DO WHAT WE DO?

Our center has almost become a referral one over the years. The clientele mostly comprise of cases that have failed at other centers and have pretty much sought treatment with us as a last resort. The pressure to deliver hence is multifold, considering that these cases may have undergone therapy for various disorders, especially severe endometriosis or Pelvic inflammatory disease and may also have inoperable abdomens in addition to being poor responders. Given these circumstances, we also have an active donor and surrogacy programme running, to accommodate influx of repeated failures at IVF owing to either a poor response, quality of embryos or implantation site. The usual categories of transfers are:

- Day 2, if the numbers of oocytes are two or less with moderate to poor quality of resultant embryos.
- Day 3, if the embryos are 2 or 3 and the embryo quality is good.
- Day 3 and Day 5/6/7, which we term as sequential, and have been successfully carrying out in chronic failures and in those whom we have a cohort of embryos that don't warrant freezing, and is based on numbers and quality.
- Blastocyst only transfers (1-2), again for chronic failures, problems with implantation site, and cases of OHSS. This also gives us extra days for luteal support.

The real indications for a single embryo transfer in order to achieve good success rates as well as reduce multiple pregnancies would be

- The younger patient (< 35 years)
- A yield of good quality blastocysts with an excess for cryopreservation
- A woman who has signed for a donor egg programme
- Previous history of miscarriages in higher order gestation
- An incompetent cervix
- Hypoplastic uteri that have been grown with hormonal therapy and
- Those with known medical disorders like diabetes and hypertension which can worsen in pregnancy.

No doubt, that barring the above mentioned scenarios; others are still being subjected to transfer of supernumerary embryos according to their previous performance and profile thereby increasing chances of multifetal gestation. We know the rates of dizygous twinning (DZ) vary while monozygous twinning (MZ) seems to be constant in ART. However the incidence of monozygosity is influenced by the techniques and transfers and is significantly higher than its natural incidence. Often a dizygous twinning and the dichorionic diamniotic variant of monozygosity are confused in diagnosis. There is also a 10-20% chance
of twin to twin transfusion with monozygous twinning and a high chance of cord entanglement in a monochorionic monoamniotic twinning, besides others(1).

It is known that these occurrences are influenced by the timing of division of pre-implantation embryos and we have observed an increase in incidence of monochorionic monoamniotic twins in triplet gestation, making it difficult to decide which fetus is to be reduced.

As per norm, they are pre-screened by nuchal translucency (NT), and in the case of twins, by both NT and triple markers, following which decisions are taken on accessibility. Mostly, in this particular scenario, if one of the monochorionic twins is reduced, there is a loss of the corresponding twin at a later date, usually in a week, thereby influencing the couples to accept the singleton fetus.

In the context of ART, there exists a great deal of debate over the factors that contribute to the increase in MZ twinning as well as the mechanisms involved. Maternal age, ovarian stimulation, zona manipulation, temperature effects, and in vitro embryo culture have all been suggested as contributory factors.

The Potential mechanisms by which MZ twins might arise following ART as reported in the article cited in the reference (1) are:

(A) DCDA (MZ) TWINS
- Suboptimal culture conditions or temperature fluctuations resulting in disruption of communication between blastomeres and the independent formation of two separate blastocysts.
- Interference with the zona by ICSI or Assisted Hatching
- Hardening of the zona caused by ovarian stimulation or sub-optimal culture conditions resulting in abnormal blastocyst hatching.
- If hatching results in bisection of the trophectoderm and inner cell mass (ICM) it may result in formation of two separate blastocysts

(B) MCDA (MZ) TWINS
- If there is disturbance of the morula it may result in disruption of communication between inner blastomeres and result in independent formation of two separate ICMs within the same blastocyst(2)
- Blastocyst collapse with adhesion of ICM cells to another point within the trophectoderm resulting in the formation and growth of a second ICM.
- Hardening of the zona resulting in abnormal blastocyst hatching.
- If hatching results in adhesion of ICM cells to another point within the trophectoderm, the formation and growth of a second ICM can result.

(C) MCMA (MZ) TWINS
- Insult to the early blastocyst resulting in disruption of communication between early ICM blastomeres and the formation of two separate embryonic disks within the same blastocyst.
- Disruption or hardening of the zona resulting in abnormal blastocyst hatching.
- If hatching results in disruption of communication between ICM cells (e.g. by apoptosis) the formation of two separate embryonic disks within the same blastocyst can result.(3)
- Research is still debating the impact of maternal age as an influence on twinning, some studies citing a 12-22% rise in women over 35 years when compared to those under 30 years, while others have found no correlation(4). Ovarian stimulation has been implicated, which seems more plausible, considering hyperstimulation with a 1.2% rise in incidence.

Schachter et al., found a Monozygous twinning rate of 0.95% of all ART pregnancies and a 1.5% rise following ovulation induction(5).

I have briefly outlined the incidence of multiple pregnancies at our centre. I need to remind that owing to our complex population our transfers are also correspondingly supernumerary.
### Statistics from August 2008 - July 2012

<table>
<thead>
<tr>
<th>Patients Underwent ART</th>
<th>4660</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancies</td>
<td>2034 (43.7%)</td>
</tr>
<tr>
<td>Multiple Pregnancies</td>
<td>482 (23.7%)</td>
</tr>
<tr>
<td>Fetal Reduction</td>
<td>225 (46.7%)</td>
</tr>
<tr>
<td>Donor Program</td>
<td>723 (35.6%)</td>
</tr>
<tr>
<td>Own Program</td>
<td>1311 (64.4%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>OUTCOME</th>
<th>IVF</th>
<th>ICSI</th>
<th>SEQ</th>
<th>BT</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Twins</td>
<td>27</td>
<td>106</td>
<td>200</td>
<td>8</td>
<td>341</td>
</tr>
<tr>
<td>Triplets</td>
<td>8</td>
<td>32</td>
<td>76</td>
<td>4</td>
<td>120</td>
</tr>
<tr>
<td>Quadruplets</td>
<td>0</td>
<td>4</td>
<td>15</td>
<td>0</td>
<td>19</td>
</tr>
<tr>
<td>Quintuplets</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>35</td>
<td>143</td>
<td>292</td>
<td>12</td>
<td>428</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Interventional 79 (35.17%)</th>
<th>Spontaneous 138 (61.3%)</th>
<th>BOTH (Int &amp; spont) 8 (3.55%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quad - Twins</td>
<td>10</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>Triplets - Twins</td>
<td>62</td>
<td>36</td>
<td>-</td>
</tr>
<tr>
<td>Triplets - Single</td>
<td>3</td>
<td>9</td>
<td>-</td>
</tr>
<tr>
<td>Twins - Single</td>
<td>2</td>
<td>89</td>
<td>-</td>
</tr>
<tr>
<td>Quin - Twins</td>
<td>2</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Quad - Trip - Twin</td>
<td>-</td>
<td>-</td>
<td>5</td>
</tr>
<tr>
<td>Trip - Twin Single</td>
<td>-</td>
<td>-</td>
<td>3</td>
</tr>
</tbody>
</table>
The general incidence over 4 years is 23.7%. The fetal reduction rate is about 46.7% of which spontaneous reduction supersedes medical reduction (61.3% versus 35.1%).

Among the multiple pregnancies cervical cerclage was done in 86.2% and of these about 45.3% had additionally had a fetal reduction. At this point I would like to include our paper on cervical cerclage in ART and the indications for which we perform this procedure on our patients (http://www.gghospital.in/Cervical.pdf).

<table>
<thead>
<tr>
<th>Outcome</th>
<th>With Cerclage-194</th>
<th>Without Cerclage-276</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivered</td>
<td>138 (71.13%)</td>
<td>4-</td>
</tr>
<tr>
<td>Mid trimester miscarriage</td>
<td>19 (9.79%)</td>
<td>36-</td>
</tr>
<tr>
<td>Hystero to my</td>
<td>4 (2.06%)</td>
<td>9-</td>
</tr>
<tr>
<td>Hysterec to my</td>
<td>1 (0.51%)</td>
<td>89-</td>
</tr>
<tr>
<td>On going</td>
<td>30 (15.46%)</td>
<td>0-</td>
</tr>
<tr>
<td>No feed back</td>
<td>30</td>
<td>-5</td>
</tr>
<tr>
<td>Trip-Twin-Single</td>
<td>-</td>
<td>-3</td>
</tr>
</tbody>
</table>

The incidence of miscarriage in mid trimester among both these categories is 9.79% and 7.6% and the carry home baby rate is about 71.13% and 72.10%.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>337 (69.91 %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivered</td>
<td></td>
</tr>
<tr>
<td>M.A</td>
<td>12 (2.48 %)</td>
</tr>
<tr>
<td>Mid trimester miscarriage</td>
<td>40 (8.29 %)</td>
</tr>
<tr>
<td>Hysterotomy</td>
<td>7 (1.45 %)</td>
</tr>
<tr>
<td>Hysterectomy</td>
<td>1 (0.02 %)</td>
</tr>
<tr>
<td>On going</td>
<td>74 (15.33 %)</td>
</tr>
<tr>
<td>No Feed Back</td>
<td>11 (2.28%)</td>
</tr>
<tr>
<td>Total</td>
<td>482</td>
</tr>
</tbody>
</table>

We have had one case of central placenta previa coupled with severe endometriosis for which a hysterectomy was inevitable owing to severe PPH. She is registered for a surrogacy programme. There were 7 cases of hysterotomy owing to failed induction for anomalous fetuses, fetal demise and Premature rupture of membrane with chorioamnionitis.
To conclude, multiple pregnancies do raise the risk in ART conceptions. However the decision between a single or multiple embryo transfer depends solely on patient profile, past performances and implantation site. The next step in decision making is on the part of the consultant and the couple. While most prefer multiple transfers thinking of twofor the price of one, there are few others who prefer to raise a single child after carefully weighing their personal circumstances. It is up to the consultants to make them aware of the associated risks and then venture in to the treatment cycle.

On the whole, the patient population differs. No two treatments can be the same. There are specific indications for performing the different procedures in the lab. The same applies to the numbers of embryos transferred. Nothing can be universally applied because ultimately we have still not arrived at clinching which embryo will certainly make a baby, although with all the research going on, we surely can predict which group of embryos is favorable for transfer and their probability in achieving a pregnancy. If multiple pregnancies are inevitable, then let us improvise management and perhaps regulate the numbers than can be carried, namely twins.

REFERENCES

DR. PRIYA SELVARAJ MD MNAMS MCE
A SCOPE OF LIFE

The latest buzzword in the field of ART as the promising new technology is the Embryoscope. This comes close at the heels of an earlier impact created by evaluation of culture media that houses developing embryos, allowing selection of the best or viable ones, by measuring important by products, namely, study of Metabolomics. Then again, it is interesting to note certain favorable points that an Embryoscope has to offer as opposed to study of the media micronutrients or metabolic products.

The Embryo is a culmination of a unique set of inheritance from two individuals and to say it in simpler terms, has a mind of its own. We may dictate the entire development or growth in an artificially created environment, yet we are dependent on tools to certify its integrity, read: repeated observations, grading, prolonged culture, biopsy, metabolomics etc. However, the biggest test is the culture conditions, gas environment, culture media and mode of fertilization. All these play a major role in generating a wide range of high to poor quality embryos or blastocysts. Of course, from the birth of the first IVF baby until now, there have been several modifications to methodology and perhaps even more, pertaining to culture conditions.

Even cryopreservation techniques have evolved from conventional slow freezing techniques to vitrification. I just used a term "conventional" which is like a pre-fix to almost all procedures in ART as the "Basics" don't change; they remain as the guide or as a comparison to newer techniques. What we tend to do is always apply them as the working standard and compare results from the newer lab practice or media or instrumentation used.

When we do that, we have not denounced old practices but acknowledge them as practices or methods that have withstood test of time in generating consistent results. We want this kind of practice: "convention" that generates "consistency".

Let's review some current basic facts concerning "integrity" of an embryo right from its journey as an individual gamete until the final stage of maturation, namely the blastocyst. Some of these statements have clinical studies to back them, while others need further more to substantiate their use in current practice.

To quote, single embryo selection, as advocated, by a pedigreed selection made in a routine tertiary care lab, namely by observing morphology and noting timing of division could influence both the data and outcome (1).

What did we begin with in terms of assessment? If we really need to complete a pedigree based selection then we ought to grade oocytes and sperms before we enable fertilization. Then, periodic evaluations follow as per conventional lab methods and may include the following.

**PN SCORING**

Nucleoli alignment: Unequal NBP (nucleolar precursor bodies) may correlate with delayed or fast rates of condensation and reflect poor developmental potential (1).

**CLEAVAGE TIMINGS**

- First check: 16-18 hours
- Second check: 25 hours
- Third check: 40-42 hours (Ideal embryo transition to 4-6 cells occurs at 31-36 hours)
- Fourth check: 62-64 hours

Thereafter a blastocyst may, according to the pre-programming, media specification and culture environment, form on day 5, 6 or 7 (when it's mostly hatching or hatched). However in most cases a blast that's conformed to the morphology expected at the above mentioned checks, throughout its transition from days 1-3, should be almost hatching on day 6.

Checking, at specified periodic intervals, key morphological characteristics which numerous studies have supported over the years, as consistent and standard, enable us to make selections for single embryo transfer. The transitions between days 1-3 are the most reliable indicators to make selections for transfer or allow for blastocysts. An early scoring with appropriate cleavage timing mostly begets good quality blasts.
In a Tertiary centre good quality blasts are generated anywhere between 20-40% of embryos handled depending on patient profile and previous performance. Hence at any given point there are reasons why we may have to deviate from a single embryo transfer in order to give the couple seeking their biological child, a fair chance, because if they generate low quality blasts, there is a need to transfer more than one (2). It seems that the transfer of such blasts gives more or less the same pregnancy rates as a day 3 embryo transfer of a similar cohort.

Let me add to the following quotes from the paper titled Morphokinetic analysis of embryo development (3): “It is widely recognized that sometimes even embryos with the perfect morphology may fail to give pregnancies as opposed to poor morphology.”

This simply means that if a couple is given a particular limited cohort to work on, we would not be discarding the embryos in view of certain time lapse images that may have captured a delayed cleavage time.

It would probably help in re-assuring the couple about expected success rate from this particular transfer with proof. The transfer per say cannot be denied altogether.

In labs that perform oocyte retrievals in the afternoon, with the corresponding time checks at mid mornings of the following day, there is no disturbance of routine or inconvenience. The time checks at the intervals mentioned above, either from the time of HCG or from the time of insemination (logical and preferred) offer similar information. Also in a well contained and orderly lab environment the temporary shifts between incubators to the microscope should not be of a great significance. This time is also used to move embryos on day 3 to the corresponding blast media and thereafter until day 5/6/7.

It has also been quoted that these “timely observations may give a very limited view of a highly dynamic process and that the most important events denoting viability occur at these 'unnoticed hours' (between observations)”. Perhaps, advantageous, since images capture the first cleavage timings, and allow for observation of asynchrony and blastomere nucleation without having to shift embryos out of the incubator right from fertilization until day 3 (if need arises). If it’s a single media from day 1 until day 6/7, there is a neat explanation of how embryos need not be removed but the media needs to be topped up in the outer well which may contain the spent metabolites.

Another advantage is the documentation of fragmentation which of course adds valuable information.

The knowledge that fragmentations appear and disappear or get reabsorbed in relation to cell division is captured to note those embryos where it appears as a transient phenomenon.

In any case this information would still be secondary assuming that if a cohort contained poor grade embryos with fragmentation on day 3, they may be cultured and observed to obtain the blast that may or may not be generated, to give ALLOWANCE for this phenomenon. This would be a norm with or without time lapse imaging.

The fact is that whether or not fragmentations appear and later get reabsorbed, without loss of cell biomass, influences our judgment only when we have embryos to spare. But if we have few embryos, this information is valuable to explain the prognosis to the couple and thereby their chances of conceiving using these embryos.

Blastomere multinucleation and correlation with pregnancy rates and duration of cleavage with timing are also possible with time lapse imaging. All these are substantiated by studies that denote multinucleation as poor grade and that those appearing at the 2 cell stage are better and generate progeny that are mononucleated and normal. However those generated at a later cleavage stage yield poor results.

Safety studies back the Embryoscope as comparable to the regular incubators. One interesting point to note is that there was no significant differences in embryo quality, blastocyst rate and pregnancy rate between the Embryoscope and standard incubators, using evaluation at 2 discrete time points (44 and 68 hours) (4). This shows that despite the course of the embryo’s journey unselected by time lapse imaging, helped generate comparable pregnancy rates and the role of Embryoscope is to fine tune our selection process and hence possibly increase pregnancy rates.
Dr. Marcos Meseguer, Senior Embryologist at IVI Valencia, credited with years of research and publications and an experienced and keen advocate of time lapse imaging agrees that although a knowledge of cleavage timings do not give you an accurate account of molecular events, it still provides valuable information on timing of second cleavage division and its influence on future implantation potential of embryos.

Moreover, the culture system is undisturbed and it's easy to change droplets or shift to a blast medium without actually moving the embryos (inner and outer well concept). Data are currently not available on arrest of embryos in a blastocyst only programme using the Embryoscope, although he agrees that it could depend on the patient's previous performances or actual factors causing the infertility. In such cases using an Embryoscope provides you with all information that is required to provide further line of treatment to the couples. He also believes that there are no particular indications to use an Embryoscope and it may be provided to all patients attending a fertility unit.

Mr. Tyl Taylor, a Senior Embryologist, NC, opines that knowledge of cleavage timings may probably tell you which cohort of embryos are capable of further division to an extent but will it concur if they would definitely end in live births remains to be answered. He feels that if an embryo deviated from the "concurred" patterns of timings and still made a blastocyst, couples may not be denied that transfer. He added that the choice remained with the consultant and the couple.

He felt basic lab practices and consistent success rates, in accordance with the current advances in lab techniques, is a pre-requisite to decide implementation of an Embryoscope programme or even a combination of this technology with an all blast programme. If labs didn't measure up to producing consistent results, giving them an Embryoscope would not alter success. He concludes, "Embryoscope concept can be a universal application, but with limited practicality. It is going to give you so much data that the chances are good that you are going to find something statistically significant even though the significance is due to chance. Remember, just because something is statistically significant, doesn't mean that it is clinically significant ".

To conclude, in ART nothing can be 100% accurate either in laboratory protocols or predictions. We are still working in an environment that's closely mimicking nature but not nature per say. No individual protocol or equipment can provide us the ultimate 100% pregnancy rates. However having said that, research is extensive and the potentials are growing by the day.

Also with experts agreeing to the fact that cleavage timings cannot reflect precise molecular events that take place at that time, the Embryoscope offers to capture time lapse images, giving you a wider account visually of exact cleavage timings and morphokinetics that may possibly add to precision in embryo selection and better pregnancy rates.

For this, the ongoing clinical trials will stand to prove it in time and also determine its application as part of standard lab practice.
REFERENCES


DR. PRIYA SELVARAJ MD MNAMS MCE
SURGICAL ABDOMEN IN NEONATES

Baby of Mrs. G, a case of twin pregnancy conceived by ICSI, was antenatally diagnosed to have Exomphalos of twin 1. Earlier fetal screening tests ruled out any other significant abnormalities. The babies were delivered by elective LSCS at 36 weeks gestation (23/11/2009) with birth weights of 2.34kg and 1.82kg respectively. On postnatal evaluation of twin 1 diagnosed with Exomphalos minor, no other dysmorphism was noted (See photo). Pre-operative evaluation also included cardiac echo and an ultrasound of the kidneys, both of which were normal.

The baby was operated upon the same day by Dr. Prasad, eminent pediatric surgeon. Intra operative findings showed an abdominal wall defect of 2.5cm diameter and a hernial sac with small bowel as its contents. The sac was opened, intestinal contents were reduced into the abdominal cavity and an umbilicoplasty was performed.

Post operatively, the baby was kept nil per oral, with parenteral support and broad spectrum antibiotics. Fluid and electrolyte homeostasis was maintained. Bilious nasogastric aspirate was replaced with corresponding IV ringer lactate. Partial parenteral nutrition with aminoven, dextrose, multivitamins and trace elements was given by central venous access.

On the 4th post-operative day, the baby developed severe abdominal distension with pneumoperitoneum (x-ray shown).

Peritoneal drainage of free air was done at the bedside. Supportive therapy for necrotizing enterocolitis included cefaperazone-sulbactam combination (80 mg/kg/day), metrogyl (7.5mg/kg/day), plasma and platelet transfusions, inotropes, oxygen and parenteral nutrition. Blood culture was sent which grew enterococci with sensitivity to vancomycin. Hence vancomycin (10mg/kg/dose) was added to the current regimen and continued for 10 days.

The general condition and abdominal signs gradually improved, though pneumoperitoneum recurred on and off for 10 days. On 21st post-operative day, after normal bowel gas pattern was established, feeds were started and advanced as tolerated. The baby was discharged on direct breast feeds on the 25th day post op day with a weight of 2.02kg.
ACASEOFANNULARPANCREAS

Baby of Mrs. D, 32 years old primigravida, conceived by ICSI, was detected to have polyhydraminos and possibly duodenal atresia during routine antenatal level 2 anomaly scan. The male infant was delivered at 32 weeks gestation with a birth weight of 1.85kg, following preterm labor.

The infant had soft abdomen, but large amount of yellowish gastric aspirate (about 60cc) on insertion of nasogastric tube. The X Ray showing double-bubble sign is shown below. The baby passed small amount of meconium. Surgical opinion was obtained. After stabilization of fluid and electrolyte status, and ruling out cardiac defects, a laparotomy was done.

At laparotomy, grossly dilated stomach and proximal duodenum, with annular pancreas and duodenal stenosis were seen. As the distal duodenum was not convenient for anastomosis, duodeno-jejunostomy was carried out (Retrocolic). The mesocolon was fixed with the stomach and the abdomen was closed in layers. The baby tolerated the procedure well.

Post operatively the infant was kept nil per oral with broad spectrum antibiotics for 10 days, after which feeds were started. During this time, electrolytes were monitored and imbalances if any were appropriately treated. Parenteral nutritional support was also given. After the 10th post-operative day, nasogastric aspirates decreased and the infant tolerated feeding well. The infant was discharged on the 14th post-operative day on direct breastfeeds.
TAKE HOME MESSAGE
The above cases illustrate management of complex surgical cases in premature, low birth weight infants, (usually associated with significant morbidity) with an aggressive approach. General principles in managing surgical conditions in neonates include:

- High resolution fetal anomaly scan to detect gut anomalies, ruling out syndrome associations
- Antenatal counseling and delivery in tertiary care facility with neonatal intensive care unit
- Timely laparotomy by experienced pediatric surgeon
- Close monitoring of fluid and electrolyte status
- Appropriate anti-microbial therapy post-operatively
- Central venous access and parenteral nutritional support
- Team work of obstetrician, neonatologist and pediatric surgeon

Overall, out of 487 pregnancies by ART in the last year, only 5 babies had major congenital anomalies requiring surgical intervention. The literature states a 2-3 % rise of birth defects in ART pregnancies in comparison to natural births. Stringent antenatal monitoring and optimal neonatal management can improve their outcomes.

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Neonatologist, G G Hospital
AN INTERESTING CASE HISTORY

37 years old Mrs. SB, married for 12 years to a cousin (3rd degree consanguinity), with previous bad obstetric history came to us once again on 12/09/2012 with an early pregnancy of 45 days. Her menstrual cycles were regular and she had no significant health conditions except for mitral valve prolapse syndrome without regurgitation that did not require active treatment. She had been treated for infertility in the past and also had missed miscarriage with twins following ovulation induction for the same in 2001. Then, subsequently she had a ruptured right ectopic pregnancy for which an emergency laparotomy was performed in 2005. At the end of 2008 she came to us for fertility treatment. After preliminary tests we asked for a karyotype analysis of the couple. The wife’s report was: mos.46, XX t (7:14) (q35:q13)/46,XX.

Owing to her previous obstetric history and the karyotype findings of a translocation the couple opted for a donor oocyte programme. Counseling was given for the same and an informed consent was obtained. The first batch of donor oocytes kept for her yielded poor quality non transferable embryos and hence having been started on progesterone and still in waiting, frozen oocytes were offered in order to complete the treatment cycle. The lower success rates associated with the use of frozen oocytes were explained and after consent, 9 oocytes were thawed using cook’s thawing media, all of which survived. These oocytes had been frozen using cook’s freezing media by conventional slow freeze method few months earlier. ICSI was performed on all 9 of which 7 fertilized. 2 embryos were arrested in PN stage yielding 5 embryos (2(4 cells grade I), 2 (5 cells grade I-II) and 1(4 cells grade I-II) which were transferred.

She became pregnant giving us the third frozen oocyte baby from our centre. Her antenatal period was uneventful and she delivered a live female baby by elective LSCS in April 2010.

Third Frozen oocyte baby from GGH

The ultrasound in her present pregnancy revealed a normal intrauterine gestational sac with fetal pole and heartbeat corresponding to the period of gestation (45 days).

Although the risks were explained to the couple, who were well informed about possibility of either a miscarriage or fetal anomalies, opted to continue with this spontaneous pregnancy. Routine antenatal reviews were undertaken and she was sent for a first trimester screening to assess nuchal translucency and also serum triple screening test.

The ultrasound at a higher centre for fetal screening revealed the following abnormalities: an increased nuchal translucency of 4.6mm, unossified nasal bone, left axis deviation with two inflows not seen clearly and a single outflow tract suggesting a complex cardiac abnormality. Owing to an abnormal scan report the blood test was withheld and a chromosomal abnormality or a single gene disorder was to be ruled out for which fetal sampling was advised. The couple opted for termination which was performed following vaginal induction with Misoprostol. The termination was uncomplicated and her general condition was good on discharge.
This history was highlighted for two interesting facts. One is the persistent abnormalities in her pregnancies while she was trying to conceive with her own gamete, thereby re-instating the fact that translocations have a major role to play and can be either lethal or produce major fetal anomalies.

This particular translocation of 7 and 14 is reported to have a low level of mosaicism in literature and according to the geneticists report; a balanced translocation involving the same may result in 7q+ and partial trisomy of short arm (7p) of chromosome 7 in the offspring. It is said to be familial in origin. In this case an early fetal anomaly was diagnosed and terminated. The other interesting fact is that she conceived in the first cycle of her donor programme using frozen oocytes, when pregnancies from this method still remain quite elusive.

DR. PRIYA SELVARAJ MD MNAMS MCE
IVF WORKSHOP 2012
DATE : March 26th - 30th 2012
VENUE : Fertility Research Centre, GG Hospital

COLLABORATION
Institute for Training & Research in reproductive Health (IRRH), Kolkata

LECTURES, DEMONSTRATION /HANDS ON
- Basic approach to infertility, Diagnostic procedures & Ovulation induction
- Ultrasound for follicle with practical demonstration
- Poly cystic ovarian syndrome (PCOS)
- Male infertility, semen analysis and sperm retrieval procedure
- Embryo grading, assessment and culture, loading, ICSI & IMSI
- Cryopreservation of oocytes, embryos and sperm (animal and human)

PARTICIPANTS
- Dr. Arunakumari Harsha Hospital, Rajahmundry
- Dr. Lakshmi R. Markani, Fernandez Hospital Pvt. Ltd, Hyderabad
- Dr. Archana Agarwal Mannat Infertility Clinic, Bangalore and
- Ms. Bindhu Moideen - Embryologist Sabine Hospital & Research Centre, Ernakulam

FACULTY
- Dr. N. Pandian, Chettinad Health City, Chennai
- Dr. S. Suresh, Mediscan Systems, Chennai
- Dr. John Edwin (Ex Dean of The Veterinary Hospital, Chennai)
- Dr. S. N. Sivaselvam and Dr. Palaniswamy from Veterinary Hospital, Chennai
- Dr. Priya Kannan, Garbarakshambigai Fertility Centre Pvt Ltd, Chennai
- Dr. Kamala Selvaraj & Dr. Priya Selvaraj, GG Hospital, Chennai

Dr. S. Suresh, Mediscan Systems, Chennai
Dr. John Edwin (Ex Dean) & Dr. S. N. Sivaselvam, Veterinary Hospital,
Chennai

Dr. Priya Kannan, Garbarakshambigai Fertility Centre Pvt Ltd, Chennai

Dr. N. Pandian, Chettinad Health City, Chennai

DISTINGUISHED VISITORS

Prof. Robert Shaw MD, FRCOG, FRCS, FACOG, past president of the Royal College of Obstetricians and Gynaecologist (UK), past president of the World Endometriosis Society (2002 - 2005) and also a founding board member of the World Endometriosis Research Foundation (July 2006 - January 2010)
Visited our centre on 10th May 2012 ahead of his talk on Recurrent Endometriosis. We had the privilege of sharing our experience with the expert in the management of Adenomyosis and severe endometriosis and outcome in ART programmes. Needless to say it was knowledge gained.

Dr. Juan Antonio Garcia Velasco, Assistant Professor of Obstetrics and Gynecology, Rey Juan Carlos University & Director, IVI- Madrid, visited our centre on 13th April 2012. The two way interaction on Surrogacy, Egg & Sperm donation programmes and cryopreservation techniques was highly beneficial, what with his expertise and experiences on the same.

**HOW TO STAY YOUNG**

- Throw out nonessential numbers. This includes age, weight and height. Let the doctors worry about them. That is why you ‘pay’ them.
- The grouches pull you down, hence surround yourself with cheerful people.
- Keep learning. Never let the brain be idle. It then becomes a devil's workshop.
- Enjoy simple pleasures in life. Money can’t buy them.
- Laugh often, long and loud, till you gasp for breath.
- Tears happen. Endure, grieve, and learn to move on. LIVE while you are ALIVE, for a lifetime.
- Surround yourself with what you love, be it family, pets, keepsakes, music, plants, hobbies or whatever. Your home is your refuge. Even better, your space.
• Cherish your health: If it is good, preserve it. If it is unstable, improve it. If it is beyond what you can improve, get help. If not write a will that does justice and serves its purpose.

• Avoid any guilt trips. Instead take a trip to the mall, or even to the neighbouring city.

**AND ALWAYS REMEMBER....**

• Tell the people that you care about, that you love them, at every opportunity.

• Life is not measured by the number of breaths we take, but by the moments that take our breath away!

• We all need to live life to its fullest each day!!

*Source: A Cheerful friend's email.*
OUR ART BABES

- **TWIN1 : MUTHUKUMARAN**
  - DOB & AGE : 02/04/1999, 13 Years
  - CONCEPTION : IVF - ET
  - CLASS : 7TH STD
  - HOBBIES - TWIN1 : CYCLE RIDES / CAR DRIVES

- **TWIN2 : NITHYASHREE**
  - DOB & AGE : 02/04/1999, 13 Years
  - CONCEPTION : IVF - ET
  - CLASS : 7TH STD
  - HOBBIES - TWIN2 : WATCHING TV / PLAYING COMPUTER GAMES

- **TWIN 1 : S. DARSHNA**
  - DOB & AGE : 27/04/2003, 10 Years
  - CONCEPTION : IVF - ET
  - CLASS : 4TH STD
  - AMBITION
    - TWIN 1 : IAS OFFICER

- **TWIN 2 : S. DHARSAAN**
  - DOB & AGE : 27/04/2003, 10 Years
  - CONCEPTION : IVF - ET
  - CLASS : 4TH STD
  - AMBITION
    - TWIN 2 : DOCTOR

- **NAME : N.T.KARTHIKHA HARSHITHA**
  - DOB & AGE : 07/03/2006, 6 Years
  - CONCEPTION : IVF ET
  - CLASS : 1ST STD
  - HOBBIES : DRAWING & COLOURING

  - AMBITION : BABY DOCTOR
  - He is 1 year and 5 months old.
  - He was born on 2010 November 12th @ GG Hospital.
  - He is the next ART babe to watch out for!!
DOB & AGE : 12/08/2002, 10 Years
CONCEPTION : IVF ET
NAME : THILOKA KURAGAMA
CLASS : 4TH STD

In 2012 at my school sports meet, I was in the school band and I was the lead drummer.

On Nov 26th 2011 in Vietnam, at the Global ART International competition I won the 4th runner up. The title is "MY WORLD & MY FUTURE"

The same year, at my school on the “English day”, I gave the welcome speech and vote of thanks and compered the proceedings.
### Monthly IUI Pregnancies (Nov 2011 - Sep 2012)

#### Monthly Pregnancies (Nov 2011 – Sep 2012)

<table>
<thead>
<tr>
<th>Months</th>
<th>Art</th>
<th>IUI</th>
<th>Natural *</th>
</tr>
</thead>
<tbody>
<tr>
<td>November</td>
<td>53</td>
<td>20</td>
<td>08</td>
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<tr>
<td>December</td>
<td>36</td>
<td>23</td>
<td>10</td>
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<tr>
<td>January</td>
<td>57</td>
<td>26</td>
<td>14</td>
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<td>February</td>
<td>47</td>
<td>14</td>
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</tr>
<tr>
<td>March</td>
<td>45</td>
<td>17</td>
<td>10</td>
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<tr>
<td>April</td>
<td>52</td>
<td>20</td>
<td>06</td>
</tr>
<tr>
<td>May</td>
<td>41</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>June</td>
<td>28</td>
<td>10</td>
<td>11</td>
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<tr>
<td>July</td>
<td>46</td>
<td>09</td>
<td>05</td>
</tr>
<tr>
<td>August</td>
<td>47</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>September</td>
<td>53</td>
<td>10</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>505</td>
<td>172</td>
<td>111</td>
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</tbody>
</table>

* Following Medical and Surgical Management
MONTHLY VARIATIONS IN ART PREGNANCIES (NOV 2011 - SEP 2012)

** Easy transfers and good quality of embryos

Total Number of pregnancies achieved: 4936
Total Number of patients delivered by ART: 2789
Total Number of babies delivered by ART: 3830
Total Number of ongoing pregnancies: 227
Total Number of Fetal wastages: 1855
Lost in follow up: 65
**ART STATISTICS (NOV 2011 - SEP 2012)**

<table>
<thead>
<tr>
<th>PROCEDURES</th>
<th>NO OF CASES</th>
<th>PREGNANCIES</th>
<th>PREG.RATE (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IUI (OWN / DONAR)</td>
<td>1660</td>
<td>172</td>
<td>10.36</td>
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<tr>
<td><strong>GENERAL</strong></td>
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<tr>
<td>ICSI ET</td>
<td>185</td>
<td>65</td>
<td>35.14</td>
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<td>IVM ICSI ET</td>
<td>1</td>
<td>1</td>
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<tr>
<td>IMSI ET</td>
<td>9</td>
<td>3</td>
<td>33.33</td>
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<tr>
<td>BT</td>
<td>9</td>
<td>5</td>
<td>55.56</td>
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<td><strong>SEQUENTIAL TRANSFERS</strong></td>
<td></td>
<td></td>
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<tr>
<td>ICSI / IMSI ET+ BT</td>
<td>274</td>
<td>181</td>
<td>66.05</td>
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<td>ICSI IVF ET + BT</td>
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<td><strong>FROZEN EMBRYOS (Slow Freeze / Vit)</strong></td>
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<td>FROZEN ICSI ET</td>
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<tr>
<td>SEQ – FROZEN ICSI ET + BT</td>
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<td>100</td>
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<td><strong>DONOR OOCYTE PROGRAMME (DOP)</strong></td>
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<tr>
<td>ICSI / IMSI ET</td>
<td>84</td>
<td>40</td>
<td>47.61</td>
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<td>BT</td>
<td>20</td>
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<tr>
<td><strong>SEQUENTIAL TRANSFERS</strong></td>
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<tr>
<td>HRT ICSI / IMSI ET + BT</td>
<td>217</td>
<td>217</td>
<td>65.44</td>
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<td>1</td>
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</tr>
<tr>
<td><strong>IVF ET + BT</strong></td>
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<tr>
<td><strong>FROZEN EMBRYOS (Slow Freeze / Vit)</strong></td>
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<td>FROZEN DET</td>
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<td>52.38</td>
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<tr>
<td>FROZEN DET + DBT</td>
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<td>25</td>
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<tr>
<td><strong>OWN + DOP</strong></td>
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</tr>
<tr>
<td>ICSI ET + BT</td>
<td>24</td>
<td>11</td>
<td>45.83</td>
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</tbody>
</table>