

ART IN LOW RESOURCE SETTINGS : SAFETY ISSUES :

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Assisted Reproductive Techniques are being very widely used in developed countries and increasingly in underdeveloped countries as efficacious treatment of infertility. However, safety issues related to ART have not been addressed adequately with reference to low resource countries.

THE ISSUES :

Safety issues affect

1. The Patient
2. Egg donor
3. Surrogate
4. ART offspring
5. The Clinician

They involve :

1. The patient herself
2. The gametes and embryos

both during the ART cycle and on a long term basis.

CONTRIBUTING FACTORS :

1. Affordability :

Some facts

1. Per capita income of India in 2006-2007 was Rs. 29,382 [USD 625]
2. The average cost of an ART cycle in India is Rs. 35,000 to 45,000 [USD 750 - 950] and the cost of drugs used for ovarian stimulation varies from Rs. 25,000 to 35,000 [500 - 750 USD] for urinary products to Rs. 60,000 to 75,000 [USD 1000 - 1250] for recombinant products.

3. No form of infertility treatment is subsidized by the government or covered under any health insurance.

A lot of couples coming for ART treatment sell / mortgage their life's earnings in a do or die effort to have a child. This puts tremendous pressure on all concerned to achieve a pregnancy. In many instances, even an unfavourable outcome [abortion, premature delivery] is acceptable, because a woman who has been able to prove her fertility commands a greater respect in her society than an infertile woman.

2. Awareness :

Awareness is directly linked to the educational status of the patients, and this being poor in low resource countries [15 % patients undergoing ART at our clinic are illiterate and 20 % have studied up to high school], awareness regarding ART procedures and its complications is also very low. We conducted a small survey of 100 patients after they completed an ART cycle at our clinic. All patients have one meeting each with the clinician, the ART coordinator and the counselor before commencing a cycle, they are shown a small video of the procedure and are made to read and sign a detailed consent form. 3 questions were asked :

1. What do you feel are the 3 major complications of ART and what is the rough incidence of these ? 25 % responded that there were no complications; others rated multiple pregnancy, OHSS, poor response and ectopic pregnancy as the major complications in that order.

2. Are you aware of the risks associated with multiple pregnancy and would you agree to transfer of fewer [2 or even 1] embryos ? 7 % responded that there are no risks, 10 % wanted twins, 50 % thought prematurity and 33% thought IUGR as the major complication. None agreed to transfer of fewer embryos !

3. Are you aware of the risks associated with the use of urinary gonadotropins and would you pay more for using rec hormones ?

17 % were aware of the risks associated with urinary products and 30 % were willing to pay more for recombinant products.

3. Lack of national databases :

Most underdeveloped countries do not have national databases or registries of neonatal and maternal morbidity and mortality especially figures on prematurity and multiple pregnancy. This makes it difficult not only for the patients but also for clinicians to counsel patients appropriately. Many patients leave the ART clinics after achieving a pregnancy and are lost to follow up. Additionally, some patients do not disclose information about their ART treatment to their treating obstetrician and their family as ART is still considered a taboo

4. Unregulated Market :

All the above three factors are compounded when the ART practice is completely unregulated. In India, we had guidelines from the Ministry of Health since 2005 and they have been waiting to be placed before parliament.

SAFETY ISSUES :

1. Number of Embryos Transferred and Multiple Pregnancy :

There has been a very slight decline in the number of embryos transferred per ET from 2004 to 2006. The percentage of cycles in which 4 embryos were transferred has declined from 22.3% in 2004 to 18.3 % cycles in 2006; 5 or more embryos were transferred in 7.3 % cycles in 2004 and 4.4 % cycles in 2006.

The incidence of twin pregnancy has remained constant at around 21 %, triplets have decreased marginally from 4.4 % in 2004 to 3.7 % in 2006 and higher order multiples have remained the same at 0.8 %. What is more significant is that the incidence of triplets and higher order multiples in Egg Donation cycles is 6.4 % and 0.5 % and in Surrogacy cycles is 4.1 % and 0.

2. Ovarian Hyperstimulation Syndrome :

At present, no data on OHSS are collected in India. This is all the more unfortunate in a country where egg sharing and egg donation are quite common.

3. Use of recombinant drugs :

Urinary [hMG and FSH] gonadotropins are still very frequently used for ovarian stimulation. Cycles with rec FSH alone have remained steady at around 22 % since 2002. The major reason behind this is the cost of the drug : 75 IU of urinary hMG/FSH is available at Rs. 477 [USD 10]; HP-hMG/FSH is available at Rs. 1200 [USD 25] and rec FSH is available at Rs. 1700 [USD 36]. Changing from urinary to rec products increases the cost of a cycle by twofold.

4. Traceability and accountability of Gametes and Embryo

One of the unique features of ART practice in India is "Batch IVF". Coupled with this is the fact that Thawed transfers account for only 8 – 9 % of all fresh stimulations. This leaves a lot of embryos generated unaccounted for, one safety aspect which has been totally ignored until now and should be very critically evaluated.

5. Surrogacy and Egg donation / sharing :

These are quite common in low resource settings; in India egg sharing, egg donation and embryo donation account for 19 % of cycles, whereas 290 surrogacy cycles were carried out in 2006. Safety issues related to this [their rights, risks, exploitation] have been by and large ignored.

The Future :

Once the ART bill is passed, a lot of this will be taken care of. A few relevant points of the Act are :

1. All ART clinics will be registered and accredited by a State Regulatory Board.
2. All ART clinics shall maintain detailed records [including DNA finger printing !!]
3. All ART clinics will put online all information available to them as and when such central facilities are available.
4. Not more than 3 embryos should be transferred at one sitting