

ASSISTED REPRODUCTION TECHNOLOGY IN A RESOURCE-LIMITED SETTING

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INTRODUCTION

The idea of Assisted Reproduction Technology (ART) (which at the moment is the highest break-through in the medical treatment of infertility) in a resource- limited setting, sends a contradictory wave of thoughts as to the desirability and affordability with such limited resources because of the high cost implication. Usually, resource- limited settings refer to low income countries, who are still contending with basic developmental issues like poverty, high unemployment, high proportion of ill health in the populace, over population and poor infrastructure¹. ART cost several thousands of Euro/dollars in high income countries where it is often a part of the spectrum of management of infertility which is both preventive and curable. In low income countries, infertility is only one of the many important health problems that people face and ART being of such high cost, cannot be a considered method for infertility treatment in view of the serious competing demand on the limited resources. It is often emphasized that the main issue in the resource limited setting is over population crisis rather than infertility whose management for now should be

by the much cheaper preventive approaches²⁻⁴.

The issue of whether or not ART is worth considering at all, for infertility management, in resource limited settings, should not be wished away with the reinstatement that infertility prevention should be the emphasis while the limited resources, should be reserved for solving the over population crisis. Such an approach is rather simplistic and devoid of the knowledge of the premium placed on child bearing in the socio-cultural setting of the people, in these resource limited countries. While the people can easily cope with overpopulation at the individual level, because of the socio cultural care for each other, they cannot cope with infertility. The individual, society and communities are devastated completely by infertility or childlessness.

In Western societies, reproduction is often a self chosen goal and largely a personal choice made by the individual or couple, hence infertility is often a problem at the individual level without societal implications⁵ Infact, there are situations in Western societies, where couple decide not have children in their marriage. In the developing countries, having children is a social obligation, a performance due to the



family (in laws) and whole community. Children secure marriage, confer social status, guarantee rights of property and inheritance, assist with labour, offer social security in old age and provide continuity of maintaining family name⁶⁻⁸. The main reason for marriage is for child bearing and not love as it is in Western countries. Often, there are no prior love plays or even familiarity between individuals in the marriage which is organised and sponsored by the families, society and community. It is only childbirth that secures the marriage union and bind families and communities together. There can never be a marriage in the developing countries in which the couple decide on voluntary childlessness. Thus, infertility in the developing countries is pervasive and a serious concern especially to the woman leading on to marital disharmony, neglect, abuse, loss of social security, polygamy and even suicide⁹⁻¹¹.

Infertility in the developing countries is therefore, not just a desire at the level of the individual (as it is in western culture). It is a huge disease burden with devastating consequences on the individual and society that deserve priority resolve amongst other disease chain¹². This is why infertility management should extend beyond prevention to include comprehensive treatment or else those presently afflicted with the disease will never be helped. Even at this, it is feared that extending infertility treatment to include ART in resource limited settings may be impracticable, for reasons of unstable infrastructure, poor staff morale and poor maintenance culture²⁻⁴. This is why it is assumed paradoxical to contemplate ART is in a resource limited setting with such obvious constrains.

This review shall include a detailed description of ART and the present

day indications. The pattern of infertility in the developing countries is critically reviewed against the background knowledge of current socio cultural correlates of infertility in a resource-limited setting to assess the need for ART for infertility management. Finally, the review shall present the outcome of ART in a resource limited setting like Nigeria with emphasis on the practice, prospects and future development of infertility management in developing countries.

Assisted Reproduction Technology (ART) Basic Knowledge

Assisted reproduction technology encompasses several techniques to by-pass the problems preventing conception through the normal sexual intercourse in a stable relationship. These techniques involve either artificial insemination or artificial fertilisation in which there is alteration in the inherent process leading unto conception and without sexual intercourse. There are several types of ART presently viz:

In vitro fertilization and Embryo Transfer (IVF and ET)

This refers to the assemblage of procedure culminating in the retrieval of human Oocyte which is approximated to potentiated Sperms in a test tube (In vitro) in a laboratory condition equilibrated to the same physiological condition as obtains in the normal human environment (in vivo). It thus involves artificial fertilisation outside the human body and without sexual intercourse.

Gamete intra-fallopian tube Transfer (GIFT)

This involves the transfer of Oocyte and potentiated sperm to the fallopian tube with the laparoscope for in vivo fertilisation and subsequent



implantation and pregnancy. Although this does not also involve sexual intercourse, the artificial fertilisation occurs in vivo within the human body.

Zygote intra fallopian tube transfer (ZIFT)

This involves the transfer of zygote (from fertilisation of Oocytes obtained through IVF and potentiated sperm) to the fallopian tube with the laparoscope. The fertilisation is done in vitro before the transfer and without sexual intercourse.

Intra uterine Insemination (I.U.I)

This involves the transfer of potentiated sperm using special insemination catheters through the cervical os into the uterine cavity using aseptic technique at the peri- ovulatory period which commonly nowadays is preceded by a super ovulation treatment (with gonadotrophin and human chorionic gonadotrophins to trigger ovulation) to facilitate release of several Oocytes to enhance the prospect of conception. It does not involve sexual intercourse but the artificial fertilisation occurs within the human body (in vivo). It should be noted that insemination of sperm at the cervix or unto the cervical os only, with whole or partially treated sperm is not grouped as Assisted Reproduction because it does not alter the inherent process leading unto conception.

Other complimentary procedure to I.V.F.

(1) Intracytoplasmic sperm injection (ICSI)

This is a complimentary procedure to IVF when there are sperm abnormalities of either low or deformed sperm. In extreme and appropriate cases spermatid or yet immature

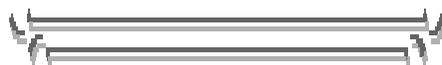
spermatozoon obtained from the epididymis may be used. It involves directly injecting a single spermatozoon, unto an Oocyte using special equipment (The ICSI machine). This is a major break-through in the treatment of male infertility.

(2) Cryo preservation and Transfer of Embryo

When there are more embryos than can be transferred in any cycle, the excessive embryo are cryopreseved by freezing in liquid nitrogen. When the frozen embryos are required later, they are thawed, and transferred into the uterus. This helps to prevent repeating the stimulation for Oocytes again. At times cryopreservation of embryo is planned when there are contraindications to embryo transfer as in fear of severe Ovarian Hyperstimulation Syndrome (OHSS) or there has been an inadequate endometrial response.

In Vitro Fertilization and Embryo transfer – Basic facts and indications

The first successful IVF in human, was in July 1978, leading to the birth of Louise Brown in Great Manchester City U.K¹³. The IVF cycle was performed in a natural cycle in which the naturally ovulated Oocyte was retrieved with the laparoscope under G.A. The IVF was performed because Lesley Brown had no tubes (which had been removed from two previous ectopic) but had normal uterine cavity and was normally ovulating. Hence the IVF by passed the damaged tubes to obtain the



ovulated Oocyte and approximate it to the sperm in vitro to obtain the embryo which was also transferred under general anaesthesia into the uterine cavity and subsequently pregnancy occurred. Without IVF Lesley Brown's chance of childbirth was zero.

In the early days, IVF was performed in natural cycles for women with damaged tubes but with normal uterus and ovulatory cycles. Later, it was found also helpful in other situations with normal tubes but with anovulation. A major break through occurred in the area of male factor treatment with the introduction of the Intracytoplasmic sperm injection (ICSI)¹⁴. With the technique of pre implantation genetic diagnosis and embryo selection, healthy babies can now be possible by avoiding transfer of embryo with genetic disease¹⁵, and with embryonic stem cell research new areas have been opened up¹⁶.

The indication for assisted reproduction has now greatly expanded to include Oocyte donation to treat premature menopause¹⁷ surrogacy for women with damaged uterus¹⁸, effective endometriosis treatment¹⁹ and even assessment and diagnosis of male factor²⁰.

IVF Procedure

At the onset, IVF was performed in the natural cycle of the woman and several days were often spent performing serial laboratory test to ascertain when ovulation will occur for laparoscopic retrieval. Often, one Oocyte was retrieved for fertilisation and therefore one embryo transferred. The success rate for this natural cycle I.V.F. was less than 5% and required tedious laboratory test and clinical skill in laparoscopic surgery. As ovulation stimulation drugs were discovered, IVF cycles were then stimulated, first with Clomiphene citrate but later with gonadotrophin in order to generate

many Oocytes and this was associated with much greater pregnancy rate²¹⁻²³. The main problem at this period, with stimulated cycles, either with clomiphene or gonadotrophins, was premature ovulation leading often to failed Oocyte retrieval but that was resolved with the introduction of L.H.RH analogues for pituitary down regulation before stimulation with HMG^{24,25}. Currently IVF procedure consist of series of steps as explained below.

Controlled ovulation stimulation

This involves the prior use of LHRH analogue for pituitary down regulation followed by gonadotrophin injection (HMG) aiming for multiple follicular growth and development and HCG administration at the appropriate time as the trigger for ovulation. This is orderwise referred to as super ovulation and is a process whereby ovulation is deliberately programmed in a woman who may have been ovulating albeit, irregularly or a woman who is Anovulatory. The aim is to stimulate the development of several mature follicles from the ovary in order to increase the chances of obtaining fertilisable eggs²⁶. The use of the LHRH analogue prevents premature ovulation (which may cause failed oocyte retrieval) and the LHRH analogue and gonadotrophins are administered till day of the HCG injection. The follicular growth is currently monitored with trans-vaginal ultrasound combined in appropriate cases with serum oestrogen measurement.²⁷.

Oocyte retrieval

Once the follicles have reached the appropriate size of about 18mm, Oocyte retrieval is performed now with transvaginal ultrasound using ultrasound guided probe in which only local analgesia like para cervical block is used on out patient basis²⁸. This has



made the procedure almost risk free and without stress to the patient.

Examination; fertilization and incubation

Once the follicles are retrieved, the fluid is examined and the oocytes are removed. The damaged or malformed ones are discarded and the others are washed and placed in Petri dishes with nutrient solution. After-wards, the Oocytes are mixed with the potentiated sperm from the male partner and equilibrated under laboratory condition to allow fertilisation to occur usually within 24 hours. The fertilised Oocyte (embryos) are then moved into an incubator for a few days to allow the cells to divide further.

Meanwhile, the woman is administered with progesterone injection often from the day of Oocyte retrieval to prepare the uterus for implantation of the embryo. In the older women (particularly recipients of oocyte donation) the progesterone administration may have began from the day of HCG administration to the oocyte donor to facilitate better endometrial preparation in the recipient. Nowadays, instead of progesterone injection, macronised progesterone pessaries (Gestones), as vaginal inserts, are used to minimise the risk in injection treatment. However, most women cannot tolerate the vaginal pessaries because of sourness in the vagina from trauma of transvaginal needle puncture in the first 5-7 days following the Oocytes retrieval. This is why there is still recourse to the progesterone injection commonly in the first one week. Thereafter, the progesterone pessary is often used for luteal support for the next 10 -12 weeks for those who achieve clinical pregnancy.

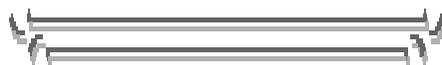
Embryo Transfer

At the 2-8 cell stage the embryo with the best chance of implanting are transferred into the uterine cavity through the undilated cervical os on the 3rd day following oocyte retrieval using a special embryo transfer catheter.

This is performed using aseptic technique under a sterile operation theatre condition. The procedure should be free of any difficulty in the identification of the cervical os, passage of the transfer catheter through the os and release of the loaded embryo into the uterine cavity which is accomplished without the catheter touching the uterine fundus or walls. Difficulty with transfer reduces the chances of successful implantation and pregnancy. Although embryo transfer is commonly performed clinically, the process can be assisted with ultrasound to guide the placement of the catheter before the release of the embryo. As much as three (but less commonly now days) four, embryos are transferred to increase the chances of implantation especially in the older women. Presently, the consensus is for the transfer of one or two embryos especially in the young woman as a way to reduce the common complication of multiple pregnancies in IVF²⁹. The remaining embryos not transferred are Cryo preserved for later use. Once an embryo implants, development continues normally in the absence of spontaneous abortion or any other complication.

Core issues in Human Reproduction and role of IVF.

The core of the reproductive process is the union of the sperm and oocytes. This union occurs often and normally naturally, at the outer third of the fallopian tube. Thus, an essential feature of this reproductive process is the adequate and appropriate



transport of the oocyte (after release from the ovary) to the outer third of the fallopian tube to be fertilised by the sperm which had found its way to the outer fluid of the tube after it had been deposited into the vagina. Hence, release and transport of the oocyte and sperm from the point of release are essential steps for the union of the oocyte and sperm for fertilization. Because, the sperm has a longer distance to transverse (from the vaginal to the outer third of the fallopian tube) motility is thus the most important quality required of the sperm to succeed in the task of union and fertilisation.

In practical realities, coital frequency is the deciding factor for the natural rate of pregnancy which means the higher coital frequency is associated with more pregnancy rate though a coital frequency of four or more per week may be associated with exhaustion in the older couple³⁰. The idea coital

frequency is 2-3 times per week evenly spaced at every 48 hours apart³⁰. In normal couples, pregnancy rate per monthly cycle with idea coital frequency is 20-25% but in six month pregnancy rate will increase to 50%, in one year it is 90% and in two years it is 96%³¹. In this context, some couples fail to conceive by chance and even success, naturally or from treatment can never be guaranteed³¹. The truth is that the human reproduction process is very inefficient with as low a pregnancy rate per monthly cycle of 25% in the ovulatory cycle of a young woman less than 30 year. For the older woman, even with ovulatory cycle pregnancy rate falls to about 12% per month.

This level of inefficiency is also greatly extended to poor conception rate in couples who had successful treatment for single cause of infertility with the conventional method, as shown in the table.

Type of single treated infertility

Conception rate as percentage of couple

Causal factor

| | 1 Cycle | 6 Cycles | 12 Cycles |
|---|---------|----------|-----------|
| 1. Anovulation (Amenorrhea; Oligomenorrhea; or normal periods). | 12% | 65% | 80% |
| 2. Unexplained infertility | 10% | 40% | 55% |
| 3. Sperm Disorder with Normal count | 5% | 10% | 20% |
| 4. Sperm Disorder with low count | 1% | 3% | 6% |
| 5. Tubal Damage | 6% | 10% | 18% |

(Cummulative conception rate from conventional management in couple with a single cause of infertility. Adopted from Hull MGR et al '85 (32).

As shown from the table above, in all of the causal factors, the best conception rate of 12% and 10% was from Anovulatory and unexplained

infertility in one cycle while all other factors in 1 cycle have a near chance pregnancy rate of 6% or less³²



It is quite obvious that left with the conventional infertility management methods, the inefficiency of the human reproduction capacity cannot be improved much even with the best of treatment. For some of the causal factors like sperm disorders and tubal damage, conventional infertility treatment does not offer better than chance occurrence of pregnancy per cycle; hence the need for Assisted Reproduction Technologies like IVF and ET. The technique of IVF allows a by-pass of some (if not all) of the insurmountable infertility causal factors by the conventional methods to allow pregnancy and child birth where otherwise the chances of birth is zero. The problems preventing the union of oocytes and sperm in the natural setting is by-passed by the super ovulation, oocyte retrieval, fertilisation and incubation and subsequently the Embryo transfer. In good IVF centres, the pregnancy rate equates to the natural pregnancy rate per monthly ovulatory cycle of 25%. At times the IVF success rate is much higher than 25% because of multiple embryo transfer which allow the conception rate to surpass the natural rate which often is monofollicular and uni-embryo implantation^{33; 34}. There is no other method of infertility treatment currently, that can achieve this same pregnancy rate per month of 25% apart from IVF. Like other methods of treatment, repeated IVF has a cumulative success rate which is virtually the same, 25% or more, for every attempt for at least the first 6-8 repeat cycles³⁵. This means a higher success rate with repeat IVF attempt.

Problems and Risks of IVF

Problems

1. Technique is complex, expensive and stressful. The cost is \$10,200 in USA

- per cycle and in Britain, it is four to five thousand pound sterling per cycle. The high cost is due to the high tech nature of the equipments, cost of the drugs, and media, and manpower cost.
2. The 25% pregnancy rate per cycle implies there is 75% failure rate. However, it is often not recalled that the natural pregnancy rate per month for a young ovulatory woman under 34 years is similarly 25% with 75% as failure rate.

Complications of IVF and ET

1. Ovarian infections, Ovarian rupture though rare, may occur
2. Ovarian Hyperstimulation syndrome (OHSS). This may occur in (0.6 – 14) % of IVF treated population³⁶. It is often a serious life threatening complication. The condition commonly occurs with the use of LHRH analogues and HMG followed by H.C.G. as trigger for ovulation. Polycystic ovary and administration of HCG appear to be a major predisposing factor for development of the full blown OHSS. Hence preventing OHSS at times involves non use or reduction in the dose of HCG or astute careful retrieval of all the oocytes followed by fertilisation and then cryopreservation of the embryo for transfer later in a non-stimulated cycle when the OHSS has subsided³⁷. In clinical practice, the predisposing factors may have been missed or were absent in the particular individual. The full blown OHSS disease many manifest (in the severe form) anytime from the 2nd or 3rd or



- even 5th day after embryo transfer with abdominal pain, abdominal distension, vomiting and respiratory difficulty associated with high packed volume level. Often, astute and aggressive treatment is required to forestall the disease process hence it is always better prevented by all means.
3. Risk of G. A., where it is used for any of the IVF procedure.
 4. Spontaneous abortion: This tends to be higher following IVF pregnancies due to factors like poor embryo malimplantation and aging of the woman.
 5. Ectopic pregnancy and at times heterotrophic pregnancy. This is often a serious problem that requires urgent attention
 6. Multiple pregnancy: This complication occurs in almost 30% of IVF pregnancies. Often due to transfer of several embryos as a way to ensure implantation and pregnancy. Approach nowadays is to transfer only one embryo for the young woman and not more than two in the older woman.
 7. Preterm delivery: This may be due to the multiple pregnancy or gross anomaly in the fetus. Adequate preparation to handle this problem with the provision of an effective and efficient neonatal intensive care unit at I.V.F. centres is important as a solution to this problem.

Pattern and trend of infertility world wide

The level and pattern of infertility vary greatly depending on the prevalence of "Core infertility" (biological variation in chromosomal, congenital and endocrinological abnormalities) and "acquired infertility" (geographical variation in infectious, environmental

and occupational factors)^{38;39}. Apart from this; the reports of causes and outcome of infertility treatments is highly variable because of the lack of a standard protocol for the investigation and treatment which makes it difficult to compare results with respect to pattern; differences and similarities. The WHO produced a standard protocol for the investigations of the infertile couple⁴⁰ which was tested in 8,456 couples from 34 centres in 25 countries world wide including four centres in Africa. The protocol standardised procedure, definitions and identification of the factor that are important in assessing the fertility status in both the males and females. The results of the study which was published in 1985 showed the pattern and trend of infertility world wide in the developed and developing countries⁴¹. African countries amongst all other developing countries were found to be peculiar in several respects, viz:

- i. African women had infertility for longer duration before consulting for assistance.
- ii. African women were much younger than their male partners almost like the men were marrying women, of the age of their grandchildren.
- iii. African women had much higher past history of S.T.D. and prior pregnancy complication.
- iv. African women had much higher secondary infertility than primary infertility.

The conclusion from the study was that infertility in African countries, were essentially due to sexually transmitted diseases and complications following induced abortions and poor maternity care which are all preventable by simple strategies⁴².

It was then recommended that approach to infertility management in



the African countries should be preventive. The issue of Assisted Reproduction Technology (ART) as treatment for infertility was emphasised as being of the least priority importance in infertility management.

Current Status of infertility in developing countries

The W.H.O. study published in 1985 involved four African countries in which 842 couples with different social and cultural background were evaluated. The studies were performed in a poly-clinic setting in which the same areas at the participating centres were used for various other purposes other than for the management of the infertility alone. In contrast, several of the other participating centres in Europe but to a lesser extent in Asia and Latin America, managed the infertility couple in their studies from centres that were dedicated for infertility because of the high premium on infertility as a reproductive health index. Such dedicated infertility programmes are uncommon in most African countries and certainly did not exist in all the African centres who participated in the W.H.O. studies, even though there is a huge burden of infertility in the gynaecological practice.

This would suggest that the findings in the socio-cultural and epidemiological correlates of the infertility in the W.H.O. studies may not have been truly comparable; unless African studies were performed in similar dedicated infertility programme. This is perhaps why African countries had strikingly different infertility findings as highlighted in the W.H.O. study. Perhaps, the findings from the WHO study if performed in similar dedicated fertility centre as in Europe etc, may have found other infertility causes that are not preventable by the recommended strategy. The WHO

recommendation of prevention as the most cost effective approach to infertility management in African countries would mean, that the prospect of infertility management in contemporary times of concurrent preventive and curative approach including with ART will never gain government support, for public funding. This is the reason for low public spending on infertility management in the developing countries. The findings from studies of the socio-cultural and epidemiological factors of infertility from a dedicated program of infertility in Nigeria did not corroborate several aspects of the prior WHO study of 1985⁴¹. Thus, the prospect of infertility management in a developing country attaining the status as in developing countries is best illustrated by the experience at a unique programme for infertility management in a University hospital in Nigeria.

A University hospital based infertility programme in Nigeria

The infertility programme is part of the department of obstetrics and gynaecology of the University of Benin Teaching Hospital Benin City, Edo State, Nigeria and is called the Human Reproduction Research Programme (H.R.R.P.). The programme has its own site building with consulting rooms, laboratories and administrative office space. Consultation for infertility is daily during the working period and the programme has its own Nurses, Laboratories Scientist, Administrative and Support staff.

Since the Programme has its own building with ample space, clients are received at the centre as couples and given assurance of strict confidentiality of information even between consorts. After the initial consultation, follow-up visit are tailored for the convenience of the couples without the usual



institutional rigidity but within the working period. Good rapport was commonly established between the couple and clinic staff after one or two visit with same staff (Nursing and Medical) unlike consultation in the routine gynaecology clinic where clients encounter different staff at each visit. This management approach encouraged the women to volunteer confidential information and truth about their age, parity and husband occupation.

The main tool for the investigation, classification and diagnosis of infertility was the World Health Organisation (WHO) format for the investigation of the infertile couple as published in 1984 by Rowe and Farley⁴⁰. All the couples were assessed by the consultants and by specially trained Nurses. After full investigation using the WHO protocol, diagnosis was established and the conventional treatment of infertility provided. The couples were followed up thereafter for pregnancy outcome. The results from the programme assessed whether the local pattern of infertility are a reflection of the WHO study over 2 decades ago on which findings and recommendation on infertility management, strategy for African countries was based.

Deduction from the University hospital based infertility Programme in Nigeria

The outcome of 10 years of infertility management involving almost 2000 consecutive couples at the programme was recently published⁴³. Although findings suggest infertility pattern similar to the prior WHO study, there are several differences. The Nigeria woman was not so much younger than her husband, the secondary infertility rate was 85.7% with primary infertility rate of only 14-3% and complications of induced abortions contributed the

highest to tubal blockage, (the commonest female causal factor) followed by vaginal deliveries attended by unskilled persons in unhygienic environment. These are all very different from the prior WHO study. It also showed that there are infertility causes that are unpreventable.

The differences in this study and others is due to the assurance of confidentiality and rapport established between patients and programme staff which led to the disclosure of the truth about the women age, parity and details of the mode and place of delivery. Culturally Nigerian women reduce their age; deny prior abortion and deliveries especially in previous relationships (because they must be seen as young and innocent of prior sexual relationship) and do not disclose the mode and place of delivery. The rapport and confidentiality essential for disclosure may not have been possible in the environment described in the WHO and other studies which may explain the marked discrepancy between this study and other studies of infertility.

The pregnancy rate of 40.1% occurred mainly from the treatment of female factors alone and spontaneous pregnancy in 7.5% attributable to the education and counselling on coital timing provided at the centre. Pregnancy rate was very poor in the female factors requiring surgery, in several of the moderate to severe male factor alone but particularly in couples with both male and female factors.

Thus, in almost 60% of the study population, the infertility program (representing the highest concentration of resources in a developing economy for most types of infertility treatment) could not help the couple achieve pregnancy and further treatment improvement is impossible with the conventional method



available. This is principally because a sizeable proportion of the infertile couples had both female and male factors and a sizable proportion with female factors required surgical treatment that were associated with poor outcome. These, are intractable to conventional infertility treatment method and are best treated with Assisted Reproduction Technology (ART).

The capacity to treat aspect of infertility unresponsive to conventional methods would improve results and therefore justify the investment. Hence the data from this study is a case for implementing ART as a key element in future infertility research and treatment. This study outcome is proof that conventional infertility treatment method has insufficient capacity for treatment of the majority of infertile couple in our environment.

Preventive versus Curative approaches to infertility management in a developing economy

The issues raised in the recommendations of ART as back up infertility treatment deserve further discussion. The data from our study confirm that secondary infertility is the main issue and can be reduced by preventive strategies like access to effective family planning, improved maternity care and Health education to reduce risky behaviour that can cause S.T.D. Not only is prevention cheap but the strategy will confer several other benefits to women's right and society, hence radical proponents of preventive strategy for infertility management, recommend total commitment of resource only to prevention⁴⁴⁻⁴⁶. This radical stance is untenable in contemporary times, because in the case of disease control with HIV/AIDS there is free distribution of antiretroviral drugs to HIV Positive

patients (instead of allowing those afflicted with HIV Virus to progress to AIDS and die) in addition to huge money spent on the campaign to promote the use of condom as prevention for the disease⁴⁷.

No matter the degree of coverage of any preventive strategy it will not apply to the several people who already now are infertile and also it is not all infertility cause that are preventable⁴⁸. A much better approach is the moderate view of infertility prevention advocating that priority should be accorded prevention, but adequate resources should be directed to curative measures to benefit the population already afflicted with infertility⁴⁹⁻⁵¹.

The other issue against curative measures for infertility is the over population issue because there is the demographic paradox that countries with the highest overall fertility rate are also those in which the prevalence of secondary infertility is highest⁵². There is therefore strong argument against infertility treatment especially with extension to ART because it would be wrong use of scare resources and worsening of the world population crisis. This over population as a reason to neglect infertility is wrong logic seeking for the few infertile women to bears the burden of world over- population in which their individual liberty for child wish is unjustly denied^{51,53,54}. More over, such an approach is highly oppressive of those who are infertile as there are better ways of population control which do not infringe upon peoples' right like educating women, providing contraception and safe abortion service⁴⁷. More recently, it was suggested that the over population problem of the world is not any more due to high fertility rate (whether in the developed or developing countries) but due to increased life expectancy



causing population growth by population aging⁵⁴.

It is therefore reasonable to suggest that for the developing economy the infertility management approach should be concurrent preventive and curative. The data from our study at the infertility programme has now defined the content of effective curative infertility management to include establishing infertility programme with competence for ART treatment because majority of the infertility causal factors are intractable to conventional treatment. Certainly the social, emotional, physical and economic consequences that infertile couple (and in particular women) face, justifies investing in treatment options like ART in developing countries^{56;57}. This was our impetus for the up grading of the infertility programme to include capacity for ART services.

IVF in Public Hospital in Nigeria: Practice, problems and prospects

After almost two decades of infertility management at the infertility programme, it was found that almost 60% of the couple could not achieve pregnancy. This is because of causal factors which are intractable to conventional methods occurring singly or in combination. In order to improve the treatment outcome, the programme was upgraded to include facilities for Assisted Reproduction technology. The programme site building was expanded to provide more space for office hysteroscopy, ultrasound with transvaginal probe and full in vitro fertilization and embryo transfer (IVF and ET) equipments and intracytoplasmic sperm injection (ICSI) machine. Full ART services including intra uterine insemination (I.U.I) and IVF and ET with ICSI began June 2007.

IVF and ET with ICSI was offered to the couple who could not achieve

pregnancy by the conventional method. The IVF and ET approach involved the standard practise of pituitary down regulation, followed by super ovulation with ganodotrophin using the long protocol during which follicular response was assessed by regular transvaginal ultrasound. Human Chronic Gonadotrophin (HCG) was administered for ovulation induction when follicles of at least 18mm diameter were obtained and Oocyte retrieval by the transvaginal route performed 35-36 hours after the HCG. The Oocytes were assessed by the embryologist, fertilised with the previously potentiated sperm and resulting embryo transferred on the third day trans- cervically using standard embryo transfer catheters. In the appropriate cases ICSI was performed when there was significant male factor. The IVF method followed the standard Western method as variously published⁵⁸⁻⁶¹.

The IVF service delivery was done in batches of 30-40 couples as a deliberate policy and involved the prior synchronisation of the menstrual cycle of the women at times across one to three cycles with sequential oestrogens and progestogens. This allowed the focalisation of all the manpower and infrastructure for the given period of Oocyte retrieval, embryo culture and transfer. It also allowed the concentration of work for a stipulated period for appropriate manpower deployment. This way, the muted fears of unstable light and water and poor staff motivation in the public hospital system was resolved because during any IVF run adequate staff and stable infrastructure is assured.

The outcome of the first year experience with IVF in a public hospital has been collated and is being published elsewhere⁶². There were 150 couples handled in 5 batches in which there were about 30 couples per



batch. The mean age of the women was 36 years with a range of 32-44 years. The mean parity was 0.7 and mean duration of infertility was 10.5 years. The women had several previous failed treatment mainly surgery (see table 2) and the commonest indication for the IVF was tubal disease and combined male and female factors. The clinical pregnancy rate was 28% per cycle in which there have been 8 deliveries so far. This result is comparable to other I.V.F centres⁶³⁻⁶⁵. The most severe problem encountered was severe Ovarian Hyperstimulation syndrome (OHSS) which occurred in two women in the series and resolved with standard management as described by Lainas 2002⁶⁵. Thus IVF Service delivery in a public hospital system in Nigeria is practicable and effective as a back up for infertility cases that are intractable to conventional treatment as in almost 60% of the infertile population. For the women who achieve pregnancy by this method there are no other ways to assist them and hence ART is a worth while investment even in our resource limited environment. The IVF and ET programme adopted the full Western style approach and achieved a pregnancy rate that is comparable to other IVF centres world wide. This fact has now broken the myth that IVF is not possible in a public hospital system as suggested by other workers^{67,68}. The strategy of batching allows the optimisation of the manpower and focused infrastructural support during an IVF run. Aside from this, batching also allowed the sufficiently large number of couples such as 40 as in our case in a single run which is useful for research and teaching the IVF knowledge. Having now established the structure for IVF at the programme, the next stage is to assess how the cost of the IVF can be reduced to

make it more affordable. This will involve reduction of cost of drugs, equipments and substantial reduction in the chargeable fee by the hospital as advocated by other workers^{50, 63,64}. It is when the cost of IVF is affordable that a truly comprehensive curative infertility treatment can be said to be available and comparable to standard of care for infertility as it is in the developed economy.

Conclusion

Infertility in developing countries is pervasive and has devastating consequences for the couple especially the woman who culturally is held culpable for the cause of the infertility. Since childbearing is the sole purpose of marriage in these settings, infertility or childlessness leads to societal disharmony, divorce, violence, suicide and other psychological disorders. It is in every way a disease burden that deserves priority attention because of the widespread effect on society and the community. This is in contrast to infertility in the Western society where the effect on society is minimal if at all, and yet infertility treatment at whatever cost including ART is never denied anyone who required it.

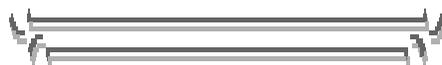
In the developing economy, infertility management has been advised to adopt the much cheaper preventive approaches because of limited funds and burden of over population. Assisted reproduction technology (ART) for infertility management, is said to be wasteful and not practicable because of poor public infrastructure low man power capacity and low staff morale. Recent studies have shown that in 60% of infertile population in some developing economy, the effective treatment is ART or most perhaps will never achieve conception. The report of IVF in a public hospital with a comparable pregnancy rate like



others IVF centres world wide confirms that IVF in a public hospital setting is practicable and worth the investment in a developing economy. What remains is the approach for IVF cost reduction to make it affordable. This is the only way that contemporary concept of infertility management will have prospect in a developing economy to be practiced appropriately in the context of the preventive and curative, including ART.

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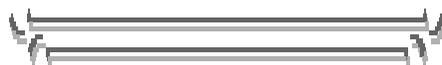
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