

Assisted reproduction in Hong Kong: status in the 1990s

Hong Kong IVF Study Group

Information on assisted reproduction in Hong Kong for the period from January 1992 through December 1993 was collected from the three centres that offer assisted reproduction. Altogether, 912 treatment cycles of in vitro fertilisation and embryo transfer, 158 treatment cycles of gamete intrafallopian transfer, and 87 cycles of zygote intrafallopian transfer were initiated during this period. The delivery rates per cycle started were 8.4% for in vitro fertilisation, 29.1% for gamete intrafallopian transfer, and 13.8% for zygote intrafallopian transfer. During the same period, 233 cycles of replacement of frozen thawed embryos were completed with a delivery rate of 11.2% per cycle. Pregnancies were also achieved using oocyte donation and micromanipulation techniques.

HKMJ 1996;2:

Key words: Reproduction techniques; Fertility agents, female; Fertilization in vitro

Introduction

Assisted reproduction was introduced in Hong Kong in 1985. The first baby conceived by in vitro fertilisation (IVF) and embryo transfer was delivered on 7th December, 1987. Three centres in Hong Kong provide assisted reproduction: the Department of Obstetrics and Gynaecology, The Chinese University of Hong Kong at the Prince of Wales Hospital; the Department of Obstetrics and Gynaecology, The University of Hong Kong at the Queen Mary Hospital, and the IVF Centre at the Hong Kong Sanatorium and Hospital. The first joint report on the results of assisted reproduction was published in 1987.¹ Since then, significant advances have been made in various aspects of assisted reproduction. These include the introduction of intratubal transfer of gametes² or embryos,³ changes in ovarian stimulation regimens with the use of gonadotrophin releasing hormone (GnRH) agonists,⁴ cryopreservation

of embryos,⁵ oocyte donation,⁶ and micromanipulation.⁷ Therefore, a further survey has been conducted into the practice and results in the three assisted centres in Hong Kong.

Subjects and methods

As part of the data collection exercise for the Asia-Oceania Federation of Obstetrics and Gynaecology, a questionnaire was designed by the Reproductive Biology Committee of the Asia-Oceania Federation of Obstetrics and Gynaecology and sent to the three centres offering assisted reproduction in Hong Kong. In the questionnaire, data were requested on IVF, gamete intrafallopian transfer (GIFT), zygote intrafallopian transfer (ZIFT), replacement of frozen thawed embryos, and micromanipulation. The information included the numbers of patients and cycles of treatment, the stimulation protocols used, the number of oocytes obtained, fertilisation rate where appropriate, the number of transfer cycles, the number of oocytes and embryos transferred, the number of clinical pregnancies, and the outcome.

Results

From January 1992 through December 1993, 912 treatment cycles of IVF, 158 treatment cycles of GIFT, and 87 cycles of ZIFT were initiated in the three Hong Kong centres. The indications for treatment are shown in Table 1. The most common indi-

Members of the IVF Study Group:

1. Department of Obstetrics and Gynaecology, Chinese University of Hong Kong, Prince of Wales Hospital:

EPL Loong, CJ Haines, TYT Chiu, SP Wong, LP Cheung

2. Department of Obstetrics and Gynaecology, University of Hong Kong, Queen Mary Hospital:

PC Ho, WK So, WSB Yeung, E Lau V Ng

3. IVF Centre, Hong Kong Sanatorium and Hospital:

CKM Leung, MKH Leong, CJY Wong, WWC Tang, MMP Chun

Correspondence to: Dr PC Ho

Department of Obstetrics and Gynaecology, University of Hong Kong, Queen Mary Hospital, Pokfulam, Hong Kong

Table 1. Indications for assisted reproduction*

	IVF [†] No. (%)	GIFT [‡] No. (%)	ZIFT [§] No. (%)
Tubo-peritoneal damage	438 (54.4)	31 (19.9)	3 (3.6)
Male infertility	69 (8.6)	67 (42.9)	34 (40.4)
Endometriosis	89 (11.1)	38 (24.3)	10 (11.9)
Unexplained infertility	159 (19.8)	42 (26.9)	17 (20.2)
Others	91 (11.3)	10 (6.4)	17 (20.2)

* One patient may have more than one indication
[†] IVF in vitro fertilisation and gamete transfer
[‡] GIFT gamete intrafallopian transfer
[§] ZIFT zygote intrafallopian transfer

Indication for IVF was tubal factor, while male factor infertility was the most common indication for GIFT and ZIFT. In 95% of the cycles, ovarian stimulation was performed with human menopausal gonadotrophin (hMG) or follicle stimulating hormone (FSH) in combination with GnRH agonists. In the remaining 5% of cycles, ovarian stimulation was performed with hMG or FSH with or without clomiphene citrate. All oocyte retrievals were performed by the transvaginal route under ultrasound guidance except in one patient, in whom a combined laparoscopic and transvaginal approach was used.

The results of the assisted reproduction procedures are shown in Tables 2 and 3. The clinical pregnancy and delivery rates were lowest with IVF and highest with GIFT. The rates of pregnancy loss were similar in the three groups.

The results of replacement of frozen thawed embryos are shown in Table 4. The clinical pregnancy rates and delivery rates per transfer were similar to those of fresh cycles. During the study period, 33 cycles of micromanipulation, including 24 cycles of subzonal sperm injection (SUZI), eight cycles of partial zona dissection (PZD) and one cycle of intracytoplasmic sperm injection (ICSI) were performed. There was one pregnancy conceived by SUZI. There were 28 cycles of oocyte donation and six patients conceived. As it takes time to collect territory-wide data, we have only analysed the data for two years. The first livebirths conceived by SUZI and ICSI in Hong Kong were delivered in 1994 and 1995, respectively, and these are not included in the

Table 2. Results of assisted reproduction in Hong Kong from January 1992 through December 1993 (I)

	IVF*	GIFT [†]	ZIFT [‡]
No. of patients	804	156	84
No. of treatment cycles initiated	912	158	87
No. of oocyte retrieval cycles	882	151	79
No. of oocytes per retrieval	6.5	10.2	8.7
Fertilization rate	69.6%	-	-
No. of transfer cycles	775	150	66
No. of embryos/oocytes per transfer	3.4	4.4	3.0

* IVF in vitro fertilisation & gamete transfer
[†] GIFT gamete intrafallopian transfer
[‡] ZIFT Zygote intrafallopian transfer

data analysis. The major landmarks in the development of assisted reproduction in Hong Kong are shown in Table 5.

Discussion

Since the first publication of IVF results in 1986, major advances have been made in the field of assisted reproduction in Hong Kong. The introduction of techniques of transfer of gametes and embryos into the fallopian tubes has improved the pregnancy rates of patients with at least one patent fallopian tube. The results of this study confirm that the results obtained with GIFT and ZIFT are better than those with IVF. However, it must be mentioned that patients treated with IVF are different to those treated with GIFT and ZIFT and differences in the patient characteristics may account for the difference in results. The clinical pregnancy rates of IVF are now better than those obtained in 1987¹ but the delivery rate is still less than 10% per cycle initiated. There is a need to improve the pregnancy rates of IVF.

Gamete intrafallopian transfer should ideally be performed in patients without tuboperitoneal factors. However, such factors were present in 19.9% of patients treated with GIFT in this series. This may explain the relatively high ectopic pregnancy rate of 4.8%. The apparently

Table 3. Results of assisted reproduction in Hong Kong from January 1992 through December 1993 (II)

	IVF* No. (%)	GIFT† No. (%)	ZIFT‡ No. (%)
No. of clinical pregnancies	107	62	16
- spontaneous abortions	27 (25.2)	13 (21.0)	3 (18.8)
- ectopic pregnancies	2 (1.9)	3 (4.8)	1 (6.3)
- deliveries	77 (72.0)	46 (74.2)	12 (75.0)
Multiple pregnancies	16 (15.0)	12 (19.4)	6 (37.5)
- twins	12 (11.2)	5 (8.1)	5 (31.3)
- triplets	4 (3.7)	5 (8.1)	1 (6.3)
- quadruplets	0 (0)	2 (3.2)	0 (0)
Clinical pregnancy rate			
- per cycle started	(11.7)	(39.2)	(18.4)
- per retrieval	(12.1)	(41.1)	(20.3)
- per transfer	(13.8)	(41.3)	(24.3)
Delivery rate			
- per cycle started	(8.4)	(29.1)	(13.8)
- per retrieval	(8.7)	(30.5)	(15.2)
- per transfer	(9.9)	(30.7)	(18.2)
* IVF	in vitro fertilization & gamete transfer		
† GIFT	gamete intrafallopian transfer		
‡ ZIFT	Zygote intrafallopian transfer		

higher incidence of ectopic pregnancy among pregnancies achieved by ZIFT is probably due to small number variation.

Another development in assisted reproduction is the use of GnRH agonists to downregulate the pituitary during ovarian stimulation.⁴ This has reduced the incidence of spontaneous luteinising hormone surges and the subsequent cancellation of cycles. It also facilitates the organisation of assisted reproduction and minimizes the need for oocyte retrieval during weekends. Our results show that in Hong Kong in the study period, 95% of the cycles were stimulated using a combination of hMG and GnRH agonists.

Our survey shows that the average number of oocytes or embryos replaced ranged from 3 to 4.4. This resulted in a multiple pregnancy rate of 15% to 37.5%, and some of these were triplets and quadruplets. The development of cryopreservation techniques has made it possible to freeze and store spare embryos. These embryos can be replaced in subsequent cycles when necessary. This survey shows that the results of replacement of frozen-thawed embryos are comparable

Table 4. Results of replacement of frozen-thawed embryos in Hong Kong from January 1992 through December 1993

	No. (%)
No. of patients	200
No. of cycles	233
No. of embryos replaced per transfer	2.6
No. of clinical pregnancies	34
- spontaneous abortions	8 (23.5)
- ectopic pregnancies	0 (0)
- deliveries	26 (76.5)
Multiple pregnancy	1 (2.9)
Clinical pregnancy rate per transfer	(14.6)
Delivery rate per transfer	(11.2)

to those obtained with fresh embryos. This further strengthens the case for limiting the number of embryos or oocytes used for replacement to avoid the risk of a multiple pregnancy.

Table 5. Milestones in assisted reproduction in Hong Kong

Event	Date
Birth of first baby conceived by IVF	7 December 1986
Birth of first baby conceived by GIFT	17 November 1987
Birth of first baby conceived by ZIFT	2 November 1989
Birth of first baby conceived by replacement of frozen thawed embryo	24 May 1990
Birth of first baby conceived by oocyte donation for premature ovarian failure	7 June 1992
Birth of first baby conceived by subzonal sperm injection	9 April 1994
Birth of first baby conceived by intracytoplasmic sperm injection	13 June 1995

The development of IVF has made it possible for women with premature ovarian failure to conceive with the use of donor oocytes. The results from this survey show that the clinical pregnancy rate (21.4%) is similar to that obtained with other techniques of assisted reproduction (11.7% in IVF to 37.5% in GIFT). The main problem in organising a donor oocyte programme is the difficulty of getting oocyte donors. In donating oocytes, the woman has to undergo ovarian stimulation and oocyte retrieval, both of which carry some risk. Therefore, only a few women agree to donate oocytes. With the introduction of cryopreservation of embryos, women undergoing treatment with IVF are also reluctant to donate some of their oocytes to other women.

Another major breakthrough in assisted reproduction was the development of micromanipulation techniques for the treatment of infertility due to subnormal semen. The three techniques used in this survey were SUZI, PZD, and ICSI. A pregnancy has been achieved now with SUZI. Recently, a baby conceived by ICSI was also born in Hong Kong. There is evidence that ICSI is the technique of choice and it has become the most commonly used micromanipulation technique worldwide.

In conclusion, this survey showed that significant advances in assisted reproduction have been made in Hong Kong. However, the success rate of IVF (compared with GIFT) is low and needs to be improved.

References

1. Mao KR, Loong EP, Lee HC, et al. Current status of in-vitro fertilisation (IVF) in Hong Kong. *J Hong Kong Med Assoc* 1987;39:144-6.
2. Asch RH, Balmaceda JP, Ellsworth LR, Wong PC. Preliminary experiences with gamete intrafallopian transfer (GIFT). *Fertil Steril* 1986;45:366-71.
3. Yovich JL, Blackledge DG, Richardson PA, Matson PL, Turner SR, Draper R. Pregnancies following pronuclear stage tubal transfer. *Fertil Steril* 1987;48:851-7.
4. Porter RN, Smith W, Craft IL, Abdulwahid NA, Jacobs HS. Induction of ovulation for in vitro fertilization using busserelin and gonadotrophins. *Lancet* 1984;2:1284-5.
5. Trounson A, Mohr L. Human pregnancy following cryopreservation, thawing and transfer of an eight-cell embryo. *Nature* 1983;305:707-9.
6. Lutjen P, Trounson A, Leeton J, Findlay J, Wood C, Renov P. The establishment and maintenance of pregnancy using in vitro fertilization and embryo donation in a patient with primary ovarian failure. *Nature* 1984;307:174-5.
7. Palermo G, Joris H, Devroey P, Van Steirteghem AC. Pregnancies after intracytoplasmic injection of single spermatozoa into an oocyte. *Lancet* 1992;340:17-8.