Are the Australian ART Results as Poor as They Appear?

INTRODUCTION

From a once preeminent position in the world of assisted reproduction, the Australian position appears to have slipped into a relatively poor rating on the international scene. Perhaps it might be fairer to say that the comparative data over the past decade show that many nations have advanced their pregnancy rates markedly, while the Australian data indicate a state of minimal progress from a position achieved in the mideighties. Is this really the case? Or is something else happening which our current data presentations fail to reveal? Let us look at both possibilities before drawing conclusions.

DATA COLLECTION IN AUSTRALIA

The first report of relevant pregnancies from in vitro fertilization/embryo transfer (IVF-ET) was published in 1981 by Professor Carl Wood's group in Melbourne (1), detailing nine clinical pregnancies from embryo transfer procedures. Rapidly many units became established within the various states of Australia, which is also credited with establishing the first comprehensive national data registry. This was organized by the AIHW National Perinatal Statistics Unit, which is funded by a grant from the Australian Institute of Health and Welfare, initially to the University of Sydney and now to the University of New South Wales, where the unit is located and functions independently of all IVF units, but to whom units are obliged to comply in providing data as an essential prerequisite to unit accreditation. This in turn is essential for unit registration, where it is required by state legislation as well as access of the unit's patients to Medicare funding.

All Australian IVF pregnancies have been included in the register, beginning with the first two pregnan-

cies reported in 1979, rising annually to record 823 viable pregnancies arising from fresh IVF-ET and 505 viable pregnancies from gamete intrafallopian transfer (GIFT) in 1996, the latest published report (2). We do not include the GIFT data in this discussion because it is currently regarded as an outmoded form of assisted reproductive technology (ART), shown by a fall of 38% from the peak of 1036 cases in 1992! The experience of many indicates that the majority of "GIFT cases" can nowadays conceive by carefully conducted ovarian stimulation, often combined with intrauterine insemination (IUI) treatment (3). Those failing to conceive after three or four failed IUI cycles are now mostly treated by IVF as the next step where fertilization problems can be appropriately identified.

It is not my intention to discuss the question of "rates" except to say that all permutations of numerator/denominator considerations are relevant to different discussions and the *embryo implantation rate* (number of pregnancy sacs arising per total number of embryos transferred) has been effectively used to compare different ART procedures within a controlled setting (4).

The Australian data report its major statistic of *viable pregnancy rate*, being the number of pregnancies advancing beyond 20 weeks of gestation per 100 treatment cycles reaching the stage of oocyte retrieval. The 1996 report reveals that this rate has now reached 11.9, a rise from 10.2 the previous year (1994), which was the first time double figures were attained (5). Of further interest during 1994 and 1995, the individual unit results for viable pregnancy rates ranged from 4.1% (of 103 treatment cycles commenced) to 29.4% (of 56 treatment cycles commenced). In fact the busiest units (more than 500 treatment cycles commenced) had results in the lower half of the scale, ranging from 7.0 to 15.4% in the period.

UK AND NORTH AMERICAN DATA COLLECTION

In the same period, the HFEA data (6) from the United Kingdom report live births of 15.4% from a total of 27,484 treatment cycles commenced. These data are considered particularly relevant in comparison to the Australian results, as supervised restrictions on embryo numbers apply similarly in the United Kingdom and Australia. In the United States and Canada for 1994, the ASRM/Society for ART Registry documents IVF *deliveries per retrieval* at a rate of 18.2% from 23,254 oocyte retrieval procedures where these were done for IVF (i.e., GIFT and ZIFT excluded) (7). It is difficult to be certain about the comparability of the North American data with the UK and Australian, data particularly with respect to numbers of embryos transferred (data not available in report) and treatments in older women. However, the embryo number question may not be a relevant concern, as many reports suggest that the chance of pregnancy peaks at two or three embryos in women under 40 years and the only significant finding for higher embryo numbers is an increase in multiple pregnancies. Furthermore, the age question appears to be biased against the North American results, given that almost 16% of the IVF cases in 1994 were performed on 3575 women aged over 40 years, with a delivery rate per retrieval of 8.3%. The Australian data for 1994 are incomplete but, for those units complying, show that 899 of 6863 IVF cycles (13.1%) were undertaken on women aged 40 years or more. Live birth rates are not given but extrapolated data suggest a delivery rate per retrieval of <7.0%.

DISCUSSION

The viable pregnancy rates therefore appear significantly lower in Australia and we have already drawn attention to the larger units being on the lower end of the spectrum, this being the reverse of HFEA data, which have consistently shown better results from the larger units (centers). However, some Australian units have argued that their data are unfairly presented in that a relatively large number of cases have a *freeze-all embryos* policy to avoid the problem of ovarian hyperstimulation syndrome (OHSS) in susceptible cases. However, this information is not readily available. Extracted data from the NPSU registers are shown in Tables I and II, where it can be seen that in 1994 68.2% of treatment cycles commenced proceeded to embryo transfer and the following year the proportion was fewer (64.6%), consistent with the increasing trend for Australian Units to use the freeze-all policy in avoiding OHSS. Tables III and IV show the comparable rates for the United Kingdom in 1995 and North America in 1994, being a significantly higher 79.3 and 77.8%, respectively, proceeding to embryo transfer. The OHSS group are known to have a significantly higher implantation rate (8) and

Table I. IVF Pregnancies in Australia Originating from Fresh Embryo Transfers to the Uterus for 1994 (Micromanipulation and Donor not Included)

	Clinical pregnancies		Live births	
Cycles	Treatment cycle commenced	Embryo transfers	Treatment cycle commenced	Embryo transfers
All centers	944/8098 (11.7%)	944/5524 (17.1%)	690/8098 (8.5%)	690/5524 (12.5%)
≥200 cycles/year	703/6225 (11.3%)	703/4188 (16.8%)	503/6225 (8.1%)	503/4188 (12%)
<200 cycles/year	241/1873 (12.9%)	241/1336 (18%)	187/1873 (10%)	187/1336 (14%)

Table II. IVF Pregnancies in Australia Originating from Fresh Embryo Transfers to the Uterus for 1995 (Micromanipulation and Donor not Included)

	Clinical pregnancies		Viable pregnancies	
Cycles	Treatment cycle commenced	Embryo transfers	Treatment cycle commenced	Embryo transfers
All centers	944/8191 (11.5%)	944/5295 (17.8%)	747/8191 (9.1%)	747/5295 (14.1%)
≥200 cycles/year	690/6024 (11.5%)	690/3788 (18.2%)	539/6024 (8.9%)	539/3788 (14.2%)
<200 cycles/year	254/2167 (11.7%)	254/1507 (16.8%)	208/2167 (9.6%)	208/1507 (13.8%)

Table III. IVF Pregnancies in the UK Originating from Fresh Embryo Transfers to the Uterus in 1995 (Micromanipulation and Donor not Included)

	Clinical pregnancies		Live birth	
Cycles	Treatment cycle commenced	Embryo transfers	Treatment cycle commenced	Embryo transfers
All centers	5,192/27,484 (18.9%)	5,192/21,805 (23.8%)	4,219/27,484 (15.4%)	4,219/21,805 (19.4%)
≥200 cycles/year	4,673/24,218 (19.3%)	4,673/19,333 (24.2%)	3,806/24,218 (15.7%)	3,806/19,333 (19.7%)
<200 cycles/year	519/3,266 (15.9%)	519/2,472 (21%)	413/3,266 (12.6%)	413/2,472 (16.7%)

Table IV. IVF Pregnancies in the United States Originating from Fresh Embryo Transfers to the Uterus (Micromanipulation and Donor not Included)

	Clinical pregnancies		Live birth	
Cycles	Treatment cycle commenced	Embryo transfers	Treatment cycle commenced	Embryo transfers
All centers	6,114/26,961 (22.7%)	6,114/20,979 (29.1%)	4,912/26,961 (18.2%)	4,912/20,979 (23.4%)

Table V. IVF and FET Data from PIVET Originating from Embryo Transfers to the Uterus (Micromanipulation and Donor Not Included)[a]

Treatment cycles	No. cycles	No. viable pregnancies (% rate)
Fresh IVF cycles	709	175 (24.6%)
Frozen cycles (arising from above)	341 (46% of cycles)	86 (25.3%)
Viable cumulative pregnancy rates per treatment cycle	709	261 (36.8%)
Estimated viable cumulative pregnancy rates per treatment cycle[a]	709	312 (44%)

[a] Two hundred additional FET cycles, with 51 additional pregnancies, calculated by 95 batches of embryos remaining in storage multiplied by 2.1 (average number of FET cycles per batch of embryos).

pregnancy rate (as well as multiple pregnancy rate) than average cases hence the Australian policy may be leading to a comparative reduction in pregnancy rates. If the IVF programs are of comparable efficiency, this should be reflected by an increased number of cycles with cryopreservation of embryos, an increased number of embryos cryopreserved per treatment cycle, a relatively higher proportion of pregnancies obtained by frozen embryo transfer (FET), and a reduction in cases of OHSS.

The FET rates for the three regions under study are shown in Table IV, where it can be seen that indeed a higher FET/fresh IVF transfer rate occurs in Australia. The FET pregnancy rates and live birth rates are similar between Australia and the United Kingdom and slightly but significantly higher in the North American data. Unfortunately data on OHSS rates are not available from any of the regions, hence it is not possible to determine if the "trade-off" of the freeze-all policy on pregnancy rates for a reduction in OHSS morbidity has been effective. However, the data presented do imply that the Australian pregnancy results would *not* be improved by scrapping the freeze-all policy, as those embryos which survived the freeze and thaw process appear to have implanted at the same rate as the fresh transfers.

If registers are going to report data to take the above considerations into account, a statistic which may be useful is the *cumulative viable pregnancy rate*, defined as the number of viable pregnancies arising from 100 treatment cycles, which includes the FET treatments arising from the single-oocyte recovery procedure. For example, PIVET data are shown in Table V. The freeze-all embryo rate during the period was 8.9%. For women under 40 years the viable pregnancy rate is 24.6% in the fresh IVF cycle and similar, at 25.3%, for frozen embryo transfers. Forty-six percent of treatment cycles have a batch of embryos cryopreserved and there are approximately 2.1 FET cycles per batch. The viable cumulative pregnancy rate for all cases (under 40 years) conducted in the period was 36.8%, but in 95 of the retrieval cycles some or all of the frozen embryo batch remains in cryostorage. The estimated viable cumulative pregnancy rate for the group is 44%.

CONCLUSIONS

In conclusion, it appears that the efficiency of IVF, when measured by the viable pregnancy rate per retrieval or per transfer, is poorer in Australia compared with the United Kingdom or North America, and this finding is not clearly due to a higher freeze-all embryos policy which prevails in Australia. To be fair the Australian data exhibit wide variability among units, with the better results arising from some of the smaller units undertaking between 100 and 300 oocyte recoveries per annum for IVF, unlike the UK experience, where larger units tend to do better. However, in comparing national data registers, the freeze-all rates should be documented and consideration given to presenting a viable cumulative pregnancy rate for a subgroup of cases which excludes major confounding variables such as advanced female age and poor responders.

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