

EDITORIAL

Assisted Reproductive Technology in Egypt, 2001: results generated from the Egyptian IVF registry

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ABSTRACT

Objective: To summarize the results of ART procedures cycles initiated in Egypt during the year 2001.

Design: The 'World Report on ART' forms, prepared by the International Committee for Monitoring Assisted Reproductive Technology (ICMART), were distributed to all IVF centers in Egypt.

Materials and methods: All IVF centers in Egypt were invited to voluntarily participate.

Main outcome measures: The total number of standard IVF, ICSI, FET after standard IVF and ICSI cycles, incidence of clinical pregnancy, abortion, delivery, stillbirth and complications rates.

Results: Data was anonymously received from 16 centers, with a total of 6,757 reported cycles. ICSI constituted 91.4%, IVF constituted 4.4%, while the frozen-thawed embryo replacement cycles represented only 4.2% of the total number of ART cycles. As for standard IVF, the clinical pregnancy rate per aspiration and per transfer was 27.5 and 27.9%, respectively. For ICSI, the corresponding rates were 33.1 and 34.7%. The distribution of singleton, twin, triplet and high-order deliveries for IVF, ICSI and FET combined was 67.2, 29.1, and 3.6 respectively. This gives a total multiple delivery rates of 32.7%. As a result of ART activities, 1,914 neonates were reported born. Complications of ART were mainly ovarian hyperstimulation syndrome, complicating 2.2% of cycles; the occurrence of bleeding in 0.27% and infection in 0.07% of all aspiration cycles.

Conclusions: This is the third consecutive report of the activities of the Egyptian IVF registry for cycles initiated during the year 2001. The clinical pregnancy rates were comparable with the previous reports. The multiple pregnancy rate is still high due to the transfer of >3 embryos. The practice of cryopreservation of embryos is still limited to only a few centers. OHSS is also high and therefore in the future preventative measures must be stricter. More efforts are needed to complete data on deliveries and perinatal mortalities.

Key words: Egypt, IVF, ICSI, registry data

INTRODUCTION

This report is the third consecutive Egyptian IVF Registry publication for Egyptian data on assisted reproduction technology (ART) for the year 2001. In 2003, the first and second reports of the Egyptian IVF Registry were collectively

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published for cycles beginning in 1999 and 2000 (1). In addition the data from the previous registries has been incorporated in the 1st report of the Middle East IVF Registry for the year 2000 (2) and the World IVF Registry 1999, 2000. Furthermore, this report is expected to be included in the upcoming Middle East and World IVF Registries.

Ever since the introduction of the first center to accommodate in-vitro fertilization (IVF) in Egypt almost twenty years ago, the IVF technique has

Table 1. Distribution of IVF Centers in Egypt.

Governorates	Number of Centers
Alexandria	9
Aswan	0
Asiut	2
Beheira	0
Beni Suef	0
Cairo	19
Dakahliya	5
Dumietta	1
Fayoum	0
Gharbiya	3
Giza	7
Ismailiya	0
Kafr El-Sheikh	0
Kalyobiya	2
Kena	0
Luxor City	0
Matroh	0
Monofiya	0
Minia	1
New Valley	0
North Sinai	0
Port Said	0
Red Sea	0
Sharkiya	2
Sohag	1
South Sinai	0
Suez	0
Total	52

become much more acceptable as a means of procreation among the medical community, patients, and society. Currently there are 52 know IVF centers operating in Egypt.

Due to the widespread IVF practice in Egypt, a national registry to represent Egyptian IVF centers became a necessity. Even though, until today there is no official governmental or governmentally affiliated body responsible for developing or maintaining an IVF registry. The "Egyptian Medical Syndicate" and the "Egyptian Ministry of Health," both whom regulate the daily operations of IVF centers in Egypt through registration and regular visits by officials, provide no specific requirements, or guidelines, for the reporting of data to a national IVF registry. However, like any other new modality of treatment, reporting of data is very important for evaluation of the efficiency of the treatment and estimation of the relative risk, which leads to continuous modifications in an attempt to improve the risk/ benefit ratio.

Table 2. Size of IVF centers as indicated by the number of cycles per year.

# of Cycles/year	Number of Centers
<100	3
100 – 199	3
200 – 499	7
500 – 999	2
>1000	1

In 2001, the Egyptian IVF Registry was formed in order to help gather information on the benefits, risks and success rates of assisted reproduction in Egypt. It is a non-governmental group independent of any current organization or society. Its primary role was to create and maintain the Egyptian IVF Registry and disseminate information pertaining to the benefits and risks involved with assisted reproduction in Egypt.

MATERIALS AND METHODS

In an effort to collect data for the year 2001, all IVF centers in Egypt were contacted through E-mails, faxes, phone calls, and personal contacts. The 'World Report on ART' forms, prepared by the International Committee for Monitoring Assisted Reproductive Technologies (ICMART), were distributed to all the centers, with a covering letter setting a date for a meeting to collect the completed anonymous forms.

The present report summarizes data from assisted reproductive treatments started during 2001. The data includes treatments from standard in vitro fertilization (IVF), intracytoplasmic sperm injection (ICSI), and frozen embryo replacement (FER) following standard IVF and ICSI, performed during the period of January 1, 2001 till December 31, 2001. Follow-up data on pregnancies and deliveries are cohort data; being collected collectively after the outcome of all pregnancies was determined. It is important to note that no oocyte donation or gamete intra-fallopian transfer (GIFT) cycles were reported in any centers in Egypt.

Table 3. Number of initiated and pick-up cycles, the number of embryos transferred and the number of clinical pregnancy (PR).

	IVF	ICSI	Total
Initiated cycles	295	6175	6470
Aspirations	262	5934	6196
Transfers (%)			
1 embryo	13 (5.0%)	498 (8.8%)	511 (8.7%)
2 embryos	49 (19.0%)	858 (15.2%)	907 (15.4%)
3 embryos	108 (41.9%)	2792 (49.4%)	2900 (49.1%)
4 embryos	65 (25.2%)	879 (15.6%)	944 (16.0%)
5 or more embryos	23 (8.9%)	591 (10.5%)	614 (10.4%)
All	258	5649	5907
Clinical pregnancies	72	1961	2033
CPR per pick-up	27.5%	33.0%	32.8%

Table 4. Frozen-thawed cycles (data provided from four (4) centers).

IVF			ICSI		
Thawings	Transfers	Clinical pregnancies	Thawings	Transfers	Clinical pregnancies
10	8	0	277	222	42

RESULTS

Response Rate

All active IVF centers in Egypt (n=52) were contacted and sent the ICMART forms. Data was collected from sixteen centers for the year 2001 and none were excluded. In addition, since not all the currently operating centers were in commission in the year 2001, a large number will be expected to participate in the upcoming registries. The geographic distribution and response rate of centers is shown in (Table 1).

Size of Clinics

The size of the centers, as indicated by the number of cycles per year, is shown in (Table 2). As in previous years, center sizes in Egypt show a parametric distribution. In addition, the largest size group still remains the category from 200 - 499 cycles per year.

Number of Treatment Cycles

The total number of cycles performed was 6,757. Table 3 shows the number of initiated and pick-up cycles, the number of embryos transferred and the number of clinical pregnancies (CPR). The clinical PR per pick-up was 27.5% in IVF and 33.0% in ICSI.

The results of frozen-thawed cycles are shown in 'Table 4.' Only 4 centers provided data for cryopreservation of embryos. The frozen-thawed cycles represented only 4.2% from the total number of ART cycles.

Table 5. Women's age at the time of retrieval.

Age	IVF	ICSI	Total
< 29	79 (30.2%)	1832 (30.9%)	1911 (30.8%)
30 - 34	104 (39.7%)	1895 (31.9%)	1999 (32.3%)
35 - 39	66 (25.2%)	1631 (27.5%)	1697 (27.4%)
> 40	13 (5.0%)	576 (9.7%)	589 (9.5%)

Table 6. Indications for ART.

INDICATION	IVF	ICSI	Total
Tubal, only	163 (61.7%)	257 (4.4%)	420 (6.9%)
Endometriosis, only	18 (6.8%)	250 (4.3%)	268 (4.4%)
Ovulation disorders, only	57 (21.6%)	269 (4.6%)	326 (5.4%)
Other female factor, only	11 (4.2%)	124 (2.1%)	135 (2.2%)
Male factor only	0 (0.0%)	3034 (52.4%)	3034 (50.2%)
Tubal + male ± Other female factor	2 (0.8%)	605 (10.4%)	607 (10.0%)
Male + other female factor, tubal excluded	0 (0.0%)	808 (14.0%)	808 (13.4%)
Infertility of unknown origin	13 (4.9%)	407 (7.0%)	420 (6.9%)
Pre-implantation genetic diagnosis	0 (0.0%)	0 (0.0%)	0 (0.0%)
Other factors	0 (0.0%)	31 (0.5%)	31 (0.5%)

Age Distribution

The women's age at the time of retrieval is shown in (Table 5). It is obvious from the results that women aged 30 - 34 years old still remain the largest group undergoing ART. Even though, there is also a trend for IVF in older women, with a large number of women aged 35 - 39 also attempting IVF. Moreover, women aged forty years and older represented 9.5% of all cycles.

Indications for ART

The indications for ART are shown in (Table 6). The male factor of infertility alone, or in association with other factors, still remains the largest indication for undergoing assisted reproduction. This represented 73.6% of all indications for IVF/ ICSI in 2001.

Table 7. Complications of ART.

Complication	IVF	ICSI	Total
Ovarian hyperstimulation syndrome:			
Total	9	136	145
Requiring hospitalization	4	26	30
Complications of oocyte retrieval:			
Total	6	16	22
Bleeding	5	12	17
Infection	0	4	4
Other	0	1	1
Maternal deaths*:			
Related to ART itself	0	0	0
Related to pregnancy	0	0	0

Risks of Treatment

The complications, such as ovarian hyperstimulation syndrome, bleeding and infection, are shown in (Table 7). Ovarian hyperstimulation syndrome still remained high, with OHSS occurring in 2.2% of initiated cycles. In addition, there was a reported occurrence of bleeding in 0.27% and infection in 0.07% of all aspiration cycles.

Pregnancies and Deliveries after Treatment

The numbers of deliveries are shown in (Table 8). Perinatal mortality is shown in (Table 9). Data on deliveries and malformations are incomplete due to inadequate follow-up. Only four centers reported on the incidence of chromosomal aberrations, and/or malformations, in IVF babies. These chromosomal aberrations and congenital malformations are presented in (Table 10).

DISCUSSION

The present report is the third consecutive report to cover ART data of treatment cycles in Egypt for the year 2001. Sixteen centers voluntarily provided data on 6,757 cycles performed between January 1, 2001 and December 31, 2001, which is an increase of 4% compared to the year 2000. Taking into consideration that even

Table 8. Number of deliveries.

	IVF	ICSI	FER	Total
Singleton deliveries	43 (75.4%)	877 (66.4%)	22 (91.7%)	942 (67.2%)
Twin deliveries	13 (22.8%)	393 (29.8%)	2 (8.3%)	408 (29.1%)
Triplet (or higher order) deliveries	1 (1.8%)	50 (3.8%)	0 (0.0%)	51 (3.6%)
All deliveries	57	1320	24	1401

FER: frozen-thawed embryo replacement

though the number of centers submitting data in 2001 is less than 2000 (16 and 18 centers, respectively), this shows an even larger increase in the usage of assisted reproduction in Egypt. Furthermore more centers are expected to participate in the future registries since they did not have data, or did not yet operate, in 2001.

Since the population of Egypt at the end of 2001 was around 66 million, it means that ART service was provided at an average rate of 102 cycles per million inhabitants. This figure should be taken with some caution since not all IVF centers in Egypt reported on the results of their activities. Therefore the true number is expected to be much higher.

In comparison with Europe, in which 289,690 ART cycles were undertaken in 2001, Egypt showed a much lower usage rate for assisted reproduction (3).

Table 9. Perinatal mortality in relation to multiple deliveries.

	Perinatal Mortality	All babies (n)	Stillborn (n)	Early neonatal death (n)
IVF	Singleton	43	0	0
	Twin	26	0	0
	Triplet	3	0	0
	Quadruplet	0	0	0
	All babies	72	0	0
ICSI	Singleton	877	5	9
	Twin	786	9	26
	Triplet	141	3	22
	Quadruplet	12	5	0
	All babies	1816	22	57
FER	Singleton	22	0	0
	Twin	4	0	0
	Triplet	0	0	0
	Quadruplet	0	0	0
	All babies	26	0	0

FER: frozen-thawed embryo replacement

The average number of treatment cycles was reported to be 829 per million inhabitants. Even though it is important to note that this was calculated only in those countries with complete coverage in their reporting and not for all of Europe.

In the United States of America, 107,587 cycles of ART treatment were reported for the year 2001 (4), with a mean of 371 cycles per million inhabitants. Again showing a higher degree of ART service compared to Egypt.

One possible explanation for the poor penetration into the Egyptian marketplace is the unequal distribution of IVF centers across the different governorates. The distribution of the IVF centers all over the country is not homogenous with only eleven out of the 27 governorates (40.7%) containing IVF Centers. Currently there are 52 know ART centers operating in Egypt. Nineteen are located in Cairo, nine in Alexandria, seven in Giza, five in Dakahliya, three in Gharbiya, two in Aslut, two in Kalyobiya and Sharkiya each, and one center in Dumietta, Minia and Sohag each.

It is important to also mention that there is no medical insurance, neither private nor governmental for ART, and patients pay the cost of the trial as well as the medications themselves.

The women's age at the time of oocyte retrieval demonstrated that women aged 30 - 34 years old still remained the largest group undergoing ART in 2001 (Table 5). In addition, women aged 29 and under accounted for 30.8% of all trials. Even though, there is also a trend for IVF in older women. Women aged 35 - 39 constituted around one fourth of all women undergoing ART. This is important because this coupled with the current high rate of 40 and above group (9.5%), we may be

Table 10. Congenital anomalies/ Chromosomal aberrations in babies born after ART.

Congenital anomalies/ Chromosomal aberrations	Woman's age	ART	Gestational age	Pregnancy outcome
Congenital Heart Disease	30	ICSI	37 wks	Live birth
Histiocytosis X (Langerhans cell histiocytosis)	33	ICSI	37 wks	Live birth
IDM, Hypoglycemia	42	ICSI	38 wks	Live birth
Klinefelter Syndrome; 47, XXY	24	ICSI	35 wks	Live birth
Klinefelter Syndrome; 47, XXY	30	ICSI	35 wks	Live birth
Multiple congenital malformations	40	ICSI	24 wks	Died
One additional marker chromosome	31	ICSI	37 wks	Live birth
Pericentric inversion of chromosome 9; (46, inv9) (p13;q43.1)	31	ICSI	37 wks	Live birth
Renal Hypoplasia	38	ICSI	26 wks	Died
Rt. undescended testis	31	ICSI	36 wks	Live birth
Rt. undescended testis (inguinal)	39	ICSI	35 wks	Live birth
Talipes	25	ICSI	38 wks	Live birth
Talipes Equino Varus	30	IVF	38 wks	Live birth
Translocation of ch. 2 & 8 ; 46, XX, t(2;8)(p36;q13)	22	ICSI	37 wks	Live birth
Translocation of ch. 7&12 ; 46, XX, t(7;12)	37	ICSI	38 wks	Live birth
Unilateral congenital cataract	35	ICSI	30 wks	Live birth
Web between Thumb	32	ICSI	38 wks	Live birth

seeing a growing market targeting relatively older women.

As for the numbers of cycles performed, the year 2001 showed an increase in the number of cycles reported as compared to the year 2000. Furthermore, since the number of centers that contributed in 2001 is less than in 2000, this can be taken a true sign of increased ART activity in Egypt.

Unfortunately, as noted by the numbers of transferred embryos, there is still a problem with transferring a large (>3) number of embryos per transfer cycle, with 26.4% of all women undergoing transfer receiving at least four embryos. Furthermore it is generally apparent that the optimum targeted number of embryos was three, with 49.1% of all women receiving this number. Lastly, only 24.1% of women received only single, or two embryo transfers. It is not clear if these were intentional low-number transfers, or if it was due to a lack of available embryos for transfer.

It is also notable that ICSI represented about 91.4% of ART cycles for the year 2001. This represents a significant predominance of ICSI as compared to standard IVF practice in Egypt. If we compare these figures with the indications of ART cycles we may find an explanation. The female factor only as a cause of infertility represented only

18.9% of cases attempting ART cycles. On the other hand, male factor alone, or in combination with other factors, represented 73.6% of the cases (Table 6).

The multiple delivery rate was still high in both IVF and ICSI. Twin deliveries represented 22.8% in IVF and 29.8% in ICSI. In addition, triplet and high-order deliveries represented 3.7% of all IVF and ICSI cycles in 2001. This is a reflection of the relatively high number of embryos transferred per cycle in all age groups. In the year 2001, 49.1% of the transfer cycles following IVF and ICSI received 3 embryos, 16.0% received 4 embryos, and 10.4% received 5 or more embryos. It is clear that the rates of multiple pregnancies are high due to the transfer of >3 embryos per cycle in Egypt, coupled with the limited availability of cryopreservation. This limited availability may play a strong role in favor of transferring these large numbers. Furthermore are the financial constraints and lack of medical insurance coverage that makes it difficult for most of the patients to afford repeating the cycle.

The reported frozen-thawed embryo replacement cycles represented only 4.2% of the total number of ART cycles. This reflects the very limited practice of cryopreservation as indicated by the fact that only 4 centers provide this service. Until recently, cryopreservation was not even

mentioned as an allowed procedure by the Egyptian Medical Syndicate.

As a result of ART in 2001, 1,914 neonates were reported born. Since the total number of all live births in Egypt for the year 2001 was 1,741,308, therefore this indicates that babies born as a result of ART represented 1 for every 910 babies born. Again this not is 100% accurate since the reporting of follow-up of pregnancies following ART cycles was reported to be very poor.

Again this not is 100% accurate since the reporting of follow-up of pregnancies following ART cycles was reported to be very poor.

The complications reported were mainly ovarian hyperstimulation syndrome, which occurred at a rate of 2.2%. This is a relatively high incidence compared to the reported incidence of 0.9% of all stimulated cycles in 20 countries in Europe, as indicated by the ESHRE registry (3). Ovarian hyperstimulation syndrome is a preventable disease and more strict precautions have to be taken for prevention. Bleeding occurred in 0.27% of aspiration cycles. In addition, infection was also rare, occurring in only 0.06% of all aspiration cycles.

The data on malformation is very deficient. Only 4 centers provided information on the number of babies born with congenital malformation, or abnormal karyotyping for the babies. This is both a result of the poor follow-up of babies born after IVF and due to the financial constraint of routine karyotyping of the offspring.

In summary, this is the third in an annual series of publications reporting the cumulative results of the work of the Egyptian IVF Registry for the year 2001. Sixteen centers participated in the registry reporting 6,757 cycles, with an overall clinical pregnancy rate of 30.7%. The multiple pregnancy and delivery rates were high, with 32.8% of deliveries being twins, triplets or high-order. The problem of multiple pregnancies needs to be resolved by reducing the number of embryos per transfer and improving the practice of cryopreservation. Rigorous efforts for the prevention of OHSS are also required. Finally, better recording systems and follow-up of pregnancies and deliveries will improve the quality and accuracy of the registry.

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Appendix 1. Egyptian IVF Registry (2001) Participating Centers

Center Name	Contact persons representing data collection
Adam International Hospital	Medhat Amer, M.D.
Alex Sydney Kiel Center	Hassan Yossef, M.D.
Alexandria IVF & ICSI Center	Hassan Ali Hassan, M.D.
Al-Rawad ART Center	Emad El-Din Khalifa, M.D.
Assaf Fertility Center	Ayman Assaf, M.D.
Cairo Fertility Center	Hussein Yossef, M.D.
Egyptian IVF-ET Center	Ragaa Mansour, M.D.
Egyptian/German Center for IVF & ICSI	Nasser Allakkany, M.D.
Faris Medical Center	Mohamed Faris, M.D.
Ganin Fertility Center	Hosam Zaki, M.D.
Hawa Mansoura Center	Mohamed El Said El Gharib, M.D.
Mansoura Fertility Center	Hamed Yossef, M.D.
Mansoura Integrated Fertility Center	Mohamed El-Said Ghanem, M.D.
Miami Infertility Center for IVF & ICSI	Hesham Ali Saleh, M.D.
Nile Badrawy Hospital	Salah Zaki, M.D.
Nozha International Hospital & IFC	Abdel Hamid Wafik, M.D.