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Assisted reproductive technologies in Africa: The African Network and Registry for ART, 2018 and 2019

BIOGRAPHY

Paversan Archary is Clinical Assistant of the African Network and Registry for ART, and regional contributor to the International Committee for Monitoring ART. He is a clinician and academic researcher at 2 Military Hospital, and Groote Schuur Hospital, University of Cape Town. His work and research focus on ART data surveillance in Africa.

Paversan Archary[a,b,*], Liezel Potgieter[a,b], Eman Elgindy[c,d], Rudolph Kantum Adageba[e], Justin Mboloko[f], Faye Iketubosin[g], Gamal Serour[h,i], Silke Dyer[a,b], on behalf of the African Network and Registry for Assisted Reproductive Technology

KEY MESSAGE

Registry data from ART procedures (2018, 2019; 18 countries) from the African Network and Registry for ART, integral to widening access to quality care in Africa. The findings of sound ART effectiveness, including in cases of single embryo transfer, a young patient population and high multiple pregnancy rates, are evident.

ABSTRACT

Research question: What were the utilization, practices and outcomes of assisted reproductive technology (ART) in Africa in 2018 and 2019?

Design: Cycle-based data (CBD) and retrospective summary data were collected cross-sectionally from voluntarily participating ART centres.

Results: During 2018, 43,958 ART procedures were reported by 67 centres in 16 countries, increasing to 45,185 procedures reported by 70 centres in 18 countries in 2019. Autologous fresh procedures predominated at 70%, whereas autologous frozen embryo transfers (FET) increased from 21.2% to 23.1% and oocyte donation cycles remained below 10%. In 2019, the mean age of women undergoing autologous fresh embryo transfer was 33.9 years and received a mean number of 2.4 embryos per transfer. The clinical pregnancy rate (CPR) per fresh embryo transfer was 42.8% in 2018 and 38.4% in 2019, with corresponding rates of 38.3% and 31.8% after FET. In both years, most ART procedures, excluding single embryo transfer (SET), were associated with a multiple delivery rate above 20%, reaching over 30% after elective dual embryo transfer in autologous cycles and after fresh oocyte donation. Multiples were predominantly born preterm with a substantially increased perinatal mortality rate. The CBD for both years showed that elective SET (eSET) achieved a high CPR without compromising safety.

Conclusion: This third report of The African Network and Registry for Assisted Reproductive Technology documents the prevailing practice of multiple embryo transfers in a cohort of relatively young women while highlighting the importance of disaggregating eSET, non-eSET and double embryo transfer. The high CPR after eSET and the increase in cryopreservation cycles are encouraging trends towards decreasing the number of embryos transferred without compromising effectiveness. Improved follow-up of ART pregnancies is required.

[a] Department of Obstetrics and Gynaecology, Groote Schuur Hospital and Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa
[b] African Network and Registry for Assisted Reproductive Technology
[c] Egypt IVF Registry
[d] Department of Obstetrics and Gynecology, Zagazig University School of Medicine, Zagazig Sharkia 44511, Egypt
[e] Fertility Society of Ghana
[f] Groupe Interafricain d'Etude, de Recherche et d'Application sur la Fertilité
[g] Association for Fertility and Reproductive Health
[h] African Federation of Fertility Societies
[i] Department of Obstetrics and Gynaecology, Al Azhar University, The Egyptian IVF-ET Center, 3 Street 161, Hadayek El-Maadi, Cairo 11431, Egypt

KEYWORDS

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*Corresponding author. E-mail address: paversan@me.com (P. Archary). https://doi.org/10.1016/j.rbmo.2023.01.014 1472-6483/© 2023 Reproductive Healthcare Ltd. Published by Elsevier Ltd. All rights reserved.
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INTRODUCTION

The disease of infertility has a significant effect on the sexual and reproductive health and rights of millions of women and men globally (*WHO, 2020*). To mitigate the effect of disease, preventative strategies must go hand in hand with equitable access to quality fertility care, including assisted reproductive technology (ART). The African Network and Registry for Assisted Reproductive Technology (ANARA) seeks to mitigate the burden of infertility disease through regional strengthening of ART (www.anara-africa.com). The objectives of ANARA are the ongoing generation of registry data on the availability, utilization, effectiveness and safety of ART, and to use these data to improve access to, and the quality of, ART in Africa. This third official data release presents information on the number, practices and outcomes of ART procedures undertaken in Africa in 2018 and 2019, and resultant babies born through to September 2020. The African Network and Registry for Assisted Reproductive Technology is in South-South cooperation with the Registro Latinoamericano de Reproducción Asistida (RLA), the Latin American Registry for ART, and in triangular cooperation with the International Committee for Monitoring ART (ICMART).

MATERIALS AND METHODS

Cross-sectional data pertaining to ART cycles conducted in the years 2018 and 2019 were collected and processed according to methods previously described (*Dyer et al., 2019*; *2020a*). Data were received in two formats and through two major avenues: cycle-based data (CBD) and retrospective summary data (RSD); as well as data from Nigerian centres collected and submitted via the Society for Assisted Reproductive Technology Clinic Outcome Reporting System. The CBD submission was via the ANARA online portal and software. This software contains measures for data validation, and captures CBD in six categories comprising autologous fresh conventional IVF and intracytoplasmic sperm injection (ICSI), frozen embryo transfers (FET), oocyte donation, preimplantation genetic testing (PGT) (without disaggregation into PGT subgroups), embryo transfers resulting from frozen–thawed oocytes, fertility preservation procedures (including oocyte, embryo, sperm freezing and ovarian tissue cryopreservation) and intrauterine inseminations. The RSD submission, submitted directly to the African Registry using standardized Microsoft Excel® data forms modified from the International Committee for Monitoring Assisted Reproductive Technologies, was available to centres not yet able to submit CBD. Retrospective summary forms did not contain data validation features and captured information on autologous ART and oocyte donation cycles only, as well as some PGT data for 2019. Lastly, the submission of the Nigerian data required a data export from the Society for Assisted Reproductive Technology Clinic Outcome Reporting System to the African Registry. As the data bridge could not be established in time for this report, only the number of procedures conducted by Nigerian ART centres could be included (TABLE 1A and TABLE 1B).

Retrospective summary data were evaluated for mathematical correctness, and errors were resolved to the extent possible. To facilitate the reporting of collective regional results, CBD were converted into summary format and pooled with the RSD. In addition, findings from CBD only are also presented, providing further details pertaining to the practices and outcomes of ART in our region. All data presented are pooled CBD and RSD, unless otherwise indicated.

Because of an established agreement between centres and countries, outcome data are presented as summary data for Africa, without disclosing specific results by country, centres, or both. Utilization of ART was calculated as previously reported by ICMART (*Dyer et al., 2020b*). Briefly, utilization of ART was calculated as the known or estimated number of ART cycles per million population per annum, with the degree of confidence reported in four categories based on the rate of reporting, e.g. number of ART procedures submitted to a registry divided by all procedures known or estimated to have been conducted in a country or region, depending on best-available data. The categories include the following: ART utilization (rate of reporting ≥95%); ART utilization estimated with high confidence (rate of reporting 66–94%); ART utilization estimated with moderate confidence (rate of reporting 34–65%); and non-estimated utilization based only on reported cycles (rate of reporting ≤33%). In this fourth category, the number of cycles conducted by participating centres is reported without attempting to extrapolate this number to a national level. For the calculation of fresh clinical pregnancy rates (CPR) and delivery rates per aspiration, total cryopreservation cycles were excluded from the denominator. As it is established that elective and non-elective single and dual embryo transfers are different entities that are associated with different outcomes (*Zegers-Hochschild et al., 2022*), cycle-based data were disaggregated by number as well as type of embryos transferred in the analysis of effectiveness in autologous cycles.

As deliveries remain poorly reported and are not yet a representative marker of effectiveness in our region, the delivery rates per embryo transfer were analysed based only on centres with 5% of pregnancies or less lost to follow-up, referred to as adjusted delivery rate per embryo transfer in the remainder of this manuscript. To monitor the degree of pregnancy follow-up in our region, the rate of reported deliveries per clinical pregnancies was also calculated as a marker, assuming that low rates are indicative of poor follow-up rather than high rates of early pregnancy losses. Cumulative pregnancy rates were calculated as the sum of all pregnancies after fresh and frozen transfers per annum over the number of aspirations conducted in the same year, recognizing that this is a pseudo marker of cumulative ART success. Collectively, data were analysed and reported descriptively.

The African Network and Registry for Assisted Reproductive Technology adheres to the International Glossary on Infertility and Fertility Care (*Zegers-Hochschild et al., 2017*) and is registered with the Human Research Ethics Committee of the Faculty of Health Sciences, University of Cape Town. Any further relevant approvals were obtained at country level.

RESULTS

Participation, procedures and utilization

Sixty-seven centres from 16 countries reported a total of 43,958 ART procedures conducted in 2018, increasing to 45,185

TABLE 1A NUMBER OF CENTRES, PROCEDURES AND ASSISTED REPRODUCTIVE TECHNOLOGY UTILIZATION, 2018

Country	Total number of centres	Participating centres	Autologous Fresh IVF/ICSI aspirations	Autologous FET transfers	Oocyte donation fresh transfers	Oocyte donation FET transfers	FTO transfers	Fertility preservation procedures	PGT[a] cycles Initiated	Total procedures	ART utilization,[b]
Benin	2	2	81	5	20	0	0	0	0	106	9[c]
Burkina Faso	1	1	93	0	63	0	0	0	0	156	8[c]
Cameroon	2	1	70	0	68	0	0	0	0	138	11[e]
Egypt	103	15	23253	6297	0	0	0	0	5	29550	296[f]
Ethiopia	1	1	254	38	0	0	0	0	0	292	3[c]
Ghana	17	6	212	21	284	10	15	6	0	548	53[e]
Kenya	10	1	52	11	8	3	0	0	0	74	1[f]
Libya	NA	1	443	119	0	0	0	0	0	562	86[f]
Mali	1	1	127	7	0	0	0	0	0	134	7[c]
Mauritius	4	1	126	44	0	0	0	0	0	170	131[f]
Nigeria	70	18	1724	148	1362	133	0	0	0	3367	17[f]
South Africa	21	15	3915	2512	630	696	66	184	124	8003	194[d]
Sudan	12	1	281	35	0	0	5	7	0	328	8[f]
Togo	2	1	140	85	51	30	0	0	0	306	77[e]
Uganda	4	1	63	7	49	0	0	0	0	119	3[f]
Zimbabwe	2	1	87	8	9	1	0	0	0	105	15[e]
Total Africa	252	67	30921	9337	2544	873	86	197	129	43958	50[g]

[a] Preimplantation genetic testing cycles included in fresh IVF and intracytoplasmic sperm injection aspirations.

[b] Calculated as the known or estimated number of assisted reproductive technology cycles per million population per annum.

[c] Utilization reported with certain confidence.

[d] Utilization estimated with high confidence.

[e] Utilization estimated with modest confidence.

[f] Non-estimated utilization based only on reported cycles.

[g] Regional utilization for Africa calculated by excluding utilization in countries with participation rate 33% or less.

ART, assisted reproductive technology; FET, frozen embryo transfer; FTO, frozen–thawed oocyte; ICSI, intracytoplasmic sperm injection; NA, not applicable; PGT, preimplantation genetic testing.

TABLE 1B NUMBER OF CENTRES, PROCEDURES AND ASSISTED REPRODUCTIVE TECHNOLOGY UTILIZATION, 2019

Country	Total number of centres	Participating centres	Autologous fresh IVF/ICSI aspirations	Autologous FET transfers	Oocyte donation fresh transfers	Oocyte donation FET transfers	FTO transfers	Fertility preservation procedures	PGT[a] cycles initiated	Total procedures	ART utilization[b]
Benin	2	1	4	0	2	0	0	0	0	6	1[e]
Burkina Faso	1	1	15	0	8	0	0	0	0	23	1[c]
Cameroon	4	1	69	8	46	0	0	0	0	123	5[f]
Cote d'Ivoire	1	1	89	37	206	123	0	0	0	455	18[c]
Egypt	103	11	17976	5182	0	0	0	0	97	23158	231[f]
Ethiopia	2	1	331	42	0	0	0	0	1	373	7[e]
Ghana	17	5	149	51	141	21	1	3	5	366	12[f]
Kenya	11	1	80	49	1	7	0	0	0	137	3[f]
Libya	NA	2	306	3	0	1	0	0	0	310	46[f]
Mali	1	1	111	19	57	0	0	0	0	187	10[c]
Mauritius	4	1	130	52	0	0	0	0	0	182	143[f]
Nigeria	70	18	1387	549	1168	164	0	0	0	3268	16[f]
South Africa	21	19	4287	2641	578	804	100	253	960	8663	164[d]
Sudan	12	2	17	6	0	0	0	1	0	24	1[f]
Togo	2	1	132	67	38	3	0	2	0	242	60[e]
Tunisia	11	2	5627	1679	0	0	0	0	8	7306	625[f]
Uganda	4	1	148	43	52	16	3	0	0	262	6[f]
Zimbabwe	2	1	82	5	8	5	0	0	0	100	14[e]
Total Africa	268	70	30940	10433	2305	1144	104	259	1071	45185	43[g]

[a] Preimplantation genetic testing cycles included in fresh IVF and intracytoplasmic sperm injection aspirations.

[b] Calculated as the known or estimated number of assisted reproductive technology cycles per million population per annum.

[c] Utilization reported with certain confidence.

[d] Utilization estimated with high confidence.

[e] Utilization estimated with modest confidence.

[f] Non-estimated utilization based only on reported cycles.

[g] Regional utilization for Africa calculated by excluding utilization in countries with participation rate 33% or less.

ART, assisted reproductive technology; FET, frozen embryo transfer; FTO, frozen–thawed oocyte; ICSI, intracytoplasmic sperm injection; NA, not applicable; PGT, preimplantation genetic testing.

ART procedures conducted by 70 centres in 18 countries in 2019. For both years, deliveries were captured through September of the following year. The proportion of centres submitting CBD increased from 58.2% to 64.3%, reporting around 20% of procedures. The number of participating centres and ART procedures by type, country and year with resultant ART utilization are presented in TABLE 1A and TABLE 1B. Throughout the results, tables and figures with the suffix 'A' present data for 2018, whereas the suffix 'B' denotes data from 2019. As in previous years, fresh autologous procedures predominated. Fertilization by ICSI was constant and high (94.3% in 2018; 94.7% in 2019) but with wide country variations (range 0–100%). The rate of autologous FET over all autologous embryo transfers increased from 28.3% in 2018 and 30.4% in 2019 (**Supplementary Figure 1A** and **Supplementary Figure 1B**). The proportion of fresh and frozen oocyte donation cycles remained stable (7.9% in 2018; 7.6% in 2019), with a rate of frozen transfers of 42.0% in both years. According to the CBD, male factor infertility was the primary or secondary indication for ART in 58.0% of autologous cycles, followed by unexplained infertility (31.8%) and tubal factor infertility (25.1%). Endometriosis was the reported indication for ART in only 6.7% of cycles.

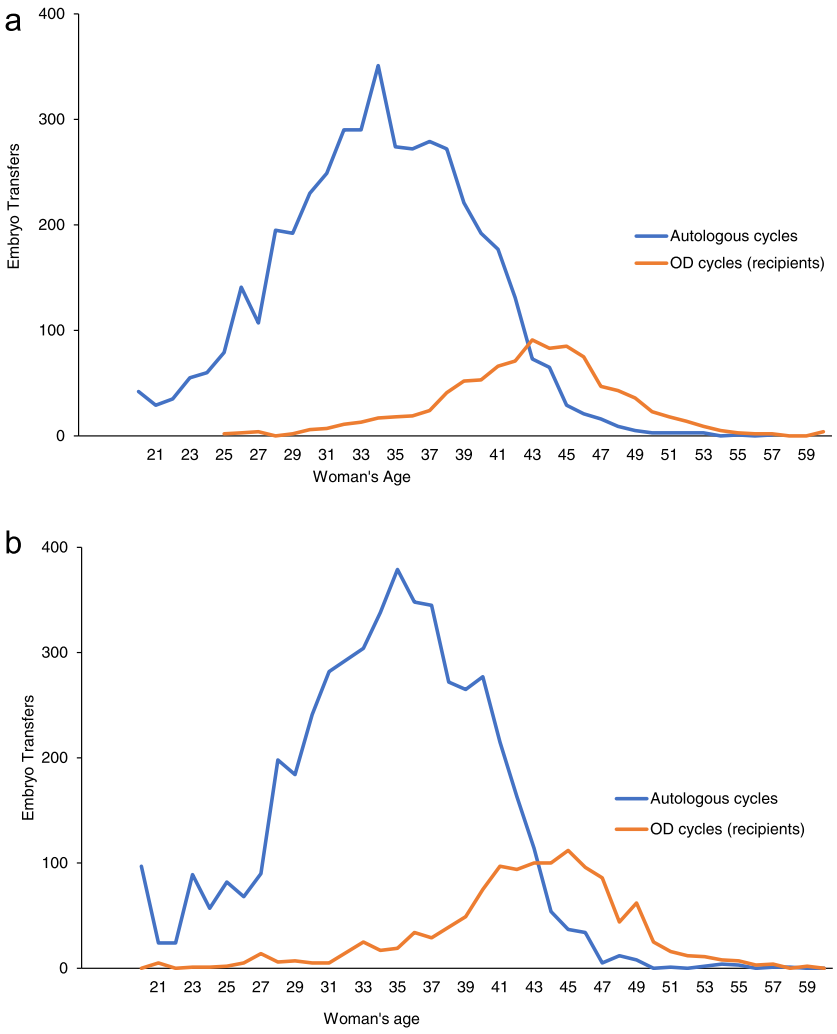

FIGURE 1 Autologous and oocyte donation fresh and frozen embryo transfers: women's age distribution at embryo transfer: (A) 2018; (B) 2019. Cycle-based data only. OD, oocyte donation.

Age

The age of women by age category, procedure and year is presented in **Supplementary Figure 1A** and **Supplementary Figure 1B**. In autologous fresh embryo transfers, a moderate decline in the youngest age category was observed (≤34 years; from 62.4–58.2%), with a concomitant increase in the oldest age category (≥40 years; from 10.5–14.2%). On the basis of CBD only, the mean age of women undergoing fresh autologous embryo transfer, however, remained constant (33.8 years in 2018; 33.9 years in 2019) and similar to the subset of women undergoing autologous embryo transfer after PGT (35.4 years in 2018; 35.5 years in 2019). The age graphs of women undergoing autologous and oocyte donation transfers is presented in FIGURE 1A and FIGURE 1B, in 2018 and 2019, respectively.

Number of embryos transferred

The distribution of number of embryos transferred by type of procedure is presented in FIGURE 2A and FIGURE 2B. In autologous fresh cycles, most cycles (75.8% in 2018; 76.3% in 2019) involved the transfer of two or three embryos, resulting in a mean number of 2.3 and 2.4, respectively; the rate of single embryo transfer (SET) remained constant (15.2% in 2018; 15.1% in 2019) as did the rate of transfers with four or more embryos (9.1% and 8.6%, respectively). In autologous FET cycles, slightly higher rates of SET were observed (17.7% in 2018; 19.7% in 2019), however, with a similar mean number of embryos transferred as in fresh cycles (2.2 in 2018; 2.3 in 2019). After oocyte donation, SET increased from 7.4% to 17.0% in fresh transfers; and from 36.1% to 38.6% in frozen transfers.

Effectiveness by procedure and age

Clinical pregnancies and deliveries stratified by procedure are presented in TABLE 2A and TABLE 2B. In autologous cycles, the CPR after fresh embryo transfer was 42.8% (2018) and 38.4% (2019), both higher compared with autologous FETs (38.3% in 2018; 31.8% in 2019). The adjusted delivery rates per embryo transfer per fresh embryo transfer was 25.2% in 2018, compared with 27.7% in 2019. Overall, the rate of clinical pregnancies with reported deliveries was less than 50% in most categories of ART procedures. The cumulative CPR per autologous aspiration was 45.8% and 40.3% in respective years.

Clinical pregnancy rates stratified by category of age and type of procedure are presented in **Supplementary Figure 2A** and **Supplementary Figure 2B**. As expected, younger age was associated with higher CPRs in autologous cycles but not in oocyte donation fresh embryo transfer

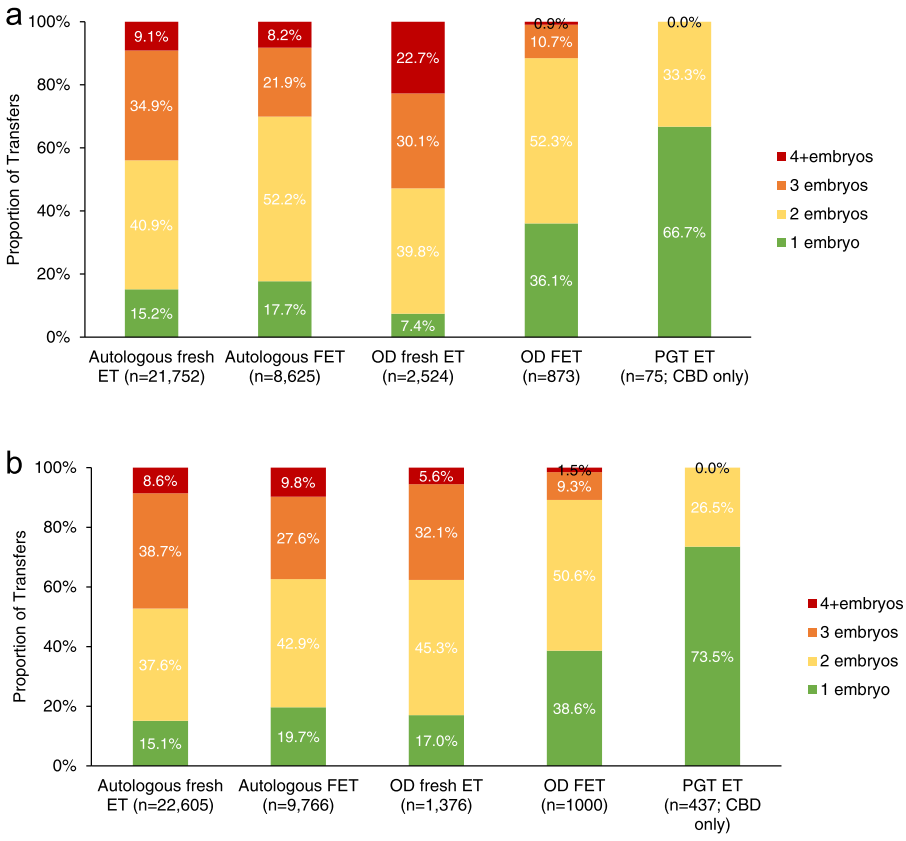

FIGURE 2 Number of embryos transferred by assisted reproductive technology procedure: (A) 2018; (B) 2019. Cycle-base data and retrospective summary data pooled. ET, embryo transfer; FET, frozen embryo transfer; OD, oocyte donation; PGT, preimplantation genetic testing.

TABLE 2A EFFECTIVENESS BY ASSISTED REPRODUCTIVE TECHNOLOGY PROCEDURE, 2018

	Autologous fresh IVF/ICSI	Autologous FET	Fresh embryo transfer after oocyte donation	FET after oocyte donation
Aspirations/thaws, *n*	30921	9488	NA	NA
Transfers, *n*	24793	9332	2544	873
Clinical pregnancies, *n*	10606	3571	893	352
Deliveries, *n*	4260	1904	568	167
CPR/aspiration[a], %	38.4	NA	NA	NA
CPR/embryo transfer, %	42.8	38.3	35.1	40.3
Adjusted delivery rate/embryo transfer,[b], %	25.2	22.0	32.6	32.9
MDR, %	17.9	14.4	38.0	22.2
Cumulative CPR/aspiration,[c],%	45.8	NA	NA	NA
Clinical pregnancy with reported delivery,[d],%	40.2	53.3	63.6	47.4

[a] Calculated as clinical pregnancies/(aspirations less total cryopreservations).

[b] Adjusted delivery rate per embryo transfer based on centres with 5% or less of clinical pregnancies lost to follow-up.

[c] Calculated as all clinical pregnancies from fresh and frozen embryo transfer cycles/aspirations.

[d] Calculated as deliveries/clinical pregnancies (%).

ART, assisted reproductive technology; CPR, clinical pregnancy rate; FET, frozen embryo transfer; ICSI, intracytoplasmic sperm injection; MDR, multiple delivery rate; NA, not applicable; PGT, preimplantaiton genetic testing.

cycles, in which CPRs above 40% were achieved in all age categories of recipients.

Effectiveness by number and type of embryos transferred

The analysis of effectiveness by number and type of embryos transferred could only be undertaken with disaggregated CBD, as RSD lacked the necessary granularity. As results for 2018 and 2019 were for the most part similar, both years were combined with findings presented in TABLE 3. A notable difference between years was the rate of blastocyst transfers, which increased in fresh cycles from 50.8% to 65.7%, and in frozen cycles from 84.3% to 91.3%. In fresh cycles, elective SET (eSET) resulted in a CPR of 38.9%, being higher than non-elective dual embryo transfer (oDET) (30.9%) but lower than elective double embryo transfer (eDET) (51.1%). The multiple delivery rate (MDR), however, was 1.3% after eSET, increasing to 34.4% after eDET. The transfer of three or more embryos provided no further increase in CPRs but introduced an important rise in triplets and higher-order pregnancies. The disaggregation of data also revealed important observations on the type of embryos transferred. In eSET and eDET cycles, the rate of blastocyst transfer was 95.0% and 87.1%, both rates substantially higher compared with all other categories of fresh autologous transfers. Moreover, the CPR after all transfers with cleavage stage embryos was 28.0% versus 44.0% after blastocyst transfers.

In frozen cycles, the rate of SET reached 42.6%, considerably higher compared with fresh SET. Frozen embryo transfer DET carried a higher CPR compared with FET SET (42.2% versus 35.1%), although again associated with a striking difference in MDRs (32.6% versus 0.5%). The transfer of additional embryos did not increase CPRs further but maintained a high MDR (>20%). When comparing FET with fresh embryo transfer in these CBD, the overall CPR after FET was 38.6% compared with 36.9% after fresh embryo transfer.

Multiple deliveries and gestational age at delivery

As seen in TABLE 2A, TABLE 2B and TABLE 3, the MDRs remained constant and high in all categories of ART procedures, with no convincing trend of any decline. Rates were particularly high in fresh oocyte donation cycles (38.0% and 31.3%) (TABLE 2A and TABLE 2B), and in autologous

TABLE 2B EFFECTIVENESS BY ASSISTED REPRODUCTIVE TECHNOLOGY PROCEDURE, 2019

	Autologous Fresh IVF/ICSI	Autologous FET	Fresh embryo transfer after oocyte donation	FET after oocyte donation	PGT[e]
Aspirations/thaws, *n*	29675	10033	NA	NA	1197
Transfers, *n*	22926	9892	1379	1000	607
Clinical pregnancies, *n*	8814	3145	564	400	291
Deliveries, *n*	2910	1394	390	197	115
CPR/aspiration[a],%	33.4	NA	NA	NA	NA
CPR/embryo transfer	38.4	31.8	40.9	40.0	47.9
Adjusted delivery rate/embryo transfer[b]	27.7	27.4	33.3	27.5	NA
MDR	25.5	22.3	31.3	20.3	22.6
Cumulative CPR/aspiration[c]	40.3	NA	NA	NA	NA
Clinical pregnancy with reported delivery[d]	33.0	44.3	69.1	49.3	39.5

[a] Calculated as clinical pregnancies/(aspirations less total cryopreservations).
[b] Adjusted delivery rate per embryo transfer based on centres with 5% or less of clinical pregnancies lost to follow-up.
[c] Calculated as all clinical pregnancies from fresh and frozen embryo transfer cycles/aspirations.
[d] Calculated as deliveries/clinical pregnancies (%).
[e] Autologous and oocyte donation cycles; 2018 and 2019 combined.
ART, assisted reproductive technology; CPR, clinical pregnancy rate; FET, frozen embryo transfer; ICSI, intracytoplasmic sperm injection; MDR, multiple delivery rate; NA, not applicable; PGT, preimplantation genetic testing.

eDET and higher order transfers as outlined above (TABLE 3).

The gestational age by order of gestation after autologous ART and aggregated for years 2018 and 2019 is presented in FIGURE 3. After both fresh and frozen transfers, 79.1% of singletons were born at term. This compared with only 39.3% of twins and 5.7% of higher order multiples. Furthermore, 12.4% of twins and 37.7% of triplets were born very or extremely preterm (<32 weeks' gestation). Gestational age data disaggregated by year and procedure (and including oocyte donation) are presented in **Supplementary Table 1A** and **Supplementary Table 1B**.

Following autologous ART, the perinatal mortality rate for all neonates with

TABLE 3 AUTOLOGOUS IVF AND INTRACYTOPLASMIC SPERM INJECTION: EFFECTIVENESS BY NUMBER OF EMBRYOS TRANSFERRED, 2018 AND 2019

Autologous transfer	All embryo transfers		Transfers with blastocysts		Clinical pregnancies and rate per embryo transfer[a]		Singleton deliveries and rate per all deliveries		Twin deliveries and rate per all deliveries		Triplet (or more) deliveries and rate per all deliveries	
Fresh	***n***	**%**	***n***	**%**	***n***	**%**	***n***	**%**	***n***	**%**	***n***	**%**
oSET	958	15.7	365	38.1	169	17.6	81	97.6	2	2.4	0	0.0
eSET	321	5.3	305	95.0	125	38.9	79	98.8	1	1.3	0	0.0
oDET	1880	30.8	983	52.3	580	30.9	241	82.0	51	17.3	2	0.7
eDET	1548	25.4	1349	87.1	791	51.1	206	65.6	105	33.4	3	1.0
TET	1155	18.9	480	41.6	491	42.5	108	71.5	35	23.2	8	5.3
QET	244	4.0	33	13.5	99	40.6	31	64.6	9	18.8	8	16.7
Total fresh	6106	100.0	3515	57.6	2255	36.9	746	76.9	203	20.9	21	2.2
FET	***n***	**%**	***n***	**%**	***n***	**%**	***n***	**%**	***n***	**%**	***n***	**%**
FET SET	1364	42.6	1316	96.5	479	35.1	188	99.5	1	0.5	0	0.0
FET DET	1569	49.0	1434	91.4	662	42.2	207	67.4	100	32.6	0	0.0
FET TET	225	7.0	93	41.3	81	36.0	10	76.9	3	23.1	0	0.0
FET QET	42	1.3	5	11.9	14	33.3	6	75.0	2	25.0	0	0.0
Total FET	3200	100.0	2848	89.0	1236	38.6	411	79.5	106	20.5	0	0.0

[a] Clinical pregnancy rate calculated per all embryos transferred, i.e. cleavage stage and blastocyst transfers combined.
DET, dual embryo transfer; eDET, elective DET; eSET, elective SET; oDET, non-elective DET; QET, transfer of four or more embryos; SET, single embryo transfer; TET, transfer of three embryos.

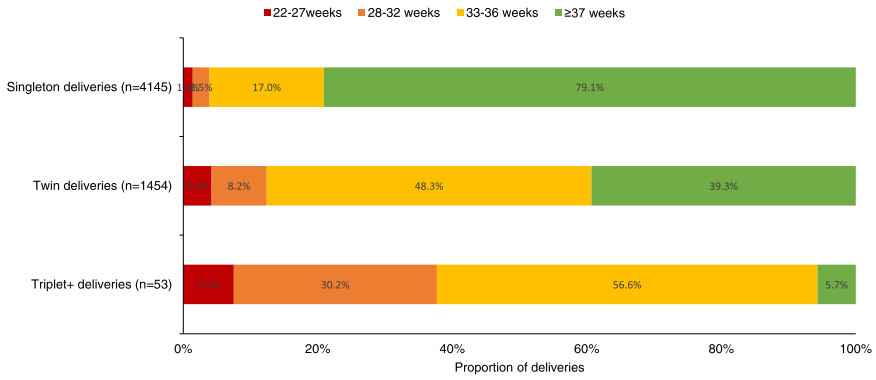

FIGURE 3 **Autologous assisted reproductive technology: gestational age by type of delivery, 2018 and 2019. Cycle-based data and retrospective summary data pooled.**

reported birth outcomes was 27.6‰ for singletons, 68.9‰ for twins, and 194.4‰ for babies born as higher order multiples (**Supplementary Table 2**).

Preimplantation genetic testing

Because few PGT procedures were reported in 2018, data for both years were aggregated and jointly presented in TABLE 2B. Two countries (Egypt and South Africa) reported 607 fresh and frozen embryo transfers after PGT resulting in a CPR per embryo transfer of 47.9% and a MDR of 22.6%. The proportion of clinical pregnancies resulting in a reported delivery was 39.5%. Autologous transfers represented 71.9% of all PGT embryo transfers.

DISCUSSION

This third report from ANARA presents the annual data for the years 2018 and 2019. The number of participating centres increased from 47 centres in 16 countries in 2017 to 70 centres in 18 countries in 2019. Approximately 65% of centres reported CBD, which represented only around 20% of reported procedures, as some large centres are yet to adopt cycle-based reporting. Although the steady growth of ANARA is encouraging, increasing the rate of participation as well as the reporting of CBD are two key objectives. To meet these, we developed an ANARA Registry Data Online course consisting of a 2-week learning module with asynchronous and synchronous learning aimed at biologists, fertility nurses and data managers. The course has been conducted three times since the end of 2021, with good attendance. The development of an advanced course is in process, and we anticipate an important rise in the number of centres reporting CBD based on this intervention.

As in our previous reports, our results indicate low rates of ART utilization and hence access to care in our region. The association between ART utilization and access to care, and the reasons for low ART utilization in our region, have been previously discussed (*Dyer et al., 2020a*; *2020b*). In addition, the index report presents new data on the indication of ART. According to these, male factor was twice as often an indication compared with tubal factor infertility. Although the exact prevalence of both factors remains to be established, they are recognized as the leading causes of infertility in Africa (*Inhorn and Patrizio, 2015*). Our findings, therefore, suggest a possible gender-bias in the utilization of ART in preference of treating male infertility. It will be important to monitor ART utilization to assess the effect of global reproductive health recommendations regarding equitable access to infertility care in general (*Starrs et al., 2018*; *WHO, 2020*) and that of infertility-related new government policies in selected African countries specifically.

An important demographic characteristic was the relatively young age of women. In 2018 and 2019, most women undergoing autologous transfers were under the age of 35 years, with a mean age just below 34 years. As expected, relevant differences in ART effectiveness were observed when stratified by category of age. In contrast, but similarly expected, the age of oocyte donation recipients was not associated with variations in CPR; however, oocyte donation represented less than 10% of ART cycles in both years, similar to the global average (*Chambers et al., 2021*). Compared with other world regions, Africa seems to have the youngest age profile among women undergoing ART. According to findings from our sibling registry in Latin America, the proportion of women aged 34 years or younger undergoing autologous fresh embryo transfers in 2019 was 25.6%, whereas that of women aged 40 years or older was 32.9%, contrasting to 62.4% and 10.5% in this report (*Zegers-Hochschild et al., 2022*). Recent data from Europe reported an age profile between Africa and Latin America, however, with substantial variations at country level (*Wyns et al., 2021*). Africa's age profile must be considered when interpreting ART practices and outcomes in our region, and when comparing these indicators to other world regions. Furthermore, it may be anticipated that Africa will follow a similar trend of delayed childbearing documented in other regions. An important opportunity hence exists to educate patients and the public on the age-related decline in fertility. This is of relevance in our region as oocyte donation is not practised in several countries where Sunni Muslims are predominant residents (*Serour and Serour, 2021*), and as access and cost barriers are unlikely to make fertility preservation a viable option for most people.

The key characteristics of ART practices in 2018 and 2019 in our region were similar to those in the preceding years, namely a preponderance of autologous fresh cycles, a high rate of fertilization by ICSI (94.7%), a gradual increase in the proportion of cryopreservation cycles and an overall low rate of oocyte donation. The high rate of fertilization by ICSI in our region has been recognized and attributed to a fear of fertilization failure in a setting in which ART is predominantly privately funded (*Dyer et al., 2020*). The transfer of multiple embryos remained the norm, reflected in a mean number of embryos transferred of 2.4 (2019) in autologous fresh cycles, with no evidence of decline since 2013 (*Dyer et al., 2019*). The mean number of embryos transferred was two or more in other ART procedures except PGT (mean 1.3 embryos per embryo transfer).

The practice of transferring multiple embryos is driven by the desire to maximize the immediate chance of pregnancy and the assumption that this chance increases proportionally to the number of embryos transferred. It is augmented by the fact that many couples may only be able to afford a single ART

cycle, as most ART treatment is privately funded, as well as an ongoing perception that multiple pregnancy is not necessarily an undesirable outcome (*Dyer et al., 2020a*; *Zegers Hochschild et al., 2022*). A recognized intervention that results in the transfer of fewer embryos is the widening of equitable access to ART without undue financial risks to households (*Chambers et al., 2020*). Another intervention is to strengthen the scientific evidence base through locally generated and applicable real-life registry data, as provided in this manuscript. To this effect, the most important key messages of this manuscript are as follows: first, that eSET is highly effective and safe; and second, that multiple gestation results in high rates of prematurity and perinatal mortality, with 60.7% of twins and 94.3% of higher order multiples born preterm. Moreover, although our documented perinatal mortality rate must be interpreted in the context of relatively small numbers, a profound difference between singletons and multiples was observed. Multiple gestation is beyond doubt a leading risk factor for adverse outcomes in mothers and offspring, a risk of particular concern in our region, as sub-Saharan Africa, together with South Asia, carries the highest burden of obstetric morbidity and mortality globally (*Aftab et al., 2021*). A recent multi-national cohort study in these two regions documented that multiple gestation carried the single highest odds ratio for maternal death, intra-partum stillbirths and neonatal deaths among all socio-economic and health variables analysed (*Aftab et al., 2021*). These findings are in keeping with a study that evaluated mortality in children under the age of 5 years in sub-Saharan Africa. The survey, which included records on 370,237 children under the age of 5 years derived from Demographic Health Survey data between 2010 and 2018, documented 27,221 deaths (7.35%). Children born as multiples represented 3.7% of the cohort and had 2.7 times the risk of death compared with singletons, a risk surpassed only by children born from birth order of four or more (*Tesfa et al., 2021*). Although ART births represent a small proportion of births in our region, the many substantial benefits of ART should not unintentionally compromise progress towards Sustainable Development Goal 3.2: to end preventable deaths of newborns and children under the age of 5 years; and to reduce neonatal mortality to less than 12/1000 live births and mortality in children under the age of 5 years to 25 out of 1000 live births or less.

When analysing the effectiveness and safety of eSET, and for the sake of reiteration, eSET, which comprised more than 90% blastocyst transfers, resulted in a higher CPR compared with oDET cycles (38.9% versus 30.9%) and a low MDR. Although the CPR after eDET was higher (51.1%), the resultant MDR was 34.4%. The transfer of three or more embryos was of no benefit to CPR, but similarly associated with a high rate of multiples. Despite these excellent results of eSET, it represented only 25.1% of all SET cycles, and only 5.3% of all autologous transfers. Our findings show similar effectiveness but lower uptake of eSET compared with results from the Latin American Registry for 2019. According to these, eSET represented 36.4% of SET cycles and resulted in a CPR of 40.4% with a MDR of 2.0%. This compared with a CPR of 30.4% in oDET and 48.5% in eDET, with a MDR of 17.5% and 25.3%, respectively (*Zegers-Hochschild et al., 2022*). Collectively, these data should give ART centres in Africa as well as Latin America the confidence, based on scientific evidence, to electively transfer a single good quality blastocyst and to counsel patients accordingly, on the risk and consequences of multiple pregnancies.

In this context, the rising proportion of FET was an encouraging finding. Cryopreservation is a prerequisite for the lowering of the rate of multiples without embryo wastage while simultaneously facilitating higher cumulative delivery rates. In oocyte donation cycles, our results documented similar effectiveness (CPR per embryo transfer) between fresh and frozen transfers but substantially lower MDRs after the latter. In autologous cycles, we observed discrepant findings between the collective data (RSD and CBD combined) and the CBD: in the former, fresh embryo transfer was associated with a higher CPR per embryo transfer compared with FET, whereas, in the latter, the reverse applied. Although the possible underlying reasons for this discrepancy cannot be ascertained from our data, they are likely to include biases in embryo selection as well as the fact that the practice of cryopreservation is still maturing in our region. With time, greater practice will result in increasing effectiveness, whereas the reverse also applies; for example, documenting rising effectiveness of fresh eSET and FET will encourage greater use of cryopreservation. Regional and local scientific meetings should hence continue to build knowledge and capabilities in cryopreservation, moving hand in hand with national and regional registry data monitoring. Strengthening the foundations of safer ART practices in this manner should not be neglected in favour of novel innovations, the benefits of which often remain to be established.

This is the first ANARA report to present findings pertaining to PGT. Reported cycles were still low in numbers and submitted by two countries only. Although our data were not disaggregated by type of PGT, it is assumed that most cycles represented PGT for aneuploidy (personal communication). As expected, the CPR per embryo transfer was higher compared with non-PGT transfers; however, cumulative live births would have been the more appropriate indicator for the evaluation of PGT effectiveness (*Kemper et al., 2020*). This is because PGT for aneuploidy can improve embryo selection but not the inherent quality of the embryo pool. Although our registry software has the capability to track cumulative live births, we have not yet collected cycles based on patient identification. Of concern, the MDR was similarly high as in non-PGT cycles, and the outcomes of pregnancies received no better surveillance. Evidently, more data over a longer period are required to derive more robust observations.

This paper shares the same strengths and limitations observed and discussed in previous reports (*Dyer et al., 2020*). Briefly, the main limitations include the fact that the findings are representative of participating centres and cannot be extrapolated to other ART centres in the region; the heterogeneous nature of our data, which comprise both retrospective summary and cycle-based reporting; the fact that data are checked for logical and mathematical correctness but without further validation; and the low proportion of pregnancies that are followed up to delivery. Conversely, the observation that most centres have adopted cycle-based reporting, the growing albeit non-linear increase in participating centres, and the fact that the African ART Registry provides the best available real-life scientific data pertaining to ART practices, effectiveness and outcomes in our region are the main strengths of this paper. Further strengths include the expertise of the authors in national, regional and global ART monitoring; the additional capabilities derived from the South-South cooperation

with the Latin American Registry, which includes but is not limited to the ongoing evolution of our registry software, and the triangular cooperation with ICMART.

In conclusion, Africa is renowned for a rich tradition of storytelling. A tradition in which families and communities come together, sharing experiences to build upon their collective knowledge. Lessons are learnt and life is adapted for the upliftment and betterment of all. This third report builds on previous data from ANARA to tell the story of ART practice in Africa. Our high rate of multiple pregnancies with poorer neonatal outcomes is an important lesson to be learnt from the prevailing practice of transferring multiple embryos into a cohort of relatively young women. A move towards the elective transfer of a single good-quality blastocyst, coupled with the cryopreservation of surplus embryo, is a valuable strategy to improve the safety of ART without compromising effectiveness. It is time for all stakeholders to listen to these stories that the data are telling, learn from their lessons and adapt practice for the betterment of all.

DATA AVAILABILITY

Data will be made available on request.

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SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.rbmo.2023.01.014.

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