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CASE REPORT

Improving access to ART in low-income settings through knowledge transfer: a case study from Zimbabwe

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ABSTRACT: It may be assumed that infertility is not a problem in resource-poor areas where fertility rates are high. However, evidence overwhelmingly shows that childlessness is highly stigmatized in these settings and that women who are unable to bear children suffer significant social and psychological consequences. The World Health Organization has recommended that infertility be considered a global health problem and stated the need for ART to be adapted to low-resource settings. This paper describes a model for improving access to ART in low-resource settings. Experienced ART health professionals from Australia and Italy representing medical science, embryology, nursing and counselling used knowledge transfer to support a clinician, a laboratory scientist and a nurse to establish an ART service in Harare, Zimbabwe. Support and mentorship provided between October 2016 and December 2017 included: hosting the clinician and the embryologist for the new service in established ART clinics for short periods and providing them with dedicated mentorship and training during their stay; funding an experienced embryologist to travel to Zimbabwe (three times) to oversee the setting up of the lab and provide hands-on embryology training; funding a scientist and a nurse to travel to Zimbabwe to troubleshoot and establish protocols for record keeping and psychosocial care; and contributing approximately AUD $15,000 to the purchase of some equipment. By 31 March 2018, the team at IVF Zimbabwe had performed 166 ART procedures, which at time of writing had resulted in 16 births and 4 ongoing pregnancies. This case study demonstrates that with mentorship and modest financial support from ART experts from high-income settings, health professionals in low-income settings can deliver affordable ART with successful outcomes.

Key words: infertility / ART / knowledge transfer / low-cost IVF / low-income country / ART access / Zimbabwe

Introduction

For most people, parenthood is a desired and expected part of adult identity and unfulfilled parenthood aspirations have far reaching social and psychological consequences for women and men. Infertility, the inability to conceive after a year or more of regular unprotected sexual intercourse (Zegers-Hochschild *et al.*, 2017), affects people worldwide. Based on population surveys it is estimated that the international prevalence of infertility is 9% on average (Boivin *et al.*, 2007) but much higher prevalence rates are reported in parts of sub-Saharan Africa (Inhorn and Patrizio, 2015). The World Health Organization has recommended that infertility be considered a global health problem and stated the need for ART to be adapted to low-resource settings (Daar and Merali, 2002; van der Poel, 2012).

While the social and psychological effects of infertility for people in high-income settings have been investigated extensively over the last three decades (Greil, 1997; Greil *et al.*, 2010; Fisher and Hammarberg, 2012), evidence about the consequences of infertility for women and men in low-income settings is more recent. Existing evidence from sub-Saharan Africa indicates that: domestic violence, union dissolutions and sexual dysfunction are more common among infertile than fertile women (Dhont *et al.*, 2011); women's treatment

WHAT DOES THIS MEAN FOR PATIENTS?

In places where most women have many children infertility may not be seen as a problem. But childlessness causes enormous pain and suffering wherever it occurs. Around the world, about one in ten couples experience infertility. In high-income countries, they can often be helped through assisted reproductive technology (ART). But in poorer countries, there are very few ART services and where there are clinics, the cost of treatment is so high that only the wealthiest can afford it. In sub-Saharan Africa access to ART treatment is particularly limited. This is partly because there is no ART expertise in most sub-Saharan countries.

This paper describes a partnership to improve access to ART in Zimbabwe. A team of health professionals from Harare, the capital of Zimbabwe, approached people with ART expertise in Australia and Italy asking them to mentor and train them in all aspects of ART.

By the end of March 2018, the team at IVF Zimbabwe had performed 166 ART procedures which, at time of writing, had resulted in 16 births and 4 ongoing pregnancies. The success rate increased over time from 6% for the first 50 stimulations (~1 pregnancy for every 17 stimulations) to 21% for the most recent 33 stimulations (about one pregnancy for every five stimulations). To avoid complications, mild stimulation protocols are used and no more than two embryos are transferred. The cost of treatment is kept as low as possible and for every eight fee-paying patients, two are treated for free.

We have shown that with mentorship and modest financial support from ART experts from high-income countries, health professionals in low-income countries can deliver affordable ART with successful outcomes.

in the community, their self-respect and understanding of womanhood depend on motherhood (Hollos *et al.*, 2009); women face greater social consequences than male partners for fertility problems (Fledderjohann, 2012); infertile women are excluded from certain social activities and traditional ceremonies (Gerrits, 1997); infertile men blame their wives for their childlessness (Folkvord *et al.*, 2005); infertile men also suffer stigmatization, verbal abuse and loss of social status (Dyer *et al.*, 2004) and poor couples often suffer catastrophic financial hardship in order to pay for infertility treatment (Dyer and Patel, 2012; Dyer *et al.*, 2013).

Most women with infertility live in the developing world and have limited access to diagnostic tests or treatment and, often, no access to ART (Fisher, 2009). In most sub-Saharan countries access to ART is either non-existent or very limited and where it is available, it is only affordable for the wealthiest (Hammarberg and Kirkman, 2013; Asemota and Klatsky, 2015; Inhorn and Patrizio, 2015; Botha *et al.*, 2018). Some of the identified difficulties in establishing and delivering ART services in the sub-Saharan region include the lack of trained embryologists, cultural and religious ambivalence about what is morally acceptable in the context of ART, the economic interests of clinic directors and dependence on international supply chains (Gerrits, 2016; Hörbst, 2016).

In the last decade, the plight of infertile women and men in low-income-settings has attracted increased attention by clinicians and academics with an interest in infertility care and a number of strategies to address it and improve access to ART have been suggested. Inhorn and Patrizio (2015) propose three directions for research and interventions: to address the preventable causes of infertility, provide support and alternatives for the infertile, and encourage new low-cost IVF initiatives. Gerrits (2012) suggests that innovative approaches, including the development of new types of partnerships (public-private, transnational, outsourcing components of treatments), exploring existing insurance mechanisms as well as alternative ways of health financing, are needed to improve access. She also advocates the development of low cost and simplified ART procedures. Asemota and Klatsky (2015) describe a three-level model for integrating infertility care into reproductive healthcare. In this model, village healthcare workers are trained to provide sexual and reproductive health education to reduce infertility at community level, midwives and health officers deliver affordable diagnostic test at district level, and specialist physicians provide ART using simplified, low-cost systems in regional referral centers.

Mechanisms for making ART more affordable and accessible have also been proposed. They include having donors from high-income countries contribute to the cost of establishing ART clinics (Cooke *et al.*, 2008) and enroling experts in reproductive medicine from high-income countries to provide training for local health professionals in all aspects of ART (Hammarberg and Kirkman, 2013). Other suggested strategies to reduce costs are to simplify the diagnostic procedures and modify the ovarian stimulation protocols (Teoh and Maheshwari, 2014) and to use basic IVF culture systems (Van Blerkom *et al.*, 2014). A multidisciplinary approach to assist developing countries in integrating infertility services into existing family planning and maternal health services is also recommended (Ombelet, 2014).

In response to the idea of ART experts from high-income countries training peers in low-income settings (Hammarberg and Kirkman, 2013), a collaboration was formed between health professionals from high- and low-income countries to establish an ART clinic in Harare, the capital of Zimbabwe. This paper describes the steps taken and the outcomes to date.

Case report

Zimbabwe is a sub-Saharan low-income country with a population of ~14.5 million of whom around 1.5 million live in the capital Harare. According to a report published in 2010 by the International Federation of Fertility Societies, Zimbabwe had one ART clinic in 2007 (Jones *et al.*, 2010). This clinic was established in the 1980s by a gynaecologist and an embryologist and was located at The Avenues Clinic, a private hospital in Harare, but ceased its operations in 2000 due to the political unrest and economic volatility in Zimbabwe at that time.

In 2015, as conditions in Zimbabwe improved, the possibility of re-opening the clinic was canvassed and a team of potential collaborators from Zimbabwe was identified by the retired gynaecologist and embryologist who started the original programme. It included an obstetrician/gynaecologist, a laboratory scientist, and a nurse none of

whom had ART experience. However, the gynaecologist had an existing practice where he was providing infertility care including diagnostic tests, ovulation induction and artificial insemination and the nurse had been involved in infertility care for many years and was aware of the psychosocial needs of infertile couples. The laboratory scientist had previous experience in tissue culture but needed specific embryology training. The gynaecologist and laboratory scientist received initial ART training at the Orange Free State Medical School in Bloemfontein, South Africa. They began treating patients in basic facilities at The Avenues Hospital in Harare in 2015. In mid-2016, the team in Zimbabwe approached ART experts in Australia to explore their willingness to provide mentorship and contribute to their continued training. The experts from Australia included a reproductive biologist, an embryologist, a practicing clinician and a nurse with counselling experience. An embryologist from Italy subsequently joined the team of mentors. Together the mentors organised a multi-stranded training and support programme with the following components:

- October 2016: the Australian embryologists spent 2 weeks in Harare trouble shooting the laboratory and training the Zimbabwean embryologist.
- February 2017: the Zimbabwean gynaecologist spent 4 weeks in Melbourne, Australia where he was mentored in the clinical aspects of ART by the Australian clinician at the Royal Women's Hospital. The mentoring reproductive biologist and nurse also provided advice relating to ways to minimise the cost of ART to make treatment accessible to more people and training in the psychosocial aspects of ART, patient-centred care and record keeping.
- March 2017: the Australian embryologist spent 2 weeks in the laboratory in Harare to fine-tune equipment to ensure optimal functioning and supervise and instruct the Zimbabwean embryologist on ICSI and embryo freezing techniques.
- April 2017: three of the Australian mentors had several meetings with the Zimbabwean team in Harare to troubleshoot and give direction and suggest solutions to problems that the team had encountered in their practice. The first baby born as a result of treatment at IVF Zimbabwe was born during this visit (at 29 weeks gestation but in good health).
- July 2017: the Zimbabwean embryologist spent 2 weeks in the laboratory at SISMER (a private ART centre) in Bologna, Italy where he was mentored by the Italian embryologist and her colleagues.
- November 2017: as part of quality assurance, the clinic sought and was approved for membership of the African Network and Registry for Assisted Reproductive Technology (ANARA, http://anara-africa.com/), a research network and a platform for communication and information sharing of the practice and outcomes of ART in Africa. They provide their data to the registry arm of ANARA, which collects and disseminates data on the availability, effectiveness and safety of ART in Africa.
- November 2017: the mentors purchased a benchtop incubator from a supplier in Brazil. It was shipped to Harare and arrived in December.
- December 2017: the Australian embryologist returned to the laboratory in Harare for 2 weeks to provide further support and mentorship, and help install the new incubator.

Some difficulties were encountered during the establishment of the clinic. This included securing the visa for the gynaecologist to travel to Australia. After multiple applications and supporting letters from the hospital in Melbourne, a visa was eventually granted after significant delay. Also, as there were no trained embryologists in Zimbabwe, the laboratory scientist had to undergo significant training before having the necessary skills to manage the laboratory. Lastly, the lack of locally available equipment, including ICSI micromanipulators, posed challenges. After hiring an ICSI micromanipulator from a tobacco research project, a good second-hand micromanipulator was purchased from California, USA. Ongoing issues include problems associated with access to a busy general operating theatre at The Avenues Hospital. This means that oocyte recovery can only begin after 6 pm and consequently that the embryology and ICSI needs to be performed very late in the evening.

The cost of treatment is kept to a minimum to make it more accessible. For their first treatment cycle, patients pay USD 3500, which covers hospital stay, medication, and gynaecologist and embryologist fees. Patients who have a failed first cycle only pay for drugs and laboratory consumables (USD 1000–USD 2000) if they return for a second cycle and in some cases, a second cycle is offered for free. For every eight fee-paying patients, two patients are treated *pro bono*.

The collaboration is based on the mutually agreed values of delivering safe and affordable ART. Hyperstimulation and multiple pregnancy are the greatest risks of ART, particularly in a low-income setting where they can be difficult to manage. To avoid these adverse outcomes, mild stimulation protocols are used and no more than two embryos are transferred. To date, no major complication has been recorded.

IVF and ICSI are used to enable fertilization, embryos are transferred on Days 2–5 depending on the patient's availability and excess embryos are cryopreserved by vitrification. Patients are generally less than 38 years of age and egg donation is practiced with older infertile women. Occasionally-sperm donation is used for severe male infertility. Sperm and egg donors are recruited by the centre. They are counselled about the implications of being a donor and then, if they decide to proceed, they are screened for HIV, hepatitis A, B and C, syphilis, herpes, cytomegalovirus and toxoplasmosis. Donors also complete a questionnaire about their medical history and sign a consent form. They are offered modest reimbursement to cover the cost of transport and loss of income.

The centre also facilitates egg sharing, where young women who have more than five eggs can share them with women who are unable to produce eggs. In these cases, the recipient pays for the donor's treatment. This practice is established in the UK and benefits both donors and recipients (Bracewell-Milnes *et al.*, 2018).

The age range of women treated to date is 25–46 years. Patients over the age of 40 years are encouraged to use donated eggs, and this has so far resulted in four live births. The most common indications for ART are male factor subfertility followed by tubal disease. African women with subfertility have a high prevalence of fibroids. Myomectomy is recommended and offered to women with submucosal fibroids distorting the endometrial lining, fibroids causing symptoms such as heavy menstrual bleeding or large fibroids which make transvaginal access to the ovaries difficult. While Ashermann syndrome is common in many sub-Saharan countries, the incidence in Zimbabwe has declined since manual vacuum aspiration and antibiotic prophylaxis was introduced as best clinical practice for miscarriage.

By the end of March 2018, the team at IVF Zimbabwe had performed 166 ART procedures on 122 women, including IVF and ICSI with own and donor eggs and/or donor sperm, and embryo freezing and thawing. At time of writing (31 August 2018), these had resulted

Table I ART procedures at IVF Zimbabwe to 31 March 2018 and outcomes to 31 August 2018

Stimulations	Procedures	hCG detected	Clinical pregnancy	Currently pregnant	Live birth	LBR per stimulation %[a]
1–50	50 IVF/ICSI	8	2	0	2	3/50, 6%
	+3 FET	2	1	1	0	
51–101	50 IVF/ICSI	15	9	0	9	10/50, 20%
	+20 FET	3	2	0	1	
102–135	33 IVF/ICSI	12	10	3	4	7/33, 21%
	+10 FET	1	1	0	0	

FET: frozen embryo transfer, LBR: live birth rate.
[a]Presuming those pregnant at time of writing have a live birth.

in 25 ultrasound verified clinical pregnancies. Of these, 4 are still ongoing and 16 have resulted in live births. Table I shows the outcomes, and also demonstrates how success rates have improved between the first 50 stimulations and the most recent 33 stimulations. ART pregnancies are considered high-risk and are managed by obstetricians in a tertiary hospital.

Egg collections and embryo transfers are currently carried out in general operating theatres at The Avenues Hospital and an adjacent space is used for the laboratory. Conditions in both theatre and laboratory are suboptimal and likely to impact on success rates. Furthermore, the lack of access to the theatre means that much laboratory work must be carried out after-hours. To improve working conditions and treatment outcomes, the team has taken a mortgage and purchased a building close to the hospital which will be fitted to accommodate consulting rooms, an andrology and biochemistry laboratory, theatre and IVF laboratory. This will significantly reduce the cost for patients as the hospital currently charges a USD 600 admission fee for egg collection and embryo transfer and is unwilling to waive this for the patients who are treated *pro bono*. The new clinic is expected to be completed in December 2018.

All collaborators on this project have provided their time *pro bono*. The financial cost to date of the knowledge transfer is approximately USD 42,000 (cost of all travel, accommodation, and the incubator), most of which was donated by the mentors.

Discussion

As this is a case study from Zimbabwe, it may not be possible to replicate exactly in another location, but it demonstrates the feasibility of knowledge transfer from high- to low-income settings. It shows that with dedicated and co-ordinated mentorship and modest financial support from ART experts in high-income settings, health professionals in low-income settings can deliver safe and affordable ART with successful outcomes. However, it is acknowledged that establishing a similar collaboration may be more difficult in places where there are existing clinics or where there are no interested local health professionals.

We believe that the personal connections that were established between the mentors and the members of the team in Zimbabwe contributed to the successful outcome of the collaboration. In addition to the face-to-face encounters, which were all very productive and gratifying, all mentors continue to offer prompt advice when contacted about clinical or laboratory problems. In return, mentors have benefited from improved understanding of conditions in low-income settings which has triggered thinking about how cost of ART can be reduced. These insights can be used to develop low-cost alternatives and improve access to ART in high-income countries where the cost often is prohibitive for people on lower incomes.

In our view, the kind of knowledge transfer described in this paper is rewarding for all involved. We, the mentors, plan to continue to support the team in Zimbabwe in the hope that they in turn will mentor others to ultimately make ART more accessible for people in the region. Ensuring support from local politicians, policy makers, healthcare providers and any existing patient organizations may increase the chance of similar initiatives being successful in other African countries. However, to significantly improve access to ART in Africa, a global project with support of local governments and healthcare providers, and with international financial support, is urgently needed.

Authors' roles

K.H. drafted the manuscript. All other authors contributed to and critically reviewed the manuscript and approved the final version.

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Conflict of interest

None of the authors declare a conflict of interest.

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