Access to Infertility Care in the Developing World: The Family Promotion Gap

Obehi A. Asemota, MD[1] Peter Klatsky, MD, MPH[1]

[1] Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, The Albert Einstein College of Medicine, Bronx, New York

Address for correspondence Peter Klatsky, MD, MPH, Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Albert Einstein College of Medicine, 1300 Morris Park Avenue, Mazer 621, Bronx, NY 10461 (e-mail: pklatsky@gmail.com).

Semin Reprod Med 2015;33:17–22

Abstract

Infertility in resource-poor settings is an overlooked global health problem. Although scarce health care resources must be deployed thoughtfully, prioritization of resources may be different for recipient and donor countries, the latter of whom focus on maternal health care, prevention, and family planning. For women and couples with involuntary childlessness, the negative psychosocial, sociocultural, and economic consequences in low-income countries are severe, possibly more so than in most Western societies. Despite the local importance of infertility, few resources are committed to help advance infertility care in regions like sub-Saharan Africa. The worldwide prevalence of infertility is remarkably similar across low-, middle-, and high-income countries. The World Health Organization (WHO) recognizes infertility as a global health problem and established universal access to reproductive health care as one of the United Nation's Millennium Developmental Goals for 2015. Currently, access to infertility care is varied and is usually only attainable by the very wealthy in low-income countries. We provide an overview on the current state of access to infertility care in low-income countries such as in sub-Saharan Africa and a rationale for providing comprehensive reproductive care and possible solutions for providing cost-effective infertility services in these settings.

Keywords

- infertility
- resource-poor setting
- reproductive health

Infertility, the inability to conceive after a year or more of regular unprotected sexual intercourse, affects approximately 9% of couples in developing countries. It affects over 72 million people worldwide, with 40 million actively seeking treatment.[1] In urban centers within sub-Saharan Africa, secondary infertility prevalence rates of 30 to 40% are reported, suggesting a disproportionate effect on people in the developing world.[2] There is also evidence that the infertility rates in low-income countries may be underestimated due to inherent limitations in population-based surveys that are used to estimate infertility prevalence rates.[3] Thus, infertility may be an even more pervasive global health problem than is generally acknowledged.

Individuals or couples living with infertility in resource-poor settings may encounter negative psychosocial, sociocultural, and economic burdens. However, infertility is rarely perceived as a major health problem because of high average fertility rates and large family sizes in sub-Saharan Africa.[4] Therefore, limited health care resources are focused on maternal health care, prevention, and family planning. The term "family planning" has become euphemistic for restricting population growth rather than encouraging or promoting planned procreation.[5] The World Health Organization (WHO) has recommended that infertility be considered a global health problem and has encouraged adaptation of assisted reproductive technologies (ARTs) for resource-poor countries; stating, "research should be directed towards finding effective, low-cost solutions to infertility and this exploration should extend to ART."[3] This article provides an overview on the current state of infertility in developing nations and a rationale for providing access to infertility care and suggests cost-effective services that could manage the often ignored global health problem of infertility in resource-poor settings.

Issue Theme Global Women's Health: Challenges and Opportunities; Guest Editor, Eli Y. Adashi, MD, MS, MA (ad eundem), CPE, FACOG

DOI http://dx.doi.org/10.1055/s-0034-1395274.
ISSN 1526-8004.

Infertility Is a Global Health Care Problem

In recent years, family planning and access to contraception have emerged as primary reproductive health and development priorities. Increasingly, contraception and access to reproductive health care are promoted to reduce maternal mortality and combat global poverty. While these are undoubtedly critical public health goals, they can overshadow a paradoxical need for infertility services for couples living in many low-income countries. In many countries with large segments of the population living in subsistence-based agricultural communities, children are not only a personal blessing, but an economic and social requirement. A review of Demographic and Health Surveys (DHS) of 190 countries suggested that the prevalence of global infertility (often cited as 9%) may be an underestimation and that childlessness in resource-poor countries is more common than what is generally cited.[1] A similar review of DHS data from 47 developing countries estimated that more than 186 million married women of reproductive age had primary or secondary infertility.[6] Unfortunately, in most of these communities, there is paucity of demographic or epidemiologic information regarding age, parity, or physiologic causes of infertility.[1]

In 1995, The United Nations International Conference on Population and Development declared that all individuals should have the right to reproduce if and when they choose; however, little is done when a couple is unable to conceive and adoption is culturally restricted.[7] Children are regarded as part of an extended family even if their parents die, and giving them up for adoption may be considered shameful.[7] The most effective and rights-respecting solution to population growth is to improve education for women and increase access to comprehensive reproductive health services; both of these strategies are associated with lower fertility rates.[8]

Infertility in sub-Saharan Africa is one of the leading drivers for women to access gynecology consultants. In Nigeria, the most common reason for which women presented for gynecology visits was to request assistance with conceiving or complaints of infertility.[5] Similarly, in Kenya, a cross-sectional online survey of 188 obstetricians and gynecologists revealed that 26% of new gynecologist consults were dedicated to assistance with infertility.[9] More commonly, however, most couples lack access to licensed physicians offering infertility services and may instead seek help outside of the formal health system either from traditional healers whose treatments are less regulated or evidence based, than from conventional services.

Current Access to Infertility Care

Despite the expense, patients will go to great lengths and assume enormous financial burdens to obtain help with infertility. Unfortunately, some leading causes of infertility, such as tubal occlusion and severe oligospermia, require access to in vitro fertilization or related ART services. In most low-income countries, such services are available only in the private sector where the cost of such services can exceed half of an average individuals' annual income, making them inaccessible, except to the very wealthy.[10,11] In Kenya, high costs of treatments, limited local services, and modest disposable income of patients in the community have been identified as major barriers to ART services.[9] Surveys of infertile women have found that they were willing to risk financial security to access infertility treatments.[12] Such surveys, validated by a prospective observational study in South Africa, found that 22% of couples accessing ART incurred catastrophic expenditures, defined as out-of-pocket payments of greater than 40% of annual nonfood expenditures.[13] This strong desire to conceive places infertile patients at risk of financial exploitation and treatment with unregulated and potentially harmful practices.[14]

Some referral clinics try to serve local populations but often lack sufficient training and may attempt procedures whose effectiveness is inadequately demonstrated and which could be potentially harmful. One approach when ART is not available is hydrotubation, where a solution containing antibiotics and steroids is infused through the cervix in an attempt to "open" blocked fallopian tubes.[15] The past decade has seen an increase in the number of private ART clinics in developing countries, despite serving a small proportion of the population.[9] Unfortunately, there has not been a corresponding growth in regulatory oversight and systems or national or professional organizations to provide this oversight.

Consequences of Infertility in Low-Income Countries

Couples with infertility in resource-poor settings often face social stigmatization, may be ostracized, and publically isolated.[16–19] Childless women often suffer physical abuse, and in more extreme cases may commit suicide.[20] Domestic violence and dissolution of marriage occur significantly more often among the infertile couples compared with couples in fecund relationships.[21] In Andhra Pradesh, India, approximately 70% of women with infertility report experiencing physical violence as a result.[7] Childless couples also face economic hardship as many families in developing countries depend on their offspring for economic survival.[3] In addition, these couples feel a deeper sense of guilt, shame, and worthlessness than do infertile couples in wealthier, Western societies with better access to care.[20,22]

Women, in particular, face economic deprivation, isolation, risk of polygamy, and domestic violence.[9] In Nigeria, nearly half of infertile women have been diagnosed with depression.[23] South African women report intense emotions such as anger, profound sadness, bitterness, loneliness, desperation, and suicidal ideation.[24] While the social burden falls disproportionately on women, infertile men are not excluded and may not be valued as adults by their communities if they are unable to have a child.[25] Such social trauma is often exacerbated by inadequate community knowledge of reproductive physiology and myths regarding the causes of infertility.[19] In some cultures, community perceptions espouse that God or their ancestors are punishing infertile couples or that evil spirits are the cause of infertility.[10] In Pakistan, a

recent survey involving 445 adults revealed that only 25% of participants could accurately identify causes of infertility, while over half of participants incorrectly assumed the use of intrauterine devices (IUDs) and oral contraceptive pills (OCPs) as a cause of infertility.[26] Such findings highlight not only the tremendous local importance of fertility, but also the lack of reproductive knowledge in many resource-poor countries, where reversible contraceptive devices and medicines may be associated with infertility and the incumbent social consequences and may represent a barrier to effective contraceptive access and utilization programs.

Causes of Infertility in Resource-Poor Countries

Few prospective or large studies have investigated the causes of infertility among women in low-resource countries. Tubal factors are often cited as the primary cause of infertility; however, the primary source of this information is outdated, published in 1985, and only included data from four urban centers in sub-Saharan Africa.[27] The high incidence of tubal disease reported by Cates and colleagues at the African sites was in contrast to the etiologies reported in industrialized countries where tubal factors were attributed to less than a third of cases.[28] The higher reported incidence of tubal occlusion in Africa could result from poor access to reproductive health care, increased prevalence of sexually transmitted infections, unsafe abortions, and postpartum pelvic infections or tuberculosis, all of which can result in tubal disease.[29–31] Few large studies have followed this 1985 report and interventions to promote condom use and prompt identification and treatment of sexually transmitted infections are likely to have decreased the current incidence of tubal infertility. Tubal obstruction is most commonly associated with infectious etiologies and while improvements have been achieved, sexually transmitted infectious diseases remain a concern. The incidence of these diseases is likely higher in urban areas and the high incidence of tubal disease in urban areas may not be seen in rural or remote areas. Few studies have been conducted and reported from rural areas or towns outside of the cities, but Mugisha and colleagues reported no increase in tubal infertility among women in rural western Uganda.[32]

One major cause of infertility in high- and low-income countries alike is anovulation, which has a prevalence rate of around 20% across the globe.[27,33] Anovulation is highly associated with obesity, particularly for women with polycystic ovary syndrome, and can present with other reproductive and health problems such as diabetes, abnormal uterine bleeding, and irregular menstrual cycles.[34,35] The increasing availability of high-caloric Western diets with cheap processed sugars has driven an increase in obesity in low-income countries and may herald a further increase in the incidence of anovulatory infertility, as well as other poor reproductive outcomes.[36] As the low-income countries globalize, the incidence of anovulation in addition to other obesity-related reproductive disorders is likely to increase as well.

Chronic anovulation not only adversely affects fecundity, but patients with oligomenorrhea can develop potentially life-threatening menorrhagia as well. Long-term, unopposed endometrial estrogen exposure can lead to endometrial hyperplasia and adenocarcinoma, which could be prevented by treatment with cyclic progestin or oral contraceptive pills. Rather than amenorrhea or irregular menses, most of these patients will present with a complaint of infertility. Lack of training in these issues represents a missed opportunity to prevent hyperplasia, menorrhagia, or to encourage lifestyle modifications that reduce the risk of developing metabolic syndrome.

Although male factors such as decreased concentration, poor motility, and ejaculatory dysfunction contribute 30 to 40% of all cases of infertility, this etiology is often underappreciated and rarely acknowledged in areas without access to training and community education. As a result, women bear the burden and blame for couples' inability to conceive.[22,37,38] In contrast to this dogma, a pilot study in rural Uganda revealed male factors, such as azoospermia or severe oligospermia, in a third of couples who underwent semen analyses.[32]

Solutions

We propose a practice model to integrate infertility care into the reproductive health package for low-income and resource-poor settings through local health care providers, district hospitals, and national referral centers (►**Table 1**).

Reproductive Health Education

Providing sexual and reproductive health education is an important strategy that can reduce the prevalence and gender-specific burden of infertility. Many couples in resource-poor settings erroneously attribute causes of infertility to modern forms of contraceptives or nonbiologic factors. Education regarding the association between sexually transmitted infections (STIs) and tubal infertility can strengthen the effectiveness of public health programs that promote condom use and reduce the spread of HIV and other infectious diseases. Incorporating basic fertility education into village health care worker training programs can disseminate this information and increase the status and credibility of local health care workers in the community. By implementing educational programs in clinics, couples can find out when and where to seek help and reduce stigma and social mythology surrounding infertility.

Local providers can be trained to provide a basic evaluation and guidance or treatment for specific causes of infertility. Technicians at district hospitals can be taught to perform semen analyses using existing equipment such as hemocytometers and microscopes that are presently available and routinely used to diagnose malaria or anemia by peripheral blood smears. Offering routine male evaluation may mitigate the blame and burden on women. Improving local access to fertility services may simultaneously strengthen the effectiveness and community "buy in" with other reproductive health interventions

Table 1 A proposed national system for improved infertility care in resource-poor settings

Level 1 (community)	Level 2 (district hospital)	Level 3 (regional referral centers)
Village health care workers	Midwives and district health officers	Specialist consultant physicians
Education	Basic infertility workup and management	Assisted reproduction
• Reproductive physiology • Causes of infertility • Promote and optimize natural fertility • Dispel myths and stigma	• Semen analysis • Basic laboratory evaluation • HSG • Ultrasound • Ovulation induction with oral agents • Possibly IUI	• IUI • IVF/ICSI • Third-party reproduction

Abbreviations: HSG, hysterosalpingography; ICSI, intracytoplasmic sperm injection; IUI, intrauterine insemination; IVF, in vitro fertilization.
Notes: Level 1: Local or village health care providers can educate patients about reproductive health, causes of and treatments for infertility, and optimize natural fertility. Level 2: Local hospitals can perform basic infertility evaluation and treatment by performing semen analysis, basic laboratory workup, HSGs, and ovulation induction with oral agents such as clomiphene citrate. Level 3: National referral hospitals will perform more sophisticated procedures such as IUI, IVF/ICSI, and third-party reproduction with donor sperm or eggs.

as health care workers share the pressing health needs and concerns of their communities.

Affordable Infertility Diagnosis

Making infertility diagnosis affordable in resource-poor countries is of paramount importance. For infertility care to be more widely accessible, a basic workup of the couple with infertility should be provided through primary health care facilities at a reasonable cost.[4,10] In addition, well-trained personnel in local hospitals should be taught how to take a menstrual history, review of endocrine symptoms, and also perform a pertinent physical examination. Where available, ultrasound and plain film hysterosalpingography (HSG) can help detect uterine abnormalities. HSG is a simple and easily performed technique that can be employed in facilities with access to plane film radiographs. This is particularly important since pelvic infections leading to tubal blockage are one of the main causes of infertility in resource-poor settings.[4] One strategy is to provide infertility evaluation in specific primary health facilities located near tertiary health care hospitals; however, such specialized reproductive health care centers may be far away from villages and may have long queues of patients waiting to be seen.[4]

Affordable Infertility Treatment

Anovulatory infertility is readily treatable and has a prevalence rate of 20 to 25% with minimal variation between countries.[33] One effective treatment, clomiphene citrate (CC), is relatively inexpensive and can achieve ovulation in over 85% of women at a dose of 150 mg or less.[39] When combined with timed intercourse, clomiphene can achieve pregnancy rates of up to 25% per cycle in anovulatory women.[30] Health care providers can also be trained to recognize patient symptoms such as weight gain, hair loss, cold intolerance, or galactorrhea that suggest hypothyroidism or hyperprolactinemia; all of which also cause anovulatory infertility. Proper training can allow targeted hormonal testing to diagnose and treat these endocrinopathies as well.

For patients with infertility despite ovulatory cycles, several treatment algorithms have been proposed. Once tubal patency is established, CC stimulation with intrauterine insemination (IUI) may be a first-line treatment for unexplained and moderate male infertility.[40] IUI is easily implemented without major expense and without expensive infrastructure and can easily be performed by trained personnel. Also integral to this training is establishing a system that assures a chain of custody of gametes. IUI also has the advantage of offering HIV sero-discordant couples a safer way to pursue a family than unprotected intercourse. Transmission of infection to the male partner can be avoided by using insemination with the partner's semen for HIV-positive women. Sperm washing prior to insemination concentrates and separates the viable sperm from infectious seminal fluid and can be used to reduce the risk of HIV transmission for IUI with sperm from HIV-positive men.[41]

Some causes of infertility such as severe male factor and tubal occlusion will require more sophisticated treatments such as ART. In Giwa-Osagie's survey-based study looking at the current state of ART access in sub-Saharan Africa, he reported in vitro fertilization (IVF) centers providing a wide array of ART services in 10 countries: Cameroon, Ghana, Guinea, Kenya, Nigeria, Senegal, Sierra Leone, Togo, Uganda, and Zimbabwe. Although most centers report adhering to guidelines set by American Society of Reproductive Medicine (ASRM) or the European Society of Human Reproduction and Embryology (ESHRE), there are few if any regulatory institutions in these communities.[42] To protect patients from unregulated, costly, and substandard care, governing bodies should be created and funded with the goal of establishing and maintaining standards for ART to prevent exploitation and help ensure that patients receive the best care possible.

Currently, ART services in resource-poor countries are primarily accessible to the very wealthy; however, strategies to provide cost-effective alternatives are increasingly within reach. The WHO, ASRM, and ESHRE have encouraged groups like the Low Cost IVF working group and The Walking Egg project to establish low-cost fertility services in developing

countries through innovation, research, training, capacity building, and service delivery.[43]

To reduce the cost of ART, minimal-stimulation IVF uses oral ovulation induction agents alone or with lower doses of urinary or recombinant gonadotropins.[44,45] Teramoto and colleagues reported live birth rates of 15% using 50 mg of CC starting on cycle day 3 with the addition of 150 IU FSH or hMG every other day beginning on cycle day 8 and a GnRH agonist used to trigger final oocyte maturation . The probability of success with these protocols is difficult to estimate due to the heterogeneity of various minimal-stimulation IVF protocols. However, studies have reported live birth rates as high as 15 to 30%.[44,45] Compared with conventional IVF, minimal-stimulation IVF has lower success rates; thus, patients should be accurately counseled about the advantages and disadvantages of minimal-stimulation IVF protocols before they are employed. Natural cycle IVF can be attempted, but is associated with high cancellation rates from premature ovulation when used without using a GnRH antagonist, the latter of which increases the associated cost.[30]

ART procedures typically require a sophisticated laboratory with expensive equipment; however, costs can be reduced by substituting expensive equipment. Instead of a laminar flow hood when handling gametes and embryos, a humidicrib—a plastic incubator designed to keep newborns warm—can be used.[46] Rather than buying and maintaining expensive incubators for culture and storage of embryos and gametes, the Petri dish with the embryos can be placed in a plastic bag and dropped into a warm bath, where culturing and incubation can be proceed effectively.[47] The use of these and other laboratory equipment substitutes could reduce the price to less than 10% of conventional laboratory costs. Other options include the INVO procedure, which employs an intravaginal device that permits fertilization and culturing of embryos, although more research is needed to evaluate the effectiveness of these techniques in resource-poor countries.[48]

More recently, von Blerkom and colleagues described a simplified culture system for IVF and embryo transfer using a closed culture system with inexpensive disposable 10-ml plain glass test tubes (366; Becton Dickson). The pilot study of this system was tested in Europe, and it resulted in 68% fertilization rates, with 88% of zygotes developing as embryos to day 3 and 7 (20%) successful live births among 35 patients. The total cost for all of the necessary equipment was approximately US $300 and also included testing and implementation.[49]

Conclusion

Involuntary childlessness in developing nations is a major reproductive health problem. Currently, infertility care in resource-poor countries is fraught with lack of training and inadequate infrastructure and delivery of unregulated treatments that place tremendous financial burdens on patients who seek treatment.[13] Although 50 to 70% of patients will require ART, many can be treated with improved education and utilization of existing resources.

We provide a potential model for integrating fertility in reproductive health services provided by local health care providers, district hospitals, and regional referral centers using a graduated approach, beginning with education and amelioration of misconceptions. Local providers working in the community can implement educational programs that may reduce myths and stigma and educate patients when and where to seek help for infertility. For patients who require more extensive infertility evaluation or treatment, referral to district hospitals for a targeted workup should be available and cost-effective treatments provided. The cost of ART may be reduced by implementing minimal stimulation protocols, as well as simplified laboratory and culture systems for IVF and embryo transfer.[49] To receive the best care possible, governing bodies should be established (and funded) and standards maintained for ART to prevent exploitation and encourage quality care. Through collective efforts of education, training of local health care providers, and use of low-cost treatment regimens and techniques, care for infertile couples can be successfully expanded around the world.

Conflict of Interest
None of the authors has any conflict of interest.

Funding
None

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