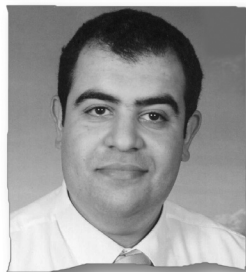


## Article

# The problem of IVF cost in developing countries: has natural cycle IVF a place?



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## Abstract

Infertility represents a national health problem in some African countries. Limited financial health resources in developing countries are a major obstacle facing infertility management. IVF is the definitive line of treatment for many couples. Stimulation cycles are associated with risks of ovarian hyperstimulation syndrome and multiple pregnancy. This study evaluates the client acceptability of stimulated versus natural cycle IVF among couples attending one infertility clinic, with respect to cost and pregnancy outcome. Of the patients who were indicated for IVF, 15% (16/107) cancelled, due mostly (12/16, 75%) to financial reasons. The majority of patients who completed their IVF treatment (82/91, 90.1%) felt the price of the medical service offered was high, and 68.1% (62/91) accepted the idea of having cheaper drugs with fewer side effects but with possibly lower chances of pregnancy. Natural cycle IVF has emerged as a potential option that might be suitable for patients worldwide, especially in developing countries.

**Keywords:** cost, developing countries, IVF, minimal stimulation, natural cycle

## Introduction

The World Health Organization (WHO) has defined sterility as an illness, if the respective couples have a desire for a child (Rowe *et al.*, 2000). False perceptions are hindering access to new research on IVF (Nature Publishing Group, 2006). Healthcare policy makers and medical professionals perceive the desire to have children as a non-authoritative preference, the fulfillment of which is optional. Many ethicists see a proclaimed human right to procreate as merely a negative right. Free IVF treatment for financially needy couples is, nevertheless, supported by many medical experts, as well as diverse patient groups (Krones *et al.*, 2006).

Infertility represents a national health problem in Africa, affecting 10–32% of couples on average (Gerai and Rushwan, 1992). Low rates of primary (3%) and high rates of secondary infertility (5–23%) could be attributed to higher rates of infection-related infertility (Larsen, 2000). Traditional and social pressures on infertile women in the African countries may cause psychosocial distress that is associated with high levels of psychiatric morbidity (Upkong and Orji, 2006). Women may become isolated and sometimes driven to suicide (Nature Publishing Group, 2006).

IVF represents the definitive line of treatment for a considerable number of couples, especially in cases of male factor and unexplained infertility. Funding of assisted reproduction techniques should be included in a publicly financed healthcare system (Devlin and Parkin, 2003; Tannsjo, 2007) or equivalent third parties (Tannsjo, 2007). The cost of IVF services would be a minute fraction of the annual cost of a typical family benefits programme, approximately US\$3393 (Collins *et al.*, 1995). Instead of this, the covering of costs of IVF by health insurance systems is regressing worldwide, especially in Europe (Krones *et al.*, 2006). In most developing countries, well-equipped infertility management settings at universities, public health insurance units and specialized clinics, funded through governmental or international funds and projects, are generally available. These systems, however, suffer limited financial resources, relatively low success rates and potential complications which make them unable to cover such an expensive intervention.

The Gross Domestic Product (GDP) measures the total

output of goods and services for final use occurring within the domestic territory of a given country (World Resources Institute, 2006). It can be taken as an economic indicator for the country. Egypt, as an example of a developing country, enjoyed a GDP of US\$78,422 million in the year 2000, compared with a GDP of US\$34,109,900 million for the whole world. Thirty-one per cent of the Egyptian population lives on less than US\$2 per day (Development Data Group, 2002). Infertility management in Egypt is affected by the low financial resources offered by public health services. IVF is a client-paid service. Assisted reproduction services are mainly offered by private centres, mostly in big cities, and by some university clinics and public health hospitals.

The use of a gonadotrophin-releasing hormone agonist (GnRHa) plus recombinant FSH (rFSH), for ovarian stimulation has been associated with a higher number of oocytes retrieved, higher quality of embryos obtained, and better pregnancy rates (Balasch *et al.*, 2003). The cost of the technology on which rFSH is based does not justify its high cost (Al-Inany *et al.*, 2003). The estimated average cost of an ongoing pregnancy is Egyptian pounds (EGP) 13,946, and EGP18,721 for a human menopausal gonadotrophin (HMG) and rFSH cycle respectively (Al-Inany, 2003). Clinical fees and drug and media costs do not comprise the whole IVF cost. Indirect expenses are brought about by waiting lists (Haimes, 1999), travel costs, leave from work and food (Kelly *et al.*, 2006). These costs are the responsibility not only of the clients, but also the clinics and the National Health Service organizations (Haimes, 1999).

The advantage of natural cycle IVF over stimulation cycle IVF is that it offers a low-risk, low-cost alternative, but large-scale prospective studies are still needed (Reyftmann *et al.*, 2007). Resorting to natural cycles reduces the cost of each treatment cycle by up to 75%. The cost of unstimulated IVF was put at just under £400, compared with £1717 for stimulated cycles, the difference being accounted for by the extra drugs (£625) and extra monitoring to avoid ovarian hyperstimulation syndrome (OHSS) (Nargund *et al.*, 2001). These advantages encourage patients to attempt consecutive cycles, with clinical pregnancy rates approaching those of stimulation IVF, especially among patients under 35 years of age (Phillips *et al.*, 2007).

Current stimulation protocols face two problems: first, the problem of IVF complications; and second, the problem of poor responders. OHSS, which affects up to 5–10% of IVF cycles, can be a life-threatening condition. Multiple gestations are the most common major complication of IVF and have a profound effect on health service costs (Bhattacharya, 2003). The medical cost per twin pregnancy was considerably higher than per singleton pregnancy (Lukassen *et al.*, 2004). A randomized controlled trial (Morgia, 2004) has proved that, in poor responders, natural-cycle IVF is at least as effective as ovarian stimulation, especially in younger patients, with a better implantation rate. High cancellation rates still make this option unattractive (Ubaldi *et al.*, 2004).

The aim of this study was to highlight the problem of IVF cost in developing countries and assess client acceptability to the idea of natural cycle IVF, in view of the cost of stimulation cycles and with respect to cost and pregnancy

outcome. As far as is known, this is the first study assessing these issues.

## Materials and methods

The study was approved by the Institutional Council of the Department of Obstetrics and Gynaecology, Assiut University. Couples attending the infertility clinic at Assiut University Hospital during June and July 2006 were approached. Patients presenting with primary or secondary infertility following regular marital life for at least 2 years and having an indication for assisted reproduction techniques, namely IVF or intracytoplasmic sperm injection (ICSI), were included. This was judged after complete history taking, physical examination and a paper-documented complete infertility work-up within the previous 6 months, either conducted within the setting of the hospital or at a licensed infertility management clinic. These patients were counselled about their participation in the study. A written informed consent was taken. Patients had the right to refuse to participate and/or withdraw from the study at any time without being denied their regular full clinical care. Personal information and medical data collected were subjected to confidentiality and were not made available to a third party. The necessity of assisted reproduction technique and the lack of the service at the University Hospital was explained for each couple.

Couples were given a telephone-based questionnaire 4 months after presentation at the clinic. All questions were asked in plain Arabic language. The questionnaire consisted of the following questions:

- (1) Did you have, or have you started, an IVF trial within the last 4 months?
- (2) If not, why not?
- (3) If you have: what was your reaction when you were told the price of the medications used for stimulation? [Couples were given the option of choosing between three reactions: surprised because the price was very high; not surprised because the price was acceptable; or not surprised because the price was low.]
- (4) What was the source of the finance for your trial? [Couples were given the opportunity to elaborate on this point.]
- (5) Do you have a solid future plan to financially cover the next trial if needed? [Yes or no.]
- (6) Do you think it is worth it to pay all this money for the whole trial in respect to the medical service and expected outcome? [Yes or no. This question focused on not only the cost of the stimulation drugs, but also on the whole financial package paid for the entire trial, including medical fees, laboratory costs and hidden costs.]
- (7) Do you accept the idea of having cheaper drugs with fewer side effects but with a possible lower chance of getting pregnant? [Yes or no.]
- (8) How would you describe the whole IVF trial? [Convenient or inconvenient.]
- (9) If you think it was inconvenient, state the most prominent cause of inconvenience. [Couples were given three options: travelling to the IVF centre; repeated medical visits; or financial cost.]

## Results

A total of 124 couples meeting the inclusion criteria were approached to participate in the study. Of these, 17 refused and 107 couples were recruited. These represent 14.4% of the whole patient pool (744 patients) presenting to the gynaecology clinic between June and December 2006. The recruited couples had indications for IVF and IVF/ICSI ranging from male factor infertility (87, 81.3%), tubal factor (12, 11.2%) and unexplained infertility (8, 7.5%). All couples were planning to pay for the costs by themselves.

There were no differences between males and females recruited regarding their age, period of infertility, type of infertility (primary or secondary) and origin of the couples. None of the couples had had an IVF trial before, although some of them had received infertility treatment services in the form of ovulation induction, intrauterine inseminations, operative laparoscopies and tubal surgery (**Table 1**).

A total of 91 couples (85%) completed an IVF trial within 4 months of their presentation. The 16 couples who did not

complete the IVF trial provided various reasons for this, but most of them (12, 75%) cancelled because of inability to pay for the treatment.

Of the couples that completed an IVF trial, 58 (63.7%) had to borrow the money for the medications from their parents, relatives and friends, or had to sell a personal asset (e.g. jewellery) to cover the expenses (21, 23.1%). About 90.1% (82 couples) were surprised to learn of the high cost of the medications. The rest of the couples (9, 9.9%) were not surprised and thought the price was acceptable and only 17 couples (18.7%) thought it was worth the cost, given the medical service and expected outcome. Sixty-two couples (68.1%) accepted the idea of having cheaper drugs with fewer side effects but with a lower pregnancy rate. Nearly half of the couples (39, 42.9%) had, at the time of the questionnaire, no solid future plan to financially cover the next trial if needed (**Table 2**).

For couples achieving a pregnancy after their first IVF trial, causes of making the IVF trial an inconvenient experience were assessed. These were cost, repeated medical visits, and travelling, in that order of priority (**Table 3**).

**Table 1.** Demographic characteristics of 107 couples presenting to the Assiut University clinic with infertility.

<i>Characteristic</i>	<i>Value</i>
Age in years (mean $\pm$ SD)	
Females	29 $\pm$ 2.3
Males	31 $\pm$ 4.3
Duration of infertility in years (mean $\pm$ SD)	4 $\pm$ 1.7
No. with primary infertility	
Females	61
Males	64
No. with secondary infertility	
Females	46
Males	43
Couple's origin ( <i>n</i> )	
Urban	42
Rural	65
Past history of infertility management ( <i>n</i> )	
Ovulation induction courses	104
Intrauterine insemination trials	18
IVF trials	0
Operative laparoscopies	49
Adhesiolysis and/or tuboplasty	70/91

**Table 2.** Breakdown of client reaction to IVF cost and natural cycle assisted reproduction among 107 couples recruited for IVF trial.

<i>Parameter</i>	<i>n</i>	<i>%</i>
Couples who cancelled the IVF trial	16/107	15.0
Cancellation due to:		
Financial reasons	12/16	75.0
Social reasons	3/16	18.8
No reason given	1/16	6.3
Couples who had an IVF trial	91/107	85.1
Reaction to high cost		
Surprised – thought the price high	82/91	90.1
Not surprised – thought the price acceptable	9/91	9.9
Not surprised – thought the price low	0/91	0.0
Accepted the idea of cheaper drugs with fewer side effects but with possibly lower chances of pregnancy	62/91	68.1
Had no future plan to financially cover subsequent trial(s) if needed	39/91	42.9
Thought it was worth it to pay all this money for the whole trial in respect of the medical service and expected outcome	17/91	18.7
Pregnancy achieved	21/91	23.1
No pregnancy	70/91	76.9

**Table 3.** Inconvenience of the IVF trial as experienced by couples achieving a pregnancy (*n* = 21) after their first IVF trial.

<i>Parameter</i>	<i>Described IVF as an inconvenient experience</i>
No. of couples (%)	14/21 (66.7)
Cause of inconvenience (%)	
Repeated medical visits	4 (28.6)
Travelling	1 (7.1)
Cost	9 (64.3)

## Discussion

The desire to have children should be considered as a normal need that ought to be met (Krones *et al.*, 2006). The overall prevalence of infertility in Egypt is 10.4%, and it is higher among married women under the age of 16 or above 30 years. While the prevalence of primary infertility is 2.5%, being higher among women under 30 years than older ages, the incidence of secondary infertility (7.9%) increases with advanced age (Mohsen *et al.*, 2001). National data about infertility in Egypt are restricted to local community studies (Mohsen *et al.*, 2001) and the national Egyptian IVF registry (Mansour and Abou-Setta, 2005). A total of 6757 cycles in the year 2000 were reported. 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%. In this study, the pregnancy rate among patients who had an IVF trial

in different settings was 23.1%. The Assiut University Hospital is an example of a tertiary care hospital in a developing country. Its infertility management setting is well equipped, although the IVF unit is still under construction.

OHSS and multiple pregnancy are the most common problems of IVF (Bhattacharya, 2003) and they increase health care costs (Koivurova *et al.*, 2004). Other financial obstacles include drugs and media used for ovarian stimulation in IVF cycles. They represent financial, social as well as medical problems on the way towards solving the infertility problem in developing countries. Minimizing these side effects without sacrificing the effectiveness of stimulation cycles is the goal of modern IVF trends.

Certain criteria can be observed from the results of this study. First, the mean age of couples seeking fertility in this study was

relatively low, which is an encouraging factor for candidates of assisted reproduction. Second is the fact that male factor infertility contributed to a large proportion of indications for assisted reproduction technology among the study group, highlighting the importance of expanding such services. It was found that 15% of recruited patients could not have their indicated IVF trial, of which 75% were unable to proceed with treatment for financial reasons. This is in accordance with Devlin and Parkin (2003) who stated that a user-payer policy may impair implementation of the service to the target group.

From a philosophical point of view, the problem of bearing the cost of IVF is a matter of debate about justice, styles of thinking for healthcare policy-makers and cultural differences of the infertile couples. Tannsjo (2007) refused to apply theories of justice where it is seen as a matter of rights, or as something resting on an agreement between rational egoists, who would rather support a healthcare system based on private insurance. Other more relevant theories included egalitarianism, which ignores infertility as a devastating event in the life of affected couples, and utilitarianism, which is the view that, through their actions, individuals ought to maximise the sum-total of wellbeing in the universe. Being childless could increase the risk of suffering from depression (Murphy, 1984). Cultural differences and the possibility of disastrous consequences for infertile women in different societies, even if they are poor, should be borne in mind (Tannsjo, 2007). Pennings and Devroey (2006) found that discounted IVF treatment was an important motive for more than two-thirds of the women who donate their oocytes. This raised a matter of justice as only women who cannot afford IVF treatment would donate. They called for more extended funding of IVF for the financially needy.

Natural cycle and mild stimulation cycles represent an interesting, not yet settled, alternative to stimulated cycles (Reyftmann *et al.*, 2007). This option has the merits of minimizing the complications of IVF, namely OHSS and multiple pregnancy. The high cumulative pregnancy rate with repeated trials together with its low cost is a high motivation for patients to attempt it repeatedly.

Data about natural cycle IVF in Egypt are lacking and only two studies, with a limited number of cycles, addressed this issue among poor (Karaki *et al.*, 2002) and low (Saleh *et al.*, 2003) responders, with a pregnancy rate of 36% per transfer. In this study, about 68% of couples receiving their first IVF trial accepted the idea of having cheaper drugs, with fewer side effects and possibly a lower chance of achieving a pregnancy in subsequent trials.

Calling for governmental funding of IVF trials should not be limited to the stimulation cycles, for two reasons. First, natural cycle IVF is still expensive in terms of medical fees, media used and laboratory charges. Second, from a utilitarian viewpoint (Tannsjo, 2007), the current cost-effectiveness of using natural cycle IVF, which has a cumulative probability of pregnancy of 46% with an associated live birth rate of 32% after four IVF cycles on average (Nargund *et al.*, 2001), is still warranted to be covered by publicly financed health insurance systems.

Medical charges are set by the marketplace and may not reflect the actual cost of providing a service, which is difficult to measure. To the client's mind, medical charges accurately

reflect the cost of healthcare services (Van Voorhis *et al.*, 1998). It was found that only 17.1% of those who had an IVF trial thought it was worth it to pay such a large sum of money in respect of the medical service and expected outcome. Notably, none of the couples in this study perceived the cost of an IVF trial to be low. Patients who became pregnant after their first trial ( $n = 21$ ) stated financial cost to be the most common cause of inconvenience. This is interesting because, to their minds, success of the procedure still did not rationalize its high cost. Lack of consideration of the differences in socioeconomic levels and the small targeted subgroups could be considered as limitations of this study.

The conclusion of this study is that the decisions of Egyptian couples for whom assisted reproduction technique is indicated are negatively affected by financial issues. The cost of IVF still far exceeds the financial capability of most of clients, who are sometimes left with the painful decision to abandon the fulfilment of their wish of procreation. Infertile couples do not perceive the cost of IVF management to be acceptable in respect of the side effects and expected outcome. Natural cycle IVF is highly acceptable in developing countries. Counselling as regards this option should include clear information about the ongoing debate regarding its effectiveness. Better cumulative pregnancy rates and safety as regards drug side effects can be addressed. Healthcare policy-makers should participate in offering advanced solutions to improve the cost-effectiveness of natural and mild stimulation methods. Moving infertility management higher up the international agenda should help ensure funding policies that allow IVF for all indicated couples.

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