

## Successful intravaginal culture of human embryos for the first time in Pakistan — An experience at the Sindh Institute of Reproductive Medicine, Karachi

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### Abstract

Approximately 10-15% of the married couples remain childless. Conventional in vitro fertilisation (IVF) has been the treatment option for most of these cases. However, it is expensive and only available to a small fraction of the infertile population. The Sindh Institute of Reproductive Medicine (SIRM), Karachi, Pakistan, has introduced a new method of IVF for the first time in Pakistan. Intravaginal culture (IVC) is a simple, reliable and cost-effective alternative to IVF. The procedure can be performed in an office set-up with minor capital equipment. Here, we report a case of a subfertile woman treated by IVC, which resulted in successful fertilisation of the eggs (fertilisation rate 71.42%) and embryo development, with an intrauterine pregnancy. Since this is the first successful case of IVC in Pakistan, comparative success rate and take-home baby rate have yet to be established.

**Keywords:** Fertilisation in vitro, Intracytoplasmic sperm injection, Intravaginal culture, Infertility, Assisted reproductive techniques, Pregnancy rate.

### Introduction

Assisted reproductive technique (ART) is the established treatment for infertility and, in most cases, the only option for childless couples to achieve parenthood. However, it is riddled with various barriers, such as accessibility, cost, as well as cultural and social factors. One of the most important barriers is finance, as ART is relatively expensive.

Keeping this in mind, the Sindh Institute of Reproductive Medicine (SIRM) was established in September 2007 with the aim of providing this facility to the low and middle socio-economic class and to transfer the technology by providing training to the interested professionals. A year later, SIRM introduced the method of intravaginal culture (IVC), which was the first of such an attempt in Pakistan.

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IVC is a different technique for the fertilisation and culture of human oocytes.<sup>1</sup> After the first IVF baby in 1978, it was introduced in 1985 and was acknowledged by the American Society for Reproductive Medicine (ASRM). It is a simple, reliable and cost-effective alternative to IVF where the vaginal cavity of the patient substitutes for the complex IVF laboratory.<sup>2</sup>

By simplifying the laboratory manipulations, the technique decreases the cost, and permits IVF standardisation. It creates a psychological comfort zone, and a high level of acceptance, permitting active participation of the mother in the process of fertilisation and early embryo development as it allays the anxiety of the couple regarding the rare possibility of gametes mix-up. In the conventional IVF procedure, the complex organisation requires a strict patient identification. During two to three days of in vitro incubation in the laboratory, the couple remains uncertain and anxious about the paternity and maternity of the fertilised embryo.

In developing countries, where infertility rate is high and access to cost-effective infertility treatment is low, IVC provides an excellent treatment option.<sup>2,3</sup> It bypasses the costly incubation period and is quicker, with a single technician carrying out all the steps in 60-90 minutes.

This procedure does not require a complex laboratory and major capital equipment. The equipment used in IVC can easily be kept in the office of the physician. Sophisticated CO<sub>2</sub> incubators with controlled continuous supply of CO<sub>2</sub>, air filtration system, alarm system and an on-call embryologist are not necessary, whereas all of these are needed for an IVF procedure.

With power shortage being an unfortunate reality in Pakistan, standby generators, equipment with extended back-ups and stabilisers are required to ensure stable and continuous supply of electricity. This also contributes to the high cost of IVF, which is unnecessary in IVC.

## Case Report

The patient was selected from the SIRM outpatient department (OPD) in September 2008. Selection criteria was of age <35 years, follicle stimulating hormone (FSH) levels of <8uIU/ml, and normal seminal fluid analysis (sperm count 20 million/ml; motility 50%; rapid linear progression (RLP) 25%; morphology 14%) or mild abnormal parameters (sperm count 10-20 million/ml; motility <50%; RLP <25%; morphology <14%).

The patient was a 23-year-old female, married for 05 years with the history of primary infertility. She had been on anti-tuberculosis therapy (ATT) for 01 year due to pulmonary tuberculosis which was completed 04 years back. Her menstrual cycle was 4/40-45 days' duration. Initial work-up showed FSH levels of 5.21 uIU/ml, luteinizing hormone (LH) 7.7 uIU/ml, and serum prolactin 31.48pg/ml. Ultrasound of the pelvis showed bilateral hydrosalpinges, while fallopian tubes blockage was demonstrated on hysterosalpingography (HSG).

After the initial work-up, controlled ovarian hyperstimulation (COH) was done with the long protocol: Gonadotropin-releasing hormone agonist (GnRH agonist; injection Suprefact 0.5cc) was started in the luteal phase (Day 21) of the preceding cycle; 150 IU of human menopausal gonadotropin (hMG) was started at day 3 of the cycle; and 10,000 international units (IU) of human chorionic gonadotropin (hCG) was given to trigger ovulation. 34 hours after the hCG injection, ultrasound-guided follicle aspiration was performed transvaginally under general anaesthesia.

Sperm preparation was performed 1 hour prior to the oocyte retrieval so that insemination could be performed immediately afterwards. Gradients of density were used to wash the sperm and select the most motile spermatozoa. The device was filled with medium without the interposition of air, as air bubbles trapped in the cumulus of the mature oocyte would bring them to the surface and, therefore, prevent fertilisation by spermatozoa. Once the device was filled with the medium, a fraction of the motile spermatozoa (30,000) was added. After follicle aspiration, oocytes were identified in the follicular fluid and immediately placed into the device. The device was closed and placed into a protective outer rigid shell, and positioned in the vaginal cavity for 03 days. Device loss during incubation was prevented by plugging the vagina with a perforated diaphragm of appropriate size. No activity restriction was required by the patient,

but she was advised to avoid baths as they could modify the temperature of incubation. On the third day, the diaphragm and the device were removed. The outer rigid shell was removed, the device was opened and the contents were observed under microscope to find the embryos. The three best embryos were loaded into a catheter and transferred immediately into the uterine cavity under ultrasound guidance.

Progesterone pessary was started from the day of the egg retrieval, and hCG injections (2500 IU; 02 doses) were given 48 hours apart starting from the day of embryo transfer (ET) for the luteal phase support.

We used the INVOcell device, which was well-accepted, non-traumatic and effective for the patient. Serum  $\beta$ -hCG was checked 15 days after the embryo transfer for the confirmation of pregnancy; it was found to be 373mIU/ml. Ultrasound was done at 6 weeks to confirm the presence of the intrauterine sac, foetal pole and the foetal heart.

## Discussion

Infertility is a common reproductive health problem in developing countries, which frequently carries negative psycho-social implications.<sup>4</sup> Keystones in the successful implementation of infertility care in low-resource settings include simplification of diagnostic and ART procedures and optimisation of these techniques in terms of availability, affordability and effectiveness.<sup>3</sup> IVC is a relatively new technique for the fertilisation and culture of human oocytes.<sup>1</sup>

A 1990 study selected 15 females for IVC, and the fertilisation rate obtained was 56%. Three intact pregnancies were recorded after ET.<sup>5</sup>

Another study showed that in a total of 45 patients, 22 were treated by IVC and 23 were treated by conventional IVF. The pregnancy rates for IVC and IVF came to 22.75% (5/22) and 17.4% (4/23), respectively.<sup>6</sup>

The fertilisation rate was 71.42% (5/7 ova) in this case report at SIRM, indicating that IVC is a valuable method.

Extracorporeal stress factors for growing the embryo, such as light and low temperature, can be minimised by IVC. The psychological factor for the patients is very important since the mother can actively participate in the early development of the conceptus and the level of satisfaction can be very high.

It has been reported that IVC yields results comparable to those obtained with classic IVF techniques.<sup>7</sup>

Furthermore, it can simplify and reduce the cost of the procedure.

### Conclusion

IVC was found to be a simple, effective and comparatively inexpensive procedure compared to the conventional IVF technique. However, in the local settings, it needs further evaluation before being extended to the common clinical practice.

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