

# Birth of first JIPMER “ICSI” Baby

Papa Dasari<sup>1,\*</sup>, Manjula Gopalakrishnan<sup>2</sup>

## ABSTRACT

Assisted reproductive techniques are becoming more and more essential for human life in the Society. Worldwide more than 5 million babies were born out of this technology after the birth of first baby Louis Brown and second Durga (India) in 1978. It is a boon for the couple in despair to have a child especially when it is provided by Govt Institutions for the less affordable people of the Society. It is essential to share provider’s experiences and expectations of the public in a fast growing biomedical field like ART. The techniques of IVF and ICSI have undergone a sea change since the initial technique of natural cycles to ovarian hyper stimulation and stem cell research. A 29 year old lady, Type I Diabetic with hirsutism, PCOS, failed IUI underwent ICSI following ovarian stimulation employing antagonist protocol after 8 years of married life. The husband is also diabetic for 13 years and suffered from post-polio residual paralysis and had asthenospermia. Frozen Embryo transfer of cleavage stage embryos was done on 31.7.2019 after endometrial preparation employing HRT. Her  $\beta$  HCG was HCG 387 on 14.8.2019 and intrauterine pregnancy was confirmed by transvaginal scan. Pregnancy and Diabetes were managed with progesterone support and Insulin therapy respectively. An alive male baby was delivered by emergency Caesarean section on 28.3.2020 at 12.34 PM for breech presentation in labour during lockdown for COVID 19. Both mother and baby were discharged home in healthy condition and the baby is one year old at the time of writing this report.

**Key words:** Bilateral Tubal block, FET, 8 celled embryo, First “ICSI” Baby, JIPMER.

## INTRODUCTION

Reproductive Physiology has undergone several manipulations from the basics and reached great heights of *in vitro*-fertilisation to begin life outside the body. Assisted Reproductive technology (ART) has become a boon for couple who fail to conceive naturally and by various other modalities of therapy for infertility. Infertility is on the rise in recent times and 1 in 6 couple experience difficulty in achieving pregnancy. On the whole 20% of infertile couple require ART to achieve successful pregnancy. Though the World’s first and second babies were born in 1978, tracking of IVF and reporting started voluntarily in 1985 and became a norm since 1992 following initiation of Fertility Clinic Success rate and Certification Act by CDC.<sup>[1]</sup> Public reporting of outcomes of ART is being encouraged to improve health outcomes.<sup>[2]</sup> With advances in ART, it is felt that there is a need to report on the actual experiences and expectations of ART.<sup>[3]</sup> Hence this case which is first to achieve in JIPMER, Puducherry, a tertiary Govt. Centre, catering free services to Public is reported.

## CASE REPORT

A 29-year-old Mrs. S, married 9 years was recruited for ART in 2019 after counselling and consent as per ICMR guidelines. Her history in chronological order is as follows: She attained menarche at 14 years of age

and her cycles were irregular since then. In 2009, at the age of 18 years she presented to Medicine OPD, JIPMER with complaints of polyphagia, polydipsia and polyuria and her random blood Sugar was 383 mg/dl and she was diagnosed as Type I DM and started on Insulin and advised diabetic diet. Fundus examination was normal. She was irregular on treatment and follow up.

In 2011 (21.6.2011) she presented to OG OPD, JIPMER for infertility of one year duration. She was diagnosed as hyperandrogenic PCOS as she had hirsutism and serum testosterone was 80.5 ng/dl and she was treated with Tab. Krimson -35 (Cyproterone acetate + Ethinyl estradiol) for 6 cycles. Later her serum testosterone reduced to 53 ng/ dl at 3 months and 38 ng/dl after 6 months; LH was 11.4IU/L FSH was 7.1 IU/. In 2012, Semen Analysis was normal and she underwent ovulation induction with clomiphene citrate for 3 cycles. Anovulation was documented. Later she was lost for follow -up.

In 2015, she underwent 3 cycles of IUI at a Private-fertility center without success. Subsequently she underwent laparoscopic evaluation which showed bilateral tubal block. She was advised IVF/ICSI which she could not afford and hence she had given up hope.

In 2018, she attended free camp of IFS (Indian Fertility Society), Puducherry chapter conducted at Kosapalayam PHC (primary Health Centre)

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and she was advised to come to ART center, JIPMER. Husband is physically handicapped due to Post-polio residual paralysis and diabetic for 13 years. His current semen analysis showed asthenospermia.

On examination, her BMI was 25 Kg/m<sup>2</sup>, hirsutism of FG Score 8, breasts and thyroid examination and systemic examination was normal. Gynecological examination revealed healthy cervix and vagina. Uterus was normal size and bilateral adnexa were palpable.

She was recruited to batch IVF in March 2019. Her hemogram, RFT, LFT were normal and HbA1C was 6.5. Cervical swab culture and semen culture were sterile. Her day 3 FSH was 8.9IU/L, LH - 11.2 IU/L, Estradiol - 60 pg/ml and AMH - 2.7 ng/dl. AFC was 11 (left ovary-4; right ovary-7). Antagonist protocol was planned. Controlled ovarian hyper stimulation was done with rFSH step up (75 to 300 IU) and hMG 150 IU was added from day 8 to Day 10. Antagonist, Cetrorelix 0.25 mg was given on Day 11 at a follicular size of 18 mm. HCG trigger was given on Day 13. Oocyte retrieval was done after 36 hours on 4.11.2019 using single lumen catheter (Cook Medical) under intravenous sedation and Para cervical block. Twelve MII Oocytes were obtained and ICSI was performed (Olympus IX71/IX51). Eight good quality embryos (Grade I) were frozen using vitrification kit (Sage Vitrification kit, Cooper Surgical).

In July 2019, endometrial preparation was undertaken by HRT cycle. Tablet estradiol valerate 6 mg and injection progesterone 50 mg intramuscular were used. ET (Endometrial thickness) was 8.3 mm with triple line on Day 7 and 11 mm on Day 13. Inj. aqueous progesterone 50 mg was administered intramuscularly for 3 days and embryo transfer was done on Day 18 (31.7.2019) at an ET of 12 mm. Three 8 celled Grade I embryos (Figure 1) were transferred using embryo transfer catheter (Gynetics) under USG guidance without any difficulty. Inj. Progesterone was continued for 14 days along with antioxidants and her medication for diabetes. Her serum  $\beta$ HCG was 387 mIU/ml on 14.8.2019. Transvaginal scan on 21.8.2019 showed single intrauterine gestational sac with yolk sac (Figure 2) and CRL measured 5 mm. She received oral progesterone (Duphastan 10 mg) twice daily for 12 weeks.

She had regular antenatal care with the same Obstetric team and her Diabetes was controlled well and fetal growth was closely monitored. She was hospitalized at 32 weeks for antenatal corticosteroids during which time she discontinued inj. Insulin by miscounseling and developed DKA which was promptly treated. Her USG at 36 weeks showed fetus in breech presentation with expected weight of 2.5 kg with normal Doppler flow and she was planned for Elective LSCS at 38 weeks on 8.4.2020. However, she went in to labour on 28.3.2020 during lockdown for COVID-19 and underwent emergency LSCS. An alive male baby, 2.6 kg was delivered at 12.34 PM with an APGAR of 7/10 at 1 min and was in NICU for 48 hr for observation and blood sugar monitoring (Figure 3A). Mother and baby (Figure 3B) were discharged on 7<sup>th</sup> post-operative day in good health.

## DISCUSSION

There are more than 70 articles that described the birth of first test tube baby, Louis brown and the scientists who made it possible underwent great criticism initially.<sup>[4,5]</sup> The history of human invitro fertilization has been recently reviewed<sup>[3]</sup> and it is reported that the first pregnancy which ended up in early embryo demise was in Melbourne, Australia and the procedure was performed in 1973 by Prof. Carl Wood and John Leeton. In 1976, Patrick Christopher Steptoe, Gynaecologist and Robert Geoffrey Edwards, a British physiologist published a report of ectopic pregnancy following transfer of a morula. In 1978, they offered IVF to Mrs. Lively Brown and John who suffered from infertility of 9 years. Bilateral tubal block was the indication and a single Oocyte was retrieved laparoscopically in a natural cycle and was fertilized in the lab and an 8 celled embryo was transferred in to the uterine cavity. During the same year

in India Dr. Subhash Mukerjee used human menopausal gonadotropin (hMG) for ovarian stimulation and retrieved the oocytes transvaginally and fertilized in lab and frozen the embryos for 53 days and then



Figure 1: Three 8 celled grade I embryos.

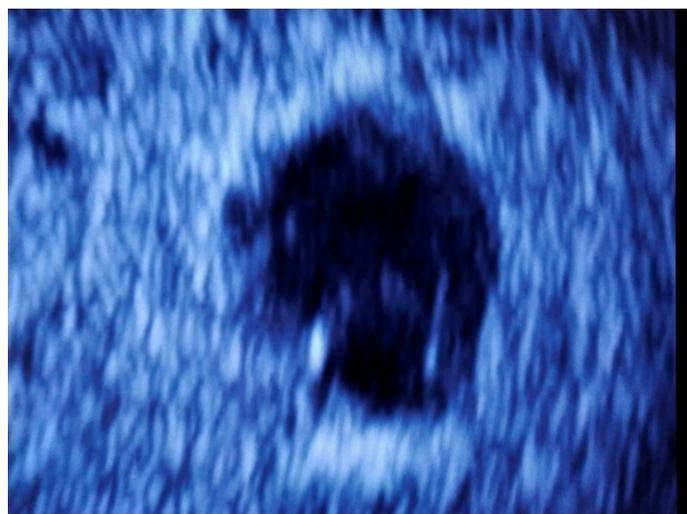


Figure 2: Transvaginal scan showing single intrauterine gestational sac with yolk sac.



Figure 3A: Newborn on the Day of Birth



**Figure 3B:** Baby at Discharge - On Day 7 of Birth.

transferred. Mr. Prabhat Kumar and Mrs. Bela Agarwal were the couple and the indication was diseased tubes.<sup>[6]</sup> He was the first one to use transvaginal aspiration and he could get 5 oocytes which were incubated initially for 4 hr and later co-incubated with husband's semen for 24 hours. He used Liquid nitrogen and dimethyl sulphoxide as cryoprotectant and performed slow freezing method. Pregnancy test was positive on 14<sup>th</sup> Feb 1978 and she was delivered by Caesarean section on 3<sup>rd</sup> October 1978 of an alive female baby named Durga. His innovation of principles of transvaginal aspiration and freezing of embryos have been refined and followed in modern era. His work which saw limelight after many years is published by Adhithya Bardwaj as the Indian IVF Saga.<sup>[7]</sup> In 1980 Edwards and Steptoe published the process of establishing full term human pregnancies using cleaving embryos grown in vitro.<sup>[8]</sup>

Advances in ART have taken place at a great speed and the history of developments have been published by many authors.<sup>[9]</sup> New inventions occurred to overcome the causes of infertility and increase fertilization rates and live birth rates. Intracytoplasmic injection (ICSI) is one such invention to ensure fertilization overcoming natural selection of sperm in IVF. The first attempt was made by Lanzendorf *et al.* in 1987 and Palermo *et al.* reported the first pregnancy in 1992.<sup>[10]</sup> The procedure requires micromanipulation using an inverted microscope and all the ART laboratories in the World have this costly equipment and special training is essential to acquire the skills to inject the sperm in to Oocyte and Clinical Embryology has emerged as a new branch of Medicine. ICSI has become the standard of care to overcome fertilization failures associated with IVF.<sup>[11]</sup> ASRM committee opinion has recently updated on this issue.<sup>[12]</sup> ICSI was followed for the present couple and frozen embryo transfer was undertaken with expectations of achieving success. Frozen embryo transfer is found to achieve higher success when compared to fresh embryo transfer.<sup>[13]</sup>

More than 8 million babies have born out of ART techniques during the last 40 years and Regulations have been in place for the past 2 decades

to control and ensure ethical practices in every country. In India ART rules and Regulations have been in place after ART Bill of 2010<sup>[14]</sup> which we followed while establishing the services. NARI (National Registry of Assisted Reproductive Technology (ART) Clinics and Banks has been established under ICMR.<sup>[15]</sup> Continuous efforts are being undertaken by Govt. of India in regulation and updating the ART clinics and also in providing these facilities to the deserving population of the society at low cost or free of cost and ours adds to one such effort. The ART services were started in JIPMER in 2018 after ensuring provision of all facilities as per ICMR guidelines and this could be achieved under some odd conditions and finally in 2020 during COVID lockdown the first birth happened and the couple was Mrs. Sangeetha and Mr. John and the baby boy was christened as Aaron Frank.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## ABBREVIATIONS

**ART:** Assisted Reproductive technology; **hMG:** Human Menopausal Gonadotropin; **ICSI:** Intracytoplasmic Injection.

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