

# Transabdominal Follicular Aspiration in IVF Treatment Cycle, an Unusual but Necessary Intervention: Experience from a Resource Limited Setting

Authors ; Osemwenkha AP Osaikhuwuomwan JA

Department of Obstetrics and Gynaecology, College of Medical Sciences, University of Benin  
Benin- City, Nigeria

## Abstract

Controlled ovarian hyperstimulation is one of the major steps in in-vitro fertilization. Inaccessibility or non visualization of developing follicles on transvaginal sonography (preferred method) may be mis-judged for poor response resulting in cycle cancellation. The need for scrupulous appraisal of proxy indicators for ovarian response viz: estradiol levels, endometrial thickness and other individual clinical characteristics are emphasized. This would prompt meticulous and assiduous trans-abdominal ultrasound follicular monitoring and oocyte retrieval as a necessary intervention to avert cycle cancellation and enhance treatment outcome.

**Keywords:** infertility, IVF-ET, ovarian stimulation, ultrasound folliculometry, cycle cancellation

## Introduction

The uptake of IVF-ET as treatment for infertility in sub-saharan African is on the ascendancy, albeit the region remains increasingly resource constrained with an attendant huge financial burden on clients accessing this treatment option; , so that clients first attempt may be the last. Thus it's imperative on caregivers in this region to facilitate measures that will enhance treatment success at each attempt. From the foregoing having ones IVF treatment cancelled can be devastating and frustrating. Cycle cancellation can occur before or after egg recovery. Cancellation before oocyte retrieval may be as a result of: poor response to the drugs used to stimulate the ovaries, a high risk of over-response to the fertility drugs and development Ovarian Hyperstimulation Syndrome (OHSS), any situation or illness which prevents egg collection going ahead at the time of oocyte maturation or post surgical adhesions/displacements preventing accessibility to ovaries, not taking hCG injection at the correct time – this triggers the release of the mature eggs before recovery and patient choice (sometimes for personal reasons postpone cycle)[1-3]

Poor response to ovarian stimulation is the commonest reason for cycle cancellation.[2,4] In order to mitigate this varying response predictors have been employed, examples include; age, body mass index, previous ovarian surgery, previous ovarian stimulation experience, basal FSH, antimullerian hormone assay, antral follicular count and serial folliculometry with ultrasound.[2,4,5] Our local experience showed that poor ovarian response to stimulation as noticed on ultrasound folliculometry was a common reason for cycle cancellation, and this was on some occasion inadvertently due to non visualization of developing follicles following ovarian displacement or encasement from previous surgery. Thus we instituted a protocol[6] where prior to cycle cancellation for poor ovarian response proxy indicators of response such as estradiol levels, basal follicle stimulating hormone or anti-mullerian hormone, endometrial thickness and other individual clinical characteristics are scrupulously appraised before a final verdict.

We present our experience in the past 24 months (July 2013 to June 2015) in a case series where meticulous review of proxy indicators for ovarian response provoked painstaking and diligent ultrasound search for the developing ovarian follicles with positive result and averting cycle cancellation.

## Case 1

Mrs E.N, 36 years old para 0<sup>+6</sup> presented for treatment 2014 with 8 years history of infertility and previous myomectomy (done 2006). She was counseled and selected for IVF-ET treatment following confirmation of bilateral tubal block. She had controlled ovarian hyperstimulation (COH) in line with our unit protocol, she was commenced on 5 ampoules of HMG (75iu per ampoule) daily. Baseline transvaginal scan (TVS) at commencement of stimulation (on day 3 of menses) showed antral follicles on both ovaries and no residual follicle or cyst. On stimulation day 5 TVS revealed tiny follicles in left ovary but the right was not visualized. On stimulation day 8, TVS revealed a poorly defined left ovary with very tiny follicles while the right ovary was not visualized. Review of stimulation day 5 estradiol level of 413pg/ml and endometrial thickness of 7.8mm were suggestive of apparent follicular development (good response); this necessitated further search using a transabdominal scan which showed 4 follicles on the right ovary and 2 follicles on the left with the largest measuring 15.5mm. On stimulation day 11 the 6 follicles were still visualized on transabdominal scan with the largest measuring 20.1mm, endometrial thickness was 10.5mm. She had i.m. HCG 10,000iu same day and oocyte retrieval done 34 hours post HCG. At oocyte retrieval (OCR) 7 follicles were aspirated transabdominally and 5 oocyte retrieved. 3 good embryos were transferred on day 3 post OCR. Pregnancy test was positive 2

weeks post embryo transfer and clinical pregnancy was confirmed by ultrasound (single live gestation) 4 weeks post transfer.

#### **Case 2**

Mrs I E a 36year old para 0<sup>+</sup> with 5 year history of infertility. She had myomectomy done 4 years prior to presentation for menorrhagia. Investigations revealed bilateral tubal block and mild oligospermia. Following clinical evaluation and discussion the couple gave informed consent for IVF-ET. She subsequently had COH in line with our protocol commencing at 5 amps(375iu) per day of HMG. On the 5<sup>th</sup> day of stimulation transvagina scan revealed multiple tiny follicles on the right ovary but the left was quiet, estradiol assay done was 456pg/ml. on the 8<sup>th</sup> day the ovaries were not visualized on TV scan but endometrial thickness was 8.1mm; a transabdominal scan was done which showed developing follicles in both ovaries, a total of 9 with the largest being 13.6mm. She continued to respond well on transabdominal folliculometry and had 12 visible follicles on the 11 day of stimulation with the largest measuring 20.5mm, she had hCG and subsequent oocyte retrieval 35 hours after. Ten follicles were aspirated transabdominally and oocyte yield was 7; of these 5 fertilized and a day 3 transfer of 3 good quality embryos. Pregnancy test was positive 2 weeks after and ultrasound confirmed viable twin pregnancy 6 weeks after embryo transfer.

#### **Case 3**

Mrs I J. a 32 year old para0<sup>+</sup> presented to the clinic with a 2 years history of infertility. Hysterosalpingogram showed bilateral tubal occlusion with uterine fibroids, semen analysis was normal. She was counseled for myomectomy prior to definitive IVF-ET treatment; she consented and had successful myomectomy. Six months after the myomectomy she commenced ovarian stimulation for IVF in line with our protocol. She was commenced on 4 amps and on the 5<sup>th</sup> day on stimulation estradiol level was 514pg/ml, follicles were scarcely visualized on transvaginal scan, the HMG was increased to 5 amps. On the 8<sup>th</sup> day on stimulation the ovaries were not visualized but endometrial thickness was 8.5mm, following detailed search on transabdominal scan 9 follicles were seen with the largest measuring 13.9mm. transabdominal folliculometry was continued and on stimulation day 12 she had over 12 follicles with the largest being 22mm, hCG was given and she went on to have transabdominal retrieval 35hours post hCG. About 18 follicles were aspirated and oocyte yield was 10 of which 6 fertilized and 3 good quality embryos were transferred on the 3<sup>rd</sup> day post OCR. Pregnancy test was negative 2 weeks after ET

#### **Case 4**

Mrs A.F. is a 39 year old para 0+0 with a five year history of infertility. She has had 2 previous myomectomy in 2003 and 2012; she also had 2 previous failed intrauterine insemination attempts. She presented desirous of IVF-ET. She was counseled and selected for IVF-ET treatment in line with our unit protocol, she was commenced on 5 ampoules of HMG(75iu per ampoule) daily. Baseline transvaginal scan (TVS) at commencement of stimulation (on day 3 of menses) showed antral follicles on both ovaries and no residual follicle or cyst. On stimulation day 5 TVS revealed tiny follicles in right ovary but the left was not visualized. On stimulation day 8, there were difficulties visualizing both ovaries. Review of stimulation day 5 estradiol level of 311pg/ml and endometrial thickness of 7.2mm were suggestive of possible follicular development necessitating further search using a transabdominal scan which showed 2 follicles on the right and 1 on the left ovary, the largest measured 12.5mm. The HMG was increased to 6 amps daily and her follicular response was monitored using the transabdominal approach. On stimulation day 11 there were 7 follicles and the largest was 20.6mm; OCR was done transabdominally 35 hours post hCG and 5 oocyte successfully fertilized. A day 3 transfer of 2 good quality embryos was done successfully, however pregnancy test was negative 2 weeks after.

#### **Discussion**

Oocyte retrieval(OCR) is one of the major steps in the process of IVF-ET. Techniques have evolved over the years for OCR; first laparoscopically, then ultrasound guided retrieval (transabdominal –transvesical, transvaginal).[7] In contemporary IVF-ET treatment cycles the transvaginal route of retrieval has become the default and preferred means of OCR albeit some clinical situations may prohibit this approach.[7,8] This series has demonstrated that in scenarios of ovarian inaccessibility transvaginally,a transabdominal ultrasound-guided follicular aspiration for oocyte retrieval can be done safely and efficiently with consequent avoidance of cycle cancellation. A previous study noted that inaccessibility to the ovaries transvaginally is uncommon but could exist especially in situations of anatomic distortions.[9] In line with this observation we noted that all four cases in this series had a prior history of abdominal surgery which likely caused anatomical displacement of the ovaries. Ovarian or pelvic surgeries have also been associated through varying mechanisms with a decline in ovarian reserve and function with consequent poor response during an IVF-ET treatment cycle.[3,10]

The pertinent import from this study is the need for rigorous appraisal of multiple proxy indices for

ovarian response as a means of follicular monitoring and treatment decisions. This was demonstrated in these cases where apparent poor response was noted on transvaginal folliculometry but on the backdrop of previous abdominal surgeries and favourable response values for estradiol and endometrial thickness the need for a more astute search for developing follicles was prompted. Estrogen is produced by developing follicles and similarly acts to cause proliferation of the endometrium. Researchers have shown that after 4 days of gonadotropin stimulation, an estradiol level of >350 pg/ml is highly predictive of successful ovarian follicular response, higher embryo grade and pregnancy outcome while a value of <75 pg/ml is predictive of a poor response and cycle cancellation.[11,12]. Also proliferation of endometrium to a thickness of at least 7mm has been associated with good follicular response and favourable IVF-ET outcome [13,14] Thus one can hypothesize that if there is a favourable estrogen level and endometrial thickness then there are follicles somewhere in the body producing them, the imperative is to look for them and prevent the devastating effect of cycle cancellation.

Transabdominal retrieval is not without complications ranging from damage to adjacent structures and contamination of follicular aspirate to multiple punctures on the abdominal skin with increased potential for discomfort, infection or scarring.[15] also previous literature documented poor oocyte yield and treatment outcome compared to transvaginal OCR.[16] In this study despite the potential for complications from pelvic adhesions we successfully aspirated follicles transabdominally under ultrasound guide without damage to other abdominal structures with appreciable oocyte yield. Similarly we had significant positive pregnancy outcome although this was not compared to transvaginal approach and we did not control for other confounders influencing IVF outcome. Albeit we can posit that transabdominal retrieval can be carried out safely and efficiently in indicated cases with good outcome.

Infertility remains a challenge in sub Saharan Africa with attendant social, psychological and economic burden on the individual involved. Cycle cancellation will further increase this burden with attendant catastrophic sequel. The need for judicious patient selection, appraisal of monitoring indices and individualization of care is emphasized as a means of improving treatment outcome and enhancing client's satisfaction.

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