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Ultrasound monitoring of ovarian follicular growth during spontaneous cycles in Nigerian women

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Summary

Thirty-nine spontaneous cycles in 34 women (22 patients from the infertility clinic and 12 normal volunteers) were serially studied by ultrasound to monitor follicular growth for ovulation prediction and detection. Ovulation was also confirmed by a mid-luteal phase progesterone assay using WHO match RIA kits. Ovulation occurred from the left ovary in 21 cycles (54%) and from the right ovary in 18 cycles (46%). The maximum follicular diameter prior to ovulation was 21.0 ± 3.48 mm with a range of 15 – 28 mm. The maximum pre-ovulatory size in the group of infertile patients 21.4mm (range 15 – 28 mm) was not statistically different from the size in normal volunteers 20.8mm (range 15.5 – 27mm) ($P > 0.5$). Bilateral ovulation occurred in two patients. Changes in shape and/or size of the follicle mostly associated with increased internal echoes were the indices of ovulation in 84.7% of cases.

Follicular diameter of 15mm may indicate imminent ovulation in Nigerian women. Infertility management procedures such as artificial insemination, timed sexual intercourse may commence just before or once this follicular size has been attained until ovulation is detected.

Résumé

39 cycles spontané en 34 femmes de clinique infertilité et douze volontés normals sont été étudiés en série par l'ultrasound à monitère le development de follicule pour la prédiction et le découverte d'ovulation. L'ovulation est été confirmé aussi par l'essai de mi-luteal phase pregesterone utilisant WHO match RIA equipments.

Ovulation est trouvé d'ovarie à gauche en 21 cycles (54%) et en 18 cycles (46%) d'ovarie à droite. Le diamètre de la follicle maximum avant l'ovulation est été 21.0 ± 3.48 mm avec une range de 15 – 28mm.

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Lé pre ovulation pointure en le groupe de femmes infertiles 21.4mm (range 15 – 28mm) n'est été pas différent de statiquement de la pointure de la follicle en les volontés normal 20.8mm (range 15.5 – 27mm) ($P > 0.05$). Les deux ovaries ont ovulé la même cycle en deux patients. Les changes de la forme ou let la pointure de la follicle pour la plupart associé avec les éches internal grossi sont été les indication d'ovulation en 84.7% de cas.

Le diamètre de la follicle de 15mm peut indiquer ovulation imminent en les femmes Nigériennes. Les précédés de management d'infertilité par exemple insemination artificiel, copulation sexuel réglé peut commencer juste avant le moment quanel la pointure de la follicle est atteint jusomà ce que l'ovulation est decouvert.

Introduction

Several methods of ovulation prediction and detection have been used within infertility management programmes[1,2,3]. In advanced countries, improved technology particularly of pelvic ultrasonography has made monitoring of follicular development more precise, convenient and reproducible. In Nigeria and other less developed countries, less specific indirect methods such as Basal Body Temperature (BBT) measurement and various hormone assays in urine and blood as well as cervical mucus scores have been used [4,5].

However, in recent times, there has been an upsurge in the utilisation of newer methods of infertility management such that there are centres that have introduced *in-vitro* fertilisation and other assisted reproductive technology programmes which may require ovarian follicular growth monitoring[6].

Discrepancies in maximum follicular diameter prior to ovulation in Caucasians[7] and the claim that local diet may affect ovarian function[8] calls for background information on follicular growth patterns in our population. This is the main thrust of this paper.

Patients, materials and methods

This cohort study was carried out on 46 menstrual cycles in 22 patients attending the infertility clinics of the department of Obstetrics and Gynaecology, and 12 volunteer students of the College of Medicine and School of Midwifery of University College Hospital (UCH) Ibadan, Nigeria over a six month period, January to June 1989. At the commencement of the study, 28 infertile but ovulating patients and 16 student volunteers participated; however 6 patients and 4 volunteers were dropped because of irregular attendance. The patients were recruited after a careful scrutiny of their medical records to exclude any major systemic disease or evidence of anovulation. Patients with gross pelvic adhesions or pathology that could make ovarian scanning difficult and those who had taken any hormonal preparations in the preceding 6 months were also excluded. All the patients were within the reproductive age group of 18-35 years and had regular cycles of 21-35 days within the preceding six months.

All the women were seen on day 6 of the menstrual cycle and then followed by ultrasonography. Trans-abdominal ultrasound scanning was carried out on each patient between 8.00 a.m. and 9.00 a.m. using a real time sector scanner (Sonoline SX-Siemens) with a 3.5 MHz transducer probe. The full bladder technique described by Donald[9] was used.

The widest diameters in 3 planes of the follicle were then measured using electronic calipers. The mean follicular diameter was then determined. Morphological changes consistent with follicular development, ovulation and development of the corpus luteum were noted. Ovulation was said to have occurred if there was collapse of a matured previously developing follicle; change in shape, reduction in size, change in the echogenic properties or disappearance of a mature follicle. The day of ovulation thus determined was defined as the 24 hour period between the visualisation of a mature follicle at one scan and the appearance of a ruptured follicle or early corpus luteum at the next scan. In other words, the day of maximal follicular diameter was designated as day zero (0), and the day of detection of follicular rupture was designated as day 0⁺. Five millilitres of blood was obtained on day 0⁺ of the cycle for the determination of plasma progesterone level. The blood samples were centrifuged at 3500 rpm for 15 minutes and the serum stored at -20°C until subsequent analysis by radioimmunoassay using the WHO matched reagent programme.

Results

A total of 46 menstrual cycles in 34 patients were studied. Twelve patients had two menstrual cycles studied. Two patients could not complete the serial scanning and in another 5 cycles the graffian follicle could not be identified and followed up consistently. These seven cycles were therefore excluded from the calculations. The results of the remaining 39 cycles which were fully studied are analysed.

The infertile patients who participated in the study were highly motivated and readily accepted the procedure because of their hope for conception. The volunteers found it exciting to view their own follicles, they were reassured of the normalcy of their follicles.

All the cycles included in the analysis were ovulatory as detected by ultrasound scan and a mid-luteal phase progesterone level more than 4.9nmol/litre. This is the value found to be consistently associated with secretory endometrium at University College Hospital Ibadan.

In all 514 ultrasound scans were performed each lasting about 5 - 7 minutes. No ovary was found dominant over the other concerning the presence of the leading follicle and therefore, the site of ovulation. In this study, ovulation occurred from the right ovary in 18 cycles (46%) and from the left ovary in 21 cycles (54%).

Comparing the maximum follicular diameters in the infertile patients (15-28mm, mean 21.4mm) and the volunteers (15.5 - 27mm, mean 20.8mm), no significant difference in the two groups was demonstrated ($P > 0.05$). Most of the patients in this study (55%) were aged 25 - 29 years.

The mean diameter of each follicle was determined daily till the day of follicular rupture. The mean and standard deviation of the mean follicular diameters are shown in Table 1. The mean and standard deviation of the maximum follicular diameters prior to rupture was 21.0 ± 3.48 mm while the range was 15-28mm. Figure 1 shows a mature follicle.

Bilateral mature follicles, one from each ovary both ovulating within 24 hours of each other were observed in two patients (5%). The rest of the patients had single follicles. The changes in ultrasonographic images of the follicles that indicated ovulation are shown in Table 2. 84.7% of the diagnoses of ovulation were made by the observation of a change in shape and or size of the follicle mostly associated with an increase in its echogenic properties (Fig. 2)

Table 1: Follicular diameters in spontaneous cycles

Days Released to Day of Rupture	-8	-7	-6	-5	-4	-3	-2	-1	0
Mean Follicular Diameters (mm).	7.0	8.5	11.2	12.0	13.8	14.4	17.4	18.9	21.0
S.D.	0.00	0.50	1.69	2.80	2.07	2.71	3.15	3.12	3.48
Range (mm)	7.0	8.0-9.0	8.5-13.0	8.5-15.0	9.0-17.0	9.0-19.5	11.0-23.0	12.0-25.0	15.0-28.0

Table 2: Ultrasonographic diagnostic criteria of ovulation

Criteria	Number	Percentage
Decrease in size \pm int. echoes	6	15.4)
Decrease in shape \pm int. echoes	12	30.8)
Decrease in shape/size	15	38.5)
Internal echoes alone	4	10.3)
Disappearance of follicle	2	5.0)



Fig 1: Mature Graafian follicle, scanned on day 13 of menstrual cycle (note regularity in shape) (B = Urinary Bladder, F = Follicle, U = Uterus)



Fig 2: Follicle after ovulation. The shape is now irregular with early internal echoes. (B = Urinary Bladder, F = Collapsed Follicle U = Uterus)

Discussion

Ultrasonography has become an important procedure in infertility management throughout the developed world and its progressive introduction in Nigeria is very encouraging. In this study ultrasonography has been used to monitor ovarian follicular development and rupture.

This study shows the average maximum diameter of the follicle prior to ovulation to be 21.0 ± 3.48 mm. These figures generally agree with those of other published data [7, 10, 11] and accords with the conclusion of Queenan *et al* [12], that no critical follicular size could serve as an index of imminent ovulation. It can be said however that follicles greater

than 15 mm in diameter can progress to ovulation.

Indeed there was fertilisation of an oocyte retrieved from a follicle whose maximum diameter was 15.5mm. This is at variance with the observation of Marinho *et al*[7] that a follicle of less than 18mm in diameter is unlikely to lead to a pregnancy. A minimum pre-ovulatory diameter of 15 mm seems to be essential for pregnancy [13, 14, 15]. However, a minimum pre-ovulatory diameter of 13.1mm for the leading follicle in induced conceptual cycles had been reported[16].

In the *in-vitro* fertilisation programme of the Royal Women's Hospital, Melbourne, Australia, the range of diameters of follicles producing fertilised oocytes was reported as 10 – 31mm [17]. Size does not usually correlate with oocyte maturation after this minimum size (15.00 mm) and no optimal follicle size guarantees the presence of a mature oocyte[15, 17]. The wide scatter of maximum follicular diameter also suggests that several ovarian scans or concomitant detection of the plasma luteinizing hormone peak level is mandatory if ovulation need to be detected or predicted within less than 24 hours of the event.

The occurrence of multiple ovulation seen in 2 cycles (5%) is not a unique phenomenon. This has been reported in 4.6 – 14.3 per cent of spontaneous menstrual cycles[12, 16, 18]. In spontaneous cycles when two or more follicles develop, there is usually one in each ovary but with ovarian stimulation, multiple mature follicles can develop in the same ovary[13, 18]. The concept of ovarian stimulation by centrally acting substances thought to be in the local diet, has been supported by higher levels of gonadotropins in patients who have had multiple pregnancy. This theory has not been borne out by the results of this study as the range of maximum follicular size does not seem to suggest increased stimulation of the ovaries. Indeed, Nylander[8] who originally published this theory has observed a decline in twinning rates in recent time and has attributed this to the move towards an European type of diet.

The most consistent ultrasonographic feature of ovulation in this study was collapse or change in shape or size of the follicle. This is similar to the findings of Queenan *et al*[12] but at variance with the findings of Marinho *et al*[7] who found that disappearance of the follicle was the most consistent feature. This however, only confirmed the variability of the ultrasonographic criteria of ovulation, and further studies on this subject need to be conducted in this region.

In conclusion, ultrasonographic services may be

capital intensive for a developing country but their accuracy and reliability in ovulation detection justifies its use in tertiary centres or specialised fertility management establishments. Patients who are undergoing pre-ovulatory ovarian scanning must be informed that it is not a guarantee of conception.

Follicular diameter of 15 mm may indicate imminent ovulation and infertility procedures such as artificial insemination, timed sexual intercourse may commence just before or once this follicular size has been attained until ovulation is detected.

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