# DIAGNOSIS OF OVULATORY DYSFUNCTION IN UNEXPLAINED INFERTILITY

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## SUMMARY

**45 women of unexplained infertility and 20 fertile controls underwent serial Transvaginal Sonography (TVS) followed by premenstrual endometrial biopsy (EB) for diagnosing Luteal phase defect (LPD) and the older methods, viz, basal body temperature (BBT) and next menstrual period (NMP) were compared with with the results.**

**Prevalence of LPD was more in infertility (30.3%) than fertile group (10%) but the difference was not statistically significant. TVS was more specific compared to NMP and BBT in diagnosing LDP. Abnormal folliculodynamics including small follicles and luteinised unruptured follicle syndrome (LUFS) have a significant association with unexplained infertility, more so with LPD.**

**Since LPD and abnormal folliculodynamics are treatable, serial sonography with timed EB is recommended in all cases of unexplained infertility before undertaking empirical and expensive treatment.**


## *INTRODUCTION*

Ovulatory dysfunction constituting abnormal folliculodynamics and luteal defects (LDP) is an important cause of unexplained infertility. Luteal phase defect (LPD) has been a controversial subject for nearly half a century (Jones 1949) owing to the lack of a diagnostic gold standard. Timed endometrial biopsy in two cycles remains the most popular method so far but only presumptive evidences of ovulation have been used like backdating from next menstrual period (NMP), basal body temperature (BBT) and LH surge which are not

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completely reliable. Now direct timing of ovulation by transvaginal sonography (TVS) is likely to increase the diagnostic accuracy besides detecting any associated follicular abnormalities. Therefore, this study was designed (1) to evaluate prevalence of LPD in infertile and fertile women, (2) to compare TVS with previous methods like NMP and BBT (3) to estimate incidence of abnormal folliculogenesis and luteinised unruptured follicle syndrome (LUFS).

## *MATERIALS AND METHODS*

**Subjects :** 45 women in the age group of 20-45 years with regular cycles of 21-35 days and with unexplained infertility (normal husband semen analysis, good postcoital test, normal HSG and/or laparoscopy; genital tuberculosis ruled out with prior endometrial biopsy) for ≥ 3 years.

**Controls :** 20 women of similar age and cycle length with atleast one childbirth < 5 years and no delivery/abortion < 1 year; no form of oral, injectable or intrauterine contraceptive used for last 1 year.

After informed consent, all women were asked to maintain BBT charts and practice abstinence/barrier contraception in the study cycle. Serial follicular monitoring was done beginning on the ninth day of the cycle till ovulation could be detected or LUFS diagnosed.

Endometrial biopsy (EB) was taken on 10th to 12th day post-ovulation and in LUFS cases 2-3 days prior to expected day of menses and the women were asked to note down NMP. Noyes et al's (1950) criteria were adopted for interpretation of the biopsy.

## *RESULTS*

Out of 45 infertile women, 4 conceived during the study cycle and were excluded from analysis. Another 8 patients had LUFS and were studied separately. Of the remaining 33 patients, 10 were diagnosed to have LPD by ultrasound (30.3%) compared to 2 out of 20 fertile controls (10%). [Fig. 1] $Chi^2$ test revealed that there was no significant difference ($P > 0.05$)

NMP diagnosed LPD in 42.4% infertile (14 out of 33) and 30% (6 out of 20) fertile women. BBT charts were maintained only by 60% women (27 infertile and 12 fertile) and of these also, 30% had inconclusive charts making it less useful in this population. In those cases where clear cut temperature elevation was noted; 42.9% (9 out of 21) infertile and 33.3% (3 out of 9) fertile women had LPD. Thus there was no statistically significant difference in the prevalence of LPD by any of the methods (Fig. 1). However, LPD was overdiagnosed in 18.8%

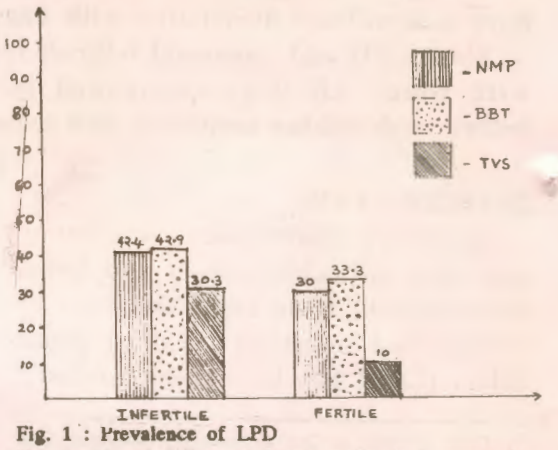


**Fig. 1 : Prevalence of LPD**
**No significant difference between the two groups by any method ($P > 0.05$)**

(10 out of 53) and 16.6% (5 out of 30) respectively by NMP and BBT - compared to TVS although no case was missed. Clearly, both NMP and BBT lack specificity compared to ultrasound.

The mean follicular size prior to rupture in infertile was 21.09 mm (SD 4.08) compared to 20.17 mm (SD 2.44) in fertile. (Table I) The difference was not statistically significant (student t test done, $p > 0.05$). However, closer look showed that in LPD group it was, 19.53 mm (SD 2.73) which was significantly different from the non-LPD group (21.13 mm SD 2.5 $p < 0.01$). Table II

The rate of follicular growth prior to

**Table I**

**Study of follicular parameters**

| | Rate of growth of follicle (mm / day) | Mean diameter of follicle at rupture (mm) | Incidence of Abnormal follicles Small (≤ 17 mm) | LUFS |
|---|---|---|---|---|
| Unexplained infertility (n = 41) | 1.9 (SD 0.8`6) | 21.09 (SD 4.08) | 6 | 8 |
| Fertile (n = 20) | 1.88 (SD 0.766) | 20.17 (SD 2.44) | 1 | 0 |
| | Student t | Student t | Fisher's exact | |
| Significance | P > 0.05 Not significant | P > 0.05 Not significant | P < 0.05 Significant | |

**Table II**

**Comparison of Folliculodynamics between LPD and Non - LPD**

| | Mean Follicular Diameter at Rupture (mm) | Mean Rate of Growth of Follicle (mm | Small Follices |
|---|---|---|---|
| LPD (n = 12) | 19.53 (SD 2.73) | 1.78 (SD 0.707) | 4 |
| Non LPD (n = 41) | 21.13 (SD 2.5) | 1.95 (SD 0.818) | 3 |
| P Value | P < 0.01 Highly significant Student t | P < 0.05 Significant Student t | P < 0.05 Significant fisher's exact |

**Table III**

**Comparison of LUFS with Fertile Controls**

| | Mean cycle length (days) | Mean max. follicular diameter (mm) | Mean rate of growth of follicle (mm / day) |
|---|---|---|---|
| LUFS (n = 8) | 30.43 (SD 2.19) | 27.28 (SD 4.44) | 2.64 (SD 0.35) |
| Fertile control (n = 20) | 26.9 (SD 2.4) | 20.17 (SD 2.44) | 1.88 (SD 0.766) |
| | Student t test | Showed P < 0.05 | |

rupture was 1.9 mm/day (SD 0.81) in infertile and 1.88 mm/day (SD 0.76) in fertile women (Student t test, p > 0.05, not significant). But in the LPD group it was 1.78 mm/day (SD 0.707) compared to 1.95 mm. day (SD 0.818) in the non-LPD group which was significant (P < 0.05) Table II.

The incidence of rupture of small follicles (≤ 17 mm) was 14.6% (6 out of 41) in the infertile as against 5% (1 out of 20 in the fertile women (Table I) LUFS was seen in 8 infertile women (19.5%) with subsequent cycles showing persistent abnormality whereas not a single case was seen among fertile women. Thus, abnormal folliculodynamics was seen in 34.1% (14 out of 41) infertile compared to only 5% (1 out of 20) fertile women. ($Chi^2$ test; P < 0.05, significant)

## *DISCUSSION*

There is no reliable method of estimating LPD resulting in a wide range of prevalence in infertility 3.5-65% (Jones 1949, Gautray et al 1981, Cumming et al 1985, Balasch et al 1985, Davidson et al 1987). Li et al (1990) found a significant number of infertile women with LPD (20%) in comparison with normal women (3.1%). But Davidson et al (1987) and Wentz et al (1990) refute this claim and in our study too, no significant difference was seen in prevalence of LPD among infertile and fertile women. However further studies with larger number of controls and utilising TVS had dating are required to conclusively establish the fact.

Shoupe et al (1989) correlated histologic dating with TVS, LH surge, BBT and NMP in 13 parous normal cycling women and demonstrated that TVS had the best correlation (96.1%). In our study also, TVS was more specific than NMP or BBT in diagnosing LPD.

Abnormal folliculodynamics occurred in a significantly higher proportion of unexplained infertility (34.1%) compared to fertile women (5%). Furthermore, when only LPD subgroup was considered, the mean follicular diameter at rupture and mean rate of follicular growth prior to rupture were both significantly lower

and rupture of small follicles (≤ 17 mm) higher (33.3%) than non-LPD group (7.3%) (Table II). These figures are similar to those of Ying et al (1988) - 39% small follicles in LPD and 9% in non - LPD while Check et al (1984) found stronger association (52%) of small follicles with LPD reiterating possible role of abnormal folliculogenesis in etiology of LPD.

Study of LUFS cycles revealed that mean cycle length (30.43 days SD 2.19), mean rate of growth of follicle (2.64 mm/ day SD 4.44) and the mean maximum diameter of follicle (27-28 mm SD 4.44) were all significantly greater in LUFS than women in fertile women (Table III). The endometrium was out of phase in 62.5% (5 out of 8 cases) when calculated from NMP. Evidently, LUFS cycles are distinctly abnormal in many respects as observed earlier by Hamilton et al (1990). Their exclusive presence in unexplained infertility and persistence in subsequent cycles suggests a causative role of LUFS in infertility.

To Conclude, TVS with EB is an accurate, easily reproducible and cost effective method of diagnosing both LPD and abnormal folliculodynamics. Since ovulatory dysfunction is potentially treatable with good results and at lesser cost (Daly et al 1991) it should be looked for in all cases of unexplained infertility before resorting to empirical treatment like IUI, IVF-ET, GIFT or ZIFT.

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