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An elevated basal FSH reflects a quantitative rather than qualitative decline of the ovarian reserve

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BACKGROUND: Many cycling women with elevated basal FSH level have been discouraged from undergoing IVF treatment. This is because elevated basal FSH is associated with poorer assisted reproduction treatment outcome. It has been argued that high FSH reflects not only reduced ovarian reserve but also poor oocyte quality. The aim of this study is to assess the value of treating cycling women who have elevated basal FSH and to assess the reasons for the reduction in both pregnancy rate (PR) and live birth rate (LBR). METHODS: Between January 1997 and December 2001, 2057 patients underwent 3401 consecutive IVF/ICSI cycles in which the basal level of FSH (days 2–4) was determined at an earlier cycle. Analysis, however, was only performed for a single cycle per patient. All cases were divided into four cohorts according to FSH levels: group A, FSH <10 IU/ml; group B, 10.1–15 IU/ml; group C, 15.1–20 IU/ml; and group D, FSH >20 IU/ml. Each group was stratified further into subgroups according to age, ≤38 and >38 years. RESULTS: Both PR (A, 32.3%; B, 19.8%; C, 17.5%; and D, 3%) and LBR (A, 24.7%; B, 13.2%; C, 13.8%; and D, 3%) were significantly reduced in the higher FSH level groups. LBR was significantly higher in the younger subgroups (A, 32.2%; B, 21.8%; C, 20%; and D, 16.7%) as compared with the older subgroups (A, 12.1%; B, 8.3%; C, 10.5%; and D, 0%). Higher levels of FSH were significantly associated with more cycle cancellation, a larger amount of gonadotrophin required to achieve follicular maturity, and a lower number of eggs collected, embryos available and embryos transferred. In all cases, however, there was no significant correlation between FSH levels and fertilization rate or miscarriage rate. Younger cycling women with elevated FSH had significantly higher LBR compared with older women with normal FSH (21.2% versus 12.1%). Furthermore, the cumulative LBR after three cycles in these younger patients with elevated FSH levels was 49.3%. CONCLUSION: Although there is a reduction in both PR and LBR associated with higher levels of basal FSH, it is clear that in cycling women, high basal FSH is not a contraindication to IVF treatment, and a respectable PR and LBR can be achieved especially in young women. The reduction in PR and LBR is due to reduced reserve rather than poor oocyte quality. Clinics refusing to treat cycling women with elevated basal FSH levels may be denying these women a reasonable, albeit low, chance of achieving a birth with their own genetic material. Clinicians should use basal FSH levels as a guide to advise patients about their chances of achieving a live birth, not to exclude patients with a predicted lower success rate from a treatment programme.

Key words: basal stimulating hormone/FSH/IVF/IVF outcome/pregnancy rate

Introduction

Determination of ovarian reserve by measuring day 3 basal FSH in normal cycling women is often used in many IVF units prior to assisted conception treatment to choose patients eligible for starting assisted reproduction technique (ART) cycles. Many cycling women with borderline elevated basal FSH have been discouraged from undertaking ART treatment because the chance of success is thought to be low, and have been directed to other modalities such as oocyte donation or adoption.

The cycle day 3 FSH level is one of the most commonly used tests for predicting success in IVF treatment. This was first described by Muasher *et al*. (1988). Lenton *et al*. (1988) demonstrated that women with an elevated cycle day 3 FSH had reduced ovarian reserve. Since then, several studies have shown that women with an elevated FSH level, independent of age, have a poor response to ovarian stimulation, leading to a lower pregnancy rate with ART (Scott *et al*., 1989; Martin *et al*., 1996; Sharif *et al*., 1998; El-Toukhy *et al*., 2002). Recently, however, El-Toukhy *et al*. (2002) argued that young age does not protect against the adverse effects of reduced ovarian reserve, suggesting that an elevated day 3 basal FSH level is associated not only with a low response, but also with poor quality oocytes leading not only to a reduction in pregnancy rate but also to a rise in miscarriage rates.

Table I. Stimulation characteristics and cycle outcome

	Group A (FSH <10.1 IU/l)	Group B (FSH 10.1–15 IU/l)	Group C (FSH 15.1–20 IU/l)	Group D (FSH >20 IU/l)
No. of patients	1721	245	58	33
Mean age ± SD[b]	35.8 ± 4.7	38.2 ± 4.4	38.8 ± 4.4	40.3 ± 4.8
Duration of infertility (mean ± SD)[b]	4.45 ± 3.7	4.57 ± 4.1	3.94 ± 2.69	4.21 ± 3.87
Cancellation rate (%)[a]	6.1	14.0	32.8	42.4
Days of taking gonadotrophins (mean ± SD)[b]	11.7 ± 2.9	11.8 ± 2.9	11.9 ± 4.0	11.6 ± 3.8
No of ampoules[c] consumed (mean ± SD)[d]	37.6 ± 15.6	49.4 ± 18.7	51.0 ± 17.2	49.1 ± 21.6
Estradiol (IU) per follicle on HCG day[e]	423.1	417.8	452.3	683.9
Average no. of oocytes collected[d]	9.9	5.6	3.8	2.5
Fertilization rate (%)[e,f]	59.5%	58.3%	60.9%	62.0%
Average no of available embryos for transfer[d]	5.53	3.14	2.92	2.15
Average no of embryos transferred[d]	2.20	1.82	1.63	1.05
Pregnancy rate per started cycle in % (*n*)[b]	32.3 (554/1721)	19.8 (48/245)	17.5 (10/58)	3.0 (1/33)
LBR per started cycle in % (*n*)[b]	24.7 (425/1721)	13.2 (32/245)	13.8 (8/58)	3.0 (1/33)
Pregnancy rate per egg collection in % (*n*)[b]	34.3 (554/1615)	23.0 (48/209)	25.6 (10/39)	5.3 (1/19)
LBR per egg collection in % (*n*)[b]	26.3 (425/1615)	15.3 (32/209)	20.5 (8/39)	5.3 (1/19)
Miscarriage rate in % (*n*)[e]	23.3 (129/554)	33.3 (16/48)	20.0 (2/10)	0 (0/1)
LBR when 1–4 eggs collected in % (*n*)[e]	10.5 (26/248)	8.5 (7/82)	19.0 (4/17)	9.1 (1/11)
Cumulative LBR after three cycles	51.2%	38.9%	36.1%	19.2%

[a]Significant statistical comparison using χ^2 cross-tabulation test with $P < 0.001$.
[b]Values are not statistically significant.
[c]Number of ampoules = in cases of pure FSH (75 IU FSH) and in cases of HMG (75 IU FSH and 75 IU LH).
[d]Significant statistical comparison using ANOVA test with $P < 0.001$.
[e]Not statistically significant.
[f]Mean no. of fertilized oocytes/mean no. of oocytes collected × 100.
[g]Mean of average amount of gonadotrophin used for stimulation.

Recently some studies have shown that women with elevated basal FSH levels can still achieve reasonable pregnancy rates with ART (Levi *et al*., 2001; Esposito *et al*., 2002; van Rooij *et al*., 2003), especially in younger women. Those cycling women who are discouraged from undertaking treatment may, therefore, be denied a reasonable chance of achieving a pregnancy with their own genetic child. In our department, we operated on the principle that if the woman was cycling regularly, then we should offer ART regardless of the basal level of FSH. The purpose of this study is to assess the value of treating cycling women who have an elevated basal FSH and to evaluate the hypothesis that the lower pregnancy rate in cycling women with elevated basal FSH levels is due to a reduced ovarian reserve (reflected by cancellation rate, dose of gonadotrophins used to stimulate the ovaries and number of eggs collected) rather than poor oocyte quality (reflected by fertilization and miscarriage rates). This would help the patient understand that if they managed to get to the stage of egg collection and eggs were obtained, then their chance of having these eggs fertilized normally would be similar to that of any other couple and that their chance of becoming pregnant was similar to that of women of their own age with a similar number of embryos generated. Moreover, should their cycle result in a pregnancy, it would not be at higher risk of miscarriage.

Materials and methods

Data of patients undergoing IVF/ICSI treatment in our unit are routinely collected prospectively and stored in a system for IVF (MedicalSys, London, UK).

Study population

Between January 1997 and December 2001, all patients underwent IVF/ICSI treatment. The most recent basal FSH level (days 2–4 of the menstrual cycle) was determined in a cycle prior to the start of IVF/ICSI treatment. There was no attempt to check the level of FSH in the treatment cycle itself. Patients were treated with either a long or short protocol. All patients, regardless of age or FSH levels, underwent ovarian stimulation.

Serum FSH level test

Serum FSH concentration was measured using a two-step chemiluminescent microparticle immunoassay (CMIA) and analysed by Abbott Architect™ System (Abbott Laboratories, IL). The analytical sensitivity of the assay was calculated to be better than 0.05 mIU/ml ($n = 36$ runs). Analytical sensitivity is defined as the concentration at 2 SDs from the ARCHITECT FSH MasterCheck™ Level 0 (0.00 mIU/ml), and represents the lowest measurable concentration of FSH that can be distinguished from zero. The specificity of the assay was determined by studying the cross-reactivity of LH, thyroid-stimulating hormone (TSH) and HCG. The percentage cross-reactivity was calculated and was shown to be 0.002% for LH, 0.043% for TSH and 0.001% for HCG. The inter- and intra-assay coefficients of variation were 2.9 and 3.8%, respectively.

Treatment protocol

Ovarian stimulation was carried out with either recombinant FSH, HMG or urinary FSH. A transvaginal scan was performed prior to ovarian stimulation to ensure the ovaries were quiescent. For the long protocol, patients were downregulated with either Nafarelin or Buserelin at mid-luteal phase. For the Cetrotide protocol, GnRH hormone antagonist was commenced when the leading follicle reached 12 mm. When follicles reached pre-ovulatory size (18–22 mm), 10 000 IU (for patients taking HMG) or 15 000 IU (for

patients taking FSH) of HCG were administrated. Oocytes were aspirated using transvaginal ultrasound guidance 34–36 h after HCG administration. Embryo transfer was performed on day 2 or day 3 using a soft catheter with transabdominal ultrasound guidance. All patients received progesterone 400 mg pessaries as supplement throughout the luteal phase. A pregnancy test was performed 2 weeks after transfer of embryos.

Definition of outcome

A mature follicle was defined as a follicle ⩾17 mm on transvaginal ultrasound scan. A miscarriage or spontaneous abortion was defined as a pregnancy lost before 24 weeks of gestation. A pregnancy was defined as a positive serum or urine HCG test and a sac seen on ultrasound scan, or an ectopic pregnancy. A live birth was defined as a pregnancy resulting in delivery of a viable infant. Twins and triplets were counted as one live birth. Fertilization rate was defined as number of two pronuclear (2 PN) embryos per number of oocytes collected × 100 for each treatment cycle including ICSI cycles. Cancellation was defined as cycle started but no egg collection performed. Treatment cycles which proceeded to egg collection but with no eggs retrieved were included as normal cycles.

Data analysis

Data were collected in the Medical System for IVF (MedicalSys, London, UK) and analysed with the Statistics Package for Social Sciences (SPSS, Surrey, UK). Descriptive statistical analysis was performed initially to examine the normality distribution of all continuous variances for parametric statistical tests. Associations between FSH values and pregnancy rates, miscarriage rates and live birth rates (LBRs) were examined with a χ^2 cross-tabulation test stratified by age. Analysis of variance (ANOVA) was then conducted to assess the relationships between FSH levels and duration and amount of gonadotrophin required to achieve follicular maturity, number of mature follicles, number of available embryos for transfer, number of oocytes collected and fertilization rate. Statistical significance was set at $P < 0.05$.

Results

Between January 1997 and December 2001, 2057 patients underwent 3401 consecutive IVF/ICSI cycles. Analysis, however, was only performed. Analyses, however, was only performed on the first treatment cycle of each patient. Thus only 2057 cycles are studied. We have analysed the data in relation to different levels of FSH and found no difference in pregnancy rate and LBR or other outcome parameters in patients with FSH <5 IU/l, those between 5 and 8 IU/l and those between 8 and 10 IU/l. We did, however, observe a significant changes if the value of FSH was >10 IU/l. All patients with FSH ⩽10 IU/l were therefore united in one group. For the purpose of analysis, the cohort was thereafter divided into four groups as follows: group A, FSH ⩽10 IU/l; group B, FSH 10.1–15 IU/l; group C, FSH 15.1–20 IU/l; and group D, FSH >20 IU/l.

Table I shows the patients' demographics, stimulation characteristics and treatment outcome in all four cohorts. Women's mean age was slightly higher in the higher FSH groups but the difference was not statistically significant. The pregnancy rate and LBR per started cycle and per egg collection were significantly lower ($P < 0.001$) in the higher FSH groups. There were no significant differences between the four groups with regard to duration of infertility, miscarriage rate, fertilization rate, serum estradiol per follicle, duration of stimulation and average number of embryos transferred. Furthermore, the mean estradiol level was not different between study groups. However, the amount of gonadotrophin required to achieve follicular maturity and the average daily dose of gonadotrophin used for stimulation were higher in the elevated FSH groups. The average number of oocytes collected and average number of available embryos for transfer were significantly reduced ($P < 0.001$) in the elevated FSH groups. The cancellation rate was significantly higher ($P < 0.001$) in the elevated FSH groups. The highest FSH level measured in a patient achieving a live birth was 32.8 IU/l. A singleton was delivered at 39 weeks. We further analysed the cumulative LBR after three cycles for each study group. This showed the same pattern, with a reduction in cumulative LBR as the level of FSH is elevated (group A = 51.2%, group B = 38.9%, group C = 36.1% and group D = 19.2%).

Tables II and III examine the relationship between age and level of FSH. Table II illustrates the effect of the level of FSH in women below and above the age of 38. In this context, the same trend as shown in Table I is apparent for the two age groups; however, in those patients aged ⩽38, the pregnancy rate and LBR were reduced, but not significantly, as FSH levels increased. An LBR of at least 20% was always achieved in patients with FSH between 10 and 20 IU/l, and 16.7% in patients with FSH >20 IU/l. The miscarriage rate and fertilization rate were not influenced by the increased FSH levels. For those patients aged >38, the pregnancy rate and LBR were significantly reduced as FSH levels increased; however, the fertilization rate was not influenced by the increased FSH levels. None of the patients with FSH >20 IU/l achieved a pregnancy in their first cycle; however, 16.7% (1/6) had a live birth in their second treatment cycle.

Table III examines the same data but illustrates the effect of age within each FSH group. As shown, age is a significant factor affecting treatment outcome. For those patients in the same FSH group, there was a marked and significant difference in the two age groups, i.e ⩽38 and >38, whereby the younger patients had a lower cancellation rate, higher numbers of eggs collected, more embryos available for transfer, higher pregnancy rate, LBR and lower miscarriage rate. It is noticeable, however, that the fertilization rate was not significantly different within any of the age subgroups.

Table IV compares the outcome for younger patients with high FSH and older patients with normal FSH. As shown, age was the most significant factor in influencing the outcome. Although younger patients with high FSH appeared to have a lower number of oocytes collected and lower number of available and transferred embryos, their pregnancy rate and LBR were both significantly higher than those of older women with normal FSH.

Discussion

Most clinics use a basal day 3 FSH level as a screening tool to assess the chance of one particular patient achieving a pregnancy or a live birth with IVF treatment. This practice is based on earlier studies showing that elevated day 3 FSH levels

Table II. Stimulation characteristics and cycle outcome of patients aged <38 and ⩾38 in all four FSH groups

	Age <38 years				Age ⩾38 years			
FSH groups	Group A	Group B	Group C	Group D	Group A	Group B	Group C	Group D
No. of patients	1082	87	20	6	639	156	38	27
Cancellation rate (%)[a]	3.9	11.5	20.0	66.7	9.7	15.4	39.5	37.0
Average no. of oocytes collected[b]	11.0	7.29	5.7	3.0	7.83	4.67	2.64	2.41
Fertilization rate (%)[c,d]	60.0	58.2	56.1	73.1	58.4	58.4	64.6	60.2
No. of embryos available for transfer[b]	6.13	3.62	4.25	4.00	4.46	2.86	2.00	1.94
Average no of embryos transferred[d]	2.24	1.87	1.94	1.67	2.13	1.80	1.42	0.95
Pregnancy rate per started cycle in % (*n*)	40.3[d] (434/1082)	29.9[d] (26/87)	25.0[d] (5/20)	16.7[d] (1/6)	18.8[a] (120/639)	14.1[a] (22/156)	13.1[a] (5/38)	0.0[a] (0/27)
LBR per started cycle in % (*n*)	32.2[d] (348/1082)	21.8[d] (19/87)	20.0[d] (4/20)	16.7[d] (1/6)	12.1[a] (77/639)	8.3[a] (13/156)	10.5[a] (4/38)	0.0[a] (0/27)
Pregnancy rate per egg collection in % (*n*)	41.5[c] (434/1035)	33.8[d] (26/77)	31.3[d] (5/11)	50.0[d] (1/2)	20.8[a] (120/577)	16.7[a] (22/132)	21.7[a] (5/23)	0.0[a] (0/27)
LBR per egg collection in % (*n*)	33.6[d] (348/1035)	24.7[d] (19/77)	25.0[d] (4/16)	50.0[d] (1/2)	13.2[a] (77/577)	9.8[a] (13/132)	17.4[a] (4/23)	0.0[a] (0/27)
Miscarriage rate (%)[a]	19.8	26.9	20.0	0	35.8	40.9	20.0	NA
Cumulative LBR after three cycles	62.1%	51.7%	37.8%	16.7%	33.1%	29.5%	32.9%	16.7%

[a]Significant statistical comparison using χ^2 cross-tabulation test with $P < 0.001$.
[b]Significant statistical comparison using ANOVA test with $P < 0.001$.
[c]Mean no. of fertilized oocytes/mean no. of oocytes collected × 100.
[d]Not statistically significant.

Table III. Stimulation characteristics and cycle outcome of patients <38 and ⩾38 years in all four FSH groups

	Group A (FSH <10.1 IU/l)		Group B (FSH 10.1–15 IU/l		Group C (FSH 15.1–20 IU/l)		Group D (FSH >20 IU/ol)	
	<38	⩾38	<38	⩾38	<38	⩾38	<38	⩾38
No. of patients	1082	639	87	156	20	38	6	27
Cancellation rate (%)[a]	3.9	9.7	11.5	15.4	20.0	39.5	66.7	37.0
Average no. of oocytes collected[b]	11.0	7.83	7.29	4.67	5.7	2.64	3.0	2.41
Fertilization rate (%)[c,d]	60.0	58.4	58.2	58.4	56.1	64.6	73.1	60.2
Available no of embryos for transfer[b]	6.13	4.46	3.62	2.86	4.25	2.00	4.00	1.94
Average no of embryos transferred[d]	2.24	2.13	1.87	1.80	1.94	1.42	1.67	0.95
Pregnancy rate per started cycle in % (*n*)	40.3 (434/1082)	18.8 (120/639)	29.9[d] (26/87)	14.1[a] (22/156)	25.0[d] (5/20)	13.1[a] (5/38)	16.7[d] (1/6)	0.0[a] (0/27)
LBR per started cycle in % (*n*)	32.2 (348/1082)	12.1 (77/639)	21.8[d] (19/87)	8.3[a] (13/156)	20.0[d] (4/20)	10.5[a] (4/38)	16.7[d] (1/6)	0.0[a] (0/27)
Pregnancy rate per egg collection in % (*n*)	41.5 (434/1035)	20.8 (120/577)	33.8[d] (26/77)	16.7a (22/132)	31.3[d] (5/11)	21.7[a] (5/23)	50.0[d] (1/2)	0.0[a] (0/27)
LBR per egg collection in % (*n*)	33.6 (348/1035)	13.2 (77/577)	24.7[d] (19/77)	9.8[a] (13/132)	25.0[d] (4/16)	17.4[a] (4/23)	50.0[d] (1/2)	0.0[a] (0/27)
Miscarriage rate (%)[a]	19.8	35.8	26.9	40.9	20.0	20.0	0	NA
Cumulative LBR after three cycles	62.1%	33.1%	51.7	29.5%	37.8%	32.9%	16.7%	16.7%

[a]Significant statistical comparison using χ^2 cross-tabulation test with $P < 0.001$.
[b]Significant statistical comparison using ANOVA test with $P < 0.001$.
[c]Mean no. of fertilized oocytes/mean no. of oocytes collected × 100.
[d]Not statistically significant.

are associated with a reduced success rate of ART (Scott and Hofmann, 1995; Balasch *et al*., 1996; Barnhart and Osherof, 1998). However, there is no clear-cut division between a normal and an elevated FSH level (van Montfrans *et al*., 2000; Esposito *et al*., 2002). It has been suggested that the reason that clinics refuse to treat patients with elevated basal FSH is to maintain the clinic's overall success rate or to improve their position in the league tables (Sharif and Afnan, 2003).

Women with elevated FSH could be a heterogeneous group. Some may have true reduced ovarian reserve, other cases may be due to the presence of heterophylic antibodies. Finally, FSH receptor polymorphism could also result in an elevated value in patients with otherwise normal ovaries (Lambalk, 2003). In this study, however, we confirm that elevated day 3 FSH levels in a previous cycle are associated with a reduction in the overall LBR if compared with women with normal basal FSH levels. Nevertheless, the LBR is reasonable, especially in cycling women under the age of 38 with FSH between 10 and 20 IU/l where the chance of a live birth is at least 20%. This is comparable with the national average LBR in the UK (HFEA Patient Guide, 2001) in patients who are not considered by most assessment to be average. In fact, two patients with FSH

Table IV. Stimulation characteristics and cycle outcome of patients <38 and FSH ⩾10 IU/l versus patients ⩾38 years and FSH <10 IU/l

	Age <38 and FSH ⩾10 IU/l	Age ⩾38 and FSH <10 IU/l	*P*-value
No. of patients)	113	639	
Mean age ± SD	33.5 ± 3.0	40.57 ± 2.2	
Duration of infertility (mean ± SD)	4.43 ± 3.2	5.31 ± 4.6	NS
Cancellation rate (%)	15.9	9.7	0.039
Days of taking gonadotrophins (mean ± SD)	12.5 ± 3.5	11.3 ± 2.5	NS
No of ampoules[a] consumed (mean ± SD)	46.0 ± 17.6	44.0 ± 16.1	NS
Estradiol (IU) per follicle on HCG day	336.82	460.46	0.184
Average no. of oocytes collected (mean ± SD)	6.77 ± 6.11	7.83 ± 5.49	0.069
Fertilization rate (%)[c]	58.1	58.4	NS
Average no. of embryos available for transfer	3.73	4.46	NS
Average no. of embryos transferred	1.88	2.13	NS
Pregnancy rate per started cycle in % (*n*)	28.3 (32/113)	18.8 (120/639)	0.016
LBR per started cycle in % (*n*)	21.2 (24/113)	12.1 (77/639)	0.008
Pregnancy rate per egg collection in % (*n*)	33.7 (32/95)	20.8 (120/577)	0.004
LBR per egg collection in % (*n*)	25.3 (24/95)	13.2 (77/577)	0.003
Miscarriage rate (%)	25.0	35.8	0.173
Cumulative LBR after three cycles	49.3%	33.1%	

[a]Number of ampoules = in cases of pure FSH (75 IU FSH) and in cases of HMG (75 IU FSH and 75 IU LH).
NS = difference not statistically significant ($P > 0.05$).

>20 IU/l achieved a live birth, one in her first cycle and the other in her second cycle, giving a cumulative LBR of 19.2%. Indeed, in patients of all groups of elevated levels of FSH (>10 IU/l) where the age was ⩽38, the LBR was in excess of 20% per single cycle, with a cumulative LBR after three cycles of 49.3%. This, we believe, is a far better choice for a significant number of women than the alternatives of oocyte donation and adoption.

In this study, there was no attempt to check the level of FSH in the treatment cycle itself. Previous studies (Scott *et al*., 1990; Martin *et al*., 1996) have demonstrated that inter-cycle variability in basal FSH values did not predict changes in ovarian response to gonadotrophin stimulation and thus may not be used to select an optimal cycle in which to stimulate an individual patient. These studies also reported that one previous elevated day 3 FSH determination dramatically decreased the chance of future IVF-ET pregnancy.

El-Toukhy *et al*. (2002) argued that young age does not protect against the adverse effects of reduced ovarian reserve, suggesting that an elevated day 3 basal FSH level is not only associated with low response, but also with poor quality oocytes. They in fact argued that patients with elevated day 3 FSH perform as badly as much older patients with normal FSH. This was not the case in this study. We have shown that although younger cycling patients with high FSH had significantly lower number of oocytes collected and a lower number of available and transferred embryos, their pregnancy rate and LBR were significantly higher and their miscarriage rate was significantly lower than older women with normal FSH. Their study was, however, a mixture of two groups, those with elevated day 3 FSH and also those with a previous poor response to stimulation and, therefore, the conclusions cannot be made (and should not have been) specific to patients with a high basal FSH level. Furthermore, the mean FSH value in all three age groups in their study was <10 IU/l.

Cycling women with elevated FSH required more ampoules for stimulation; this could be due to a true poor response or a possible bias due to knowledge in advance of a basal FSH value encouraging the clinician to prescribe a higher dose of gonadotrophins. The fact, however, is that regardless of the increasing dose of gonadotrophins, there was a higher cancellation rate and the ultimate number of eggs collected was progressively reduced in the elevated FSH groups. The fertilization rate, however, was the same in all groups, indicating that oocyte quality is not affected by the basal FSH level. This finding is in keeping with the findings of Sharif *et al*. (1998). Overall, however, the number of embryos available for transfer was lower for those patients with a high basal FSH, and thus the number of embryos to choose from and the number of embryos transferred were lower in that group. This resulted in a lower pregnancy rate. This implies that elevated basal FSH is associated with low ovarian reserve, but is not synonymous with poor oocyte quality. This finding is illustrated in several other studies (Check *et al*., 2002; Esposito *et al*., 2002; van Rooij *et al*., 2003).

It is of interest to note that the fertilization rate was affected neither by the level of FSH nor the age of the women. The miscarriage rate, however, was affected by age but not by the FSH level. Within the same age group, it was shown that the miscarriage rate does not increase with an increase in basal FSH level; however, the miscarriage rate does significantly increase with increased age. The increased miscarriage rate is therefore associated with age-related changes in the structure of the chromosomes of the oocytes. Furthermore, high FSH therefore does not reflect ageing oocytes, it is just that fewer are produced. This finding contradicts that of El-Toukhy *et al*. (2002) who showed that poor responders have a high miscarriage rate regardless of age. However, they did not compare the miscarriage rate with a normal control group. In addition, as mentioned above, their population was a mixture of patients

with high FSH as well as poor responders with a normal FSH. Nasseri *et al*. (1999) found an increased incidence of abnormal karyotype in the abortuses of patients with elevated FSH and/or estradiol. We have no data regarding the karyotype of the abortuses, but the miscarriage rate was no different between the different levels of FSH within the same age group. Furthermore, they did not find a significant difference in the incidence of abnormal karyotype in women aged ⩽35 years.

From the data in this study, we can conclude that an elevated basal FSH level does not indicate deterioration of oocyte and embryo quality. The fertilization rate does not decrease and the miscarriage rate is not increased. Our finding implies that the reduction in pregnancy rate is a result of a reduced number of oocytes collected and subsequently the limited choice of embryos available to be transferred. This was clearly demonstrated in cycles in which only 1–4 eggs were collected. In those patients, there was no significant difference in the LBR between all FSH groups. This further confirms that the observed reduction in LBR in the overall data was due to lower quantity of eggs rather than poor quality of these eggs. In other words, patients assume an LBR related to their age and the number of eggs they produce rather than the level of FSH.

Clinicians should therefore advise patients with a high basal FSH level to expect a lower pregnancy rate, due to the fewer eggs they will produce, as compared with their counterparts of similar age who produce a higher number of eggs. Clinicians and patients alike should therefore accept that patients with a high FSH level will have poorer ovarian response and be prepared to go ahead and undergo egg collection when a small number of follicles has developed.

In summary, cycling women with high basal day 3 FSH will have a lower chance of achieving a live birth, but there is still a reasonable chance of success even with FSH levels up to 20 IU/l. In the current system, many women with elevated FSH are led to believe that they are unsuitable for IVF treatment and would have no chance of a successful outcome. Therefore, these women are forced to consider other treatment options to provide them with the chance of motherhood, although not with their own genetic child. For these women, a chance, although a reduced one of achieving a pregnancy with their own genetic child is a precious and important opportunity for them to consider. Some woman may feel that a lower chance is better than no chance at all. The level of basal FSH should not be used as a screening tool to select patients for treatment; instead it should be used as additional information to counsel patients appropriately regarding the realistic chance of conception as well as aiding the clinician in determining the appropriate dose of gonadotrophins.

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