Discrimination between chronological and ovarian age in infertile women aged 35 years and older: predicting pregnancy using basal follicle stimulating hormone, age and number of ovulation induction/intra-uterine insemination cycles*

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A marked decline in fertility rates has been demonstrated in women >35 years of age. We have previously demonstrated the importance of basal follicle stimulating hormone (FSH) concentrations plus chronological age to predict pregnancies in women aged ≥40 years undergoing ovulation induction therapy. The purpose of the current study was to extend our previous study and determine the impact of age, basal FSH concentrations and ovulation induction/intra-uterine insemination (IUI) treatment cycles on pregnancy rates in infertile women aged ≥35 years. This prospective observational study was performed at a tertiary university fertility centre. Assessments of basal hormonal status and ovulation induction protocols were performed. The main outcome measured was clinical pregnancies. A total of 770 treatment cycles in 179 women aged ≥35 years were analysed. The impact of basal FSH concentrations on treatment outcomes could be bifurcated into a favourable group (FSH ≤23 mIU/ml) and a poor prognosis group (FSH ≥24 mIU/ml). A multivariate logistic regression model was generated which accurately predicted pregnancies. There was a high degree of correlation between predicted pregnancies and observed pregnancies ($r = 0.86$).

We conclude that age, number of treatment cycles and the interaction term basal FSH × age are useful and significant predictors of pregnancies in patients aged ≥35 years undergoing ovulation induction/IUI therapy.

Key words: FSH/maternal age/ovulation induction

Introduction

A marked decline in fecundity and fertility rates has been demonstrated in women aged >35 years (Mosher and Pratt, 1990, 1991). Follicular atresia, increased spontaneous abortion rates, decreasing endometrial receptivity and decline in oocyte quality have been implicated in this decline (Federation CECOS, 1982; Richardson et al., 1987; Wilcox et al., 1988; Navot et al., 1991; Buyalos et al., 1992; Meldrum 1993). We have previously demonstrated the importance of basal follicle stimulating hormone (FSH) concentrations and chronological age to predict pregnancies in women aged ≥40 years undergoing ovulation induction therapy (Pearlstone et al., 1992). The probability of a clinical pregnancy per treatment cycle fell sharply as a function of patient age and increasing FSH concentrations in these infertile patients. Presently, there are limited data available with which to counsel 35—40 year old patients regarding their individual chances of achieving pregnancy while undergoing ovulation induction/intra-uterine insemination (IUI) therapy. The current investigation was undertaken with two objectives: firstly to define quantitatively the impact of basal FSH on prognosis in patients ≥35 years of age undergoing ovulation induction/IUI therapy, and secondly to determine the utility of basal FSH, age and the number of previous treatment cycles in predicting the probability of pregnancy in women aged ≥35 years undergoing ovulation induction/IUI.

Materials and methods

Subjects and study design

The study population consisted of women aged ≥35 years undergoing infertility treatment at the University of California, Los Angeles Fertility Center, CA, USA, from January 1989 to May 1993. Patients were randomly selected to represent a diverse clinical infertility outpatient practice. Patients who met the criteria for ovulation induction/IUI and/or IUI treatment, regardless of diagnosis, were selected. A number of patients were referred from outside institutions for fertility management, and no effort was made to include prior treatment protocols in this analysis. However, clomiphene citrate was not used if the patient had documented failure with clomiphene citrate in the past. Basal FSH measurements were prospectively obtained on cycle day 2 or 3 in these women as part of an institutional review board-approved protocol. Participation in the study was voluntary, and only patients aged ≥35 years with prospective sampling of basal FSH were studied. All couples were diagnosed as infertile based on inability to conceive after a minimum of 1 year of unprotected intercourse. Diagnostic evaluation included assessment of ovulation, a semen analysis, evaluation of the luteal phase, exclusion of cervical factor, and confirmation of tubal patency by hysterosalpingography and/or laparoscopy. Laparoscopy was performed in a selective manner congruent with published protocols (Navot et al., 1987; Collins and Rowe, 1989).

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Table I. Characteristics of the 179 infertility patients aged >35 years undergoing ovulation induction/infra-uterine insemination (IUI)*

<table>
<thead>
<tr>
<th>Diagnoses</th>
<th>No. of patients</th>
<th>Age (mean ± SD)</th>
<th>No. of cycles</th>
<th>Basal FSH (mIU/ml) (± mean SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anovulation</td>
<td>32</td>
<td>40 ± 2</td>
<td>116</td>
<td>14.4 ± 13</td>
</tr>
<tr>
<td>Tubal factor (unilateral)</td>
<td>19</td>
<td>42 ± 3</td>
<td>106</td>
<td>16.5 ± 11</td>
</tr>
<tr>
<td>Male factor</td>
<td>14</td>
<td>41 ± 3</td>
<td>71</td>
<td>15.6 ± 7</td>
</tr>
<tr>
<td>Endometriosis</td>
<td>44</td>
<td>42 ± 3</td>
<td>261</td>
<td>17.0 ± 11</td>
</tr>
<tr>
<td>Natural cycle/IUI</td>
<td>20</td>
<td>41 ± 2</td>
<td>74</td>
<td>17.1 ± 11</td>
</tr>
<tr>
<td>Clomiphene citrate/IUI</td>
<td>97</td>
<td>41 ± 3</td>
<td>405</td>
<td>15.8 ± 10</td>
</tr>
<tr>
<td>Clomiphene citrate/HMG + IUI</td>
<td>18</td>
<td>40 ± 3</td>
<td>55</td>
<td>17.8 ± 14</td>
</tr>
<tr>
<td>HMG/IUI</td>
<td>44</td>
<td>41 ± 3</td>
<td>236</td>
<td>17.4 ± 12</td>
</tr>
</tbody>
</table>

*No statistically significant differences in age or basal FSH between diagnostic categories or types of treatment protocols were observed at the P < 0.05 level using analysis of variance.

Patients were classified into one of six diagnostic categories contingent on their primary infertility diagnosis (Table I). The women in this study had regular menstrual cycles of 24–35 days, with the exception of patients classified as having ovulatory dysfunction. This group included patients with oligo-ovulation secondary to either polycystic ovarian syndrome, hypothalamic amenorrhoea or hyperprolactinaemia. These women did not demonstrate elevated FSH and luteinizing hormone (LH) concentrations indicative of the premenopausal state. Diagnosis of male factor subfertility was predicated on at least two semen analyses separated by a minimum of 3 months which confirmed any of the following abnormalities: sperm density <20 × 10^6/ml, 1 h motility <50% or <50% normal morphology. Couples with severe male factor infertility (sperm density <1 × 10^6/ml) were excluded from this analysis. Donor insemination was referred to those patients with no known female factors undergoing such therapy. Endometriosis was diagnosed by laparoscopy and classified in accordance with the revised classification of the American Fertility Society (1985). Couples without evidence of abnormalities throughout their evaluation were classified as having unexplained infertility. The infertility diagnoses, age, number of ovulation induction/IUI cycles and basal FSH concentrations are summarized in Table I. The data in this study represent an extension of our previous study, which examined women aged >40 years (Pearlstone et al., 1992), and now includes women 35–39 years of age.

Ovulation induction protocols

Stimulated cycles employed clomiphene citrate (Serophene; Serono Laboratories, Norwell, MA, USA) and/or human menopausal gonadotrophin (HMG, Pergonal or Metrodin; Serono). Clomiphene citrate was administered orally in doses ranging from 50 to 150 mg/day for 5 days, with therapy initiated on cycle day 3, 4, or 5. Transvaginal ultrasound examinations were performed to assess follicular development. HMG therapy was started on cycle day 2 in cycles in which this was the sole treatment, or on the sixth day of stimulation immediately following 5 days of clomiphene citrate in combined clomiphene citrate/HMG cycles. HMG was given at an individualized dose ranging from one to four ampoules per day, with a usual starting dose of two ampoules. In selected cycles bromocriptine and pulsatile gonadotrophin-releasing hormone (GnRH) were used. Ampoules of Pergonal contained 75 IU of FSH and 75 IU of LH and those of Metrodin contained 75 IU of FSH. Human chorianic gonadotrophin (HCG) was administered as 10 000 IU i.m. when the lead follicle(s) attained a mean diameter of 16 mm in HMG cycles or 18 mm in clomiphene citrate and clomiphene citrate/HMG cycles. Alternatively, in some patients home urinary LH assays were used to detect the LH surge. All patients received IUIs, which were performed the morning after the LH surge detection or 36–40 h after the injection of HCG. All donor cycles utilized cryopreserved semen for insemination. The characteristics of patients undergoing different treatment protocols are summarized in Table I.

Outcomes

Clinical pregnancies were defined by a positive serum HCG with sonographic confirmation of a gestational sac or pathological confirmation of choriocarcinoma villi or a surgical specimen of an ectopic gestation. The clinical pregnancy rate was defined as the number of clinical pregnancies divided by the number of treatment cycles performed. Spontaneous abortion referred to pregnancies ending prior to 20 weeks gestation. Livebirths referred to pregnancies resulting in the delivery of a viable infant. In our prior study there were no statistically significant differences between treatment protocol and outcome as measured by pregnancy rates in women aged >40 years (Pearlstone et al., 1992).

FSH assays

FSH assays were performed by a single laboratory using commercially available radioimmunoassay kits (Amerlex; Amersham Corp., Arlington Heights, IL, USA). The second IRP-HMG standard was used. Assay sensitivity was 2 mIU/ml. Intra-assay and inter-assay variability did not exceed 7 and 9.1% respectively. Our laboratory changed standards for FSH analysis in May 1993 (from second IRP-HMG to second IRP 78/549) and we concluded the study in order to reduce introduction of assay bias into the data set.

Statistical analysis

The unit of analysis was a woman, i.e. her attributes (age, basal FSH) and the cumulative probability of pregnancy after 4.3 ovulation induction/IUI treatment cycles. This number represents the mean number of treatment cycles undergone by women in our study. Our analyses assume that the woman conceived after the last cycle recorded. A woman's post-pregnancy treatment cycles were excluded from the database. Analysis of variance was used for the comparisons of means. One-sided hypothesis testing was prospectively used in the cases of chronological age and basal FSH because the alternative considerations were not biologically plausible (Hassard, 1991). Otherwise, two-tailed analyses were employed. Statistical significance was defined as P < 0.05, except in our logistic regression model which allowed for a P ≤ 0.1 level for the interaction term, basal FSH × age,
had been unsuccessful, thereby contributing to the low observed other infertility practices because prior infertility treatments were unsuccessful. Patients studied at our institution were usually referred from other infertility practices because prior infertility treatments were unsuccessful. FSH and pregnancy rates
Analyses of 179 women aged ≥35 years (range 35–48 years) with an average of 4.3 ovulation induction/IUI cycles were examined. There were 29 clinical pregnancies in 770 treatment cycles, resulting in an overall pregnancy rate of 3.8% per cycle. There were no differences in the mean age or basal FSH as a function of infertility diagnosis or ovulation induction protocol (Table I). When clinical pregnancies were plotted separately as a function of basal FSH and patient age, graphic analysis revealed cutoff values of 23 mIU/ml and 44 years respectively (Figure 1). As expected, the pregnancy rates declined with an increase in the patient’s age (7.1% per treatment cycle in patients aged 35–38 years compared to 2.0% per cycle in women aged 41–44 years; P < 0.01).

Results
FSH and pregnancy rates
Analyses of 179 women aged ≥35 years (range 35–48 years) with an average of 4.3 ovulation induction/IUI cycles were examined. There were 29 clinical pregnancies in 770 treatment cycles, resulting in an overall pregnancy rate of 3.8% per cycle. There were no differences in the mean age or basal FSH as a function of infertility diagnosis or ovulation induction protocol (Table I). When clinical pregnancies were plotted separately as a function of basal FSH and patient age, graphic analysis revealed cutoff values of 23 mIU/ml and 44 years respectively (Figure 1). As expected, the pregnancy rates declined with an increase in the patient’s age (7.1% per treatment cycle in patients aged 35–38 years compared to 2.0% per cycle in women aged 41–44 years; P < 0.01).

Patients studied at our institution were usually referred from other infertility practices because prior infertility treatments had been unsuccessful, thereby contributing to the low observed pregnancy rates and increased spontaneous abortion rates. No pregnancies were observed in patients who were ≥44 years (Figure 1). When all patients’ ages and basal FSH were plotted there was a significant correlation between increasing age and FSH concentrations (r = 0.21, P ≤ 0.005). However, when only the ages and basal FSH concentrations of patients who became pregnant were compared, there was no significant relationship observed (r = 0.18, P > 0.4). We initially divided patients into three groups according to their basal FSH concentrations: <15, 15–23 and ≥23 mIU/ml (Table II). The mean clinical pregnancy rate in patients whose basal FSH fell in the <15 mIU/ml group was 4.6 ± 1.9% and was similar to the pregnancy rate per treatment cycle for patients whose basal FSH was 16–23 mIU/ml (3.9 ± 2.5%, P = 0.34). No pregnancies occurred in patients whose basal FSH was ≥24 mIU/ml. Thus, the relative effect of basal FSH concentrations on the ability to achieve pregnancy allowed patients to be divided into two groups: a group with a favourable prognosis, with a basal FSH <23 mIU/ml, and a group with a poor prognosis, with FSH ≥24 mIU/ml.

Discrimination between chronological and functional ovarian age
Multivariate analysis was performed for the probability of achieving a clinical pregnancy using the chronological age at the start of the treatment cycle, basal FSH concentrations and prior number of completed ovulation induction/IUI cycles. Three statistically significant prognostic variables were calculated: age (P < 0.05), cycle number (P < 0.02), and the interaction term of age and basal FSH concentration (P < 0.09). The equation quantifying this relationship is

\[
\text{logit} = 0.7 - (0.001 \times \text{age} \times \text{FSH}) - (0.51 \times \text{age}) + (0.113 \times \text{cycles}).
\]

Where \(\text{logit} = \frac{\text{p}}{1 - \text{p}}\) and \(\text{p} = \text{probability of pregnancy}\).

These data were used to develop a multivariate logistic regression model which accurately predicted pregnancies based on the ability to achieve pregnancy allowed patients to be divided into two groups: a group with a favourable prognosis, with a basal FSH <23 mIU/ml, and a group with a poor prognosis, with FSH ≥24 mIU/ml.

Table II. Multivariate logistic regression model\(^*\) for the probability of a clinical pregnancy after a patient has undergone 4.3 ovulation induction/intra-uterine insemination (IUI) cycles in three representative basal follicle stimulating hormone (FSH) concentration categories (<15, 15–23 and ≥23 mIU/ml)

<table>
<thead>
<tr>
<th>FSH concentration (mIU/ml)</th>
<th>Age group</th>
<th>No. of predicted pregnancies</th>
<th>No. of observed pregnancies</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;15</td>
<td>35–36</td>
<td>2.4</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>37–38</td>
<td>1.4</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>39–40</td>
<td>6.8</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>41+</td>
<td>10.1</td>
<td>12</td>
</tr>
<tr>
<td>15–23</td>
<td>35–36</td>
<td>0.4</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>37–38</td>
<td>0.2</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>39–40</td>
<td>1.9</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>41+</td>
<td>3.4</td>
<td>7</td>
</tr>
<tr>
<td>≥23</td>
<td>35–36</td>
<td>0.1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>37–38</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>39–40</td>
<td>0.3</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>41+</td>
<td>1.6</td>
<td>0</td>
</tr>
</tbody>
</table>

\(^*\)The estimated probability of pregnancy = 1/(1 + e^{-\text{logit score}}), where \text{logit} = 0.7 - (0.001 \times \text{cycle} \times \text{FSH}) - (0.51 \times \text{age}) + (0.113 \times \text{cycles}).

\(^*\)Determined using the second IRP-HMG standard.
on basal FSH, patient age at the start of each cycle, and the number of completed treatment cycles. In our model, for each jump in age category (35-36, 37-38, 39-40 years) the probability of pregnancy was reduced ~3% (assumes the number of cycles was held constant and basal FSH concentrations were <15 mIU/ml). If basal FSH concentrations were 15-23 mIU/ml and cycles were held constant, then for each age category (35-36, 37-38, 39-40 years) the probability of pregnancy was ~6% lower compared to basal FSH of <15 mIU/ml (as above) and the fall in probability of occurrence of pregnancy for each increase in age group was 2%. Finally, when basal FSH values exceeded 23 mIU/ml, our model predicted a significant fall in the probability of pregnancy for each increase in age group, with the 35-37 year old group having a probability of occurrence of pregnancy less than half that of the group with basal FSH <15 mIU/ml. We determined, however, that FSH concentrations ≥24 mIU/ml were incompatible with pregnancy in our population.

In our model, increasing the number of cycles increased the probability of pregnancy by increasing the exposure of the spermatozoon to an egg for fertilization. It is important to understand that our study addressed the likelihood of conception after a defined number of treatment cycles; we were not analysing pregnancy rate per cycle. In our model, the Goodness of Fit statistic $G^2 = 150.9$, df = 173 - 4 = 169 and the corresponding $P$ value was 0.84. A low $P$ value would have meant that we could reject the null hypothesis, i.e. that the model fitted the data. However, we had a high $P$ value and did not reject the null hypothesis, i.e. the model fitted the data. As shown in Table II, there was a high degree of correlation between the predicted number of pregnancies and observed pregnancies ($r^2 = 0.86$, $P = 0.001$). Only the number of treatment cycles, age and the interaction term basal FSH×age were found to be significantly predictive of clinical pregnancy rates. Infertility diagnoses, type of treatment protocol and method and timing of inseminations did not predict the likelihood of achieving pregnancy in this infertile population nor in that of our previous study (Pearlstone et al., 1992). Using this prognostic model, a graph was constructed (Figure 2). Four age groups were selected: 35, 37, 39 and 41 years. Basal FSH concentrations ranging from 2 to 24 mIU/ml are shown, and the number of completed treatment cycles was set at 4.3 cycles. We chose 4.3 completed treatment cycles because this represented the mean number of treatment cycles our patients had received. Using this model, the probability of pregnancy declined as chronological age and basal FSH increased.

Figure 3 represents the data reanalysed to include number of completed treatment cycles (0, 1, 2, 3, 4). Here, we find evidence supporting our model which predicts an effect of the number of treatment cycles a patient undergoes on her chances for pregnancy and how changes in her basal FSH influence these effects. This demonstrates an increase in the probability of pregnancy as the number of treatment cycles increases. Our model does not calculate the point of diminishing returns where positive outcomes can no longer be expected. This visual representation of the logistic regression model can be used to help a patient understand how her attributes (age, basal

![Figure 2](image_url)

**Figure 2.** A logistic regression model for the probability of a clinical pregnancy as a function of patient age, basal follicle stimulating hormone (FSH) concentrations and number of prior treatment cycles. The model assumes an average of 4.3 prior ovulation induction/intra-uterine insemination (IUI) cycles and the age of the infertile patients to be ≥35 years. FSH values were derived using the second IRP-HMG standard. The multivariate logistic equation used was $P = 1/(1 + e^{-\text{logit score}})$ where $P = \text{probability of pregnancy and logit} = 0.7 - (0.001 \times \text{age} \times \text{FSH}) - (0.51 \times \text{age}) + (0.113 \times \text{cycles})$.

![Figure 3](image_url)

**Figure 3.** Effect of number of ovulation induction/intra-uterine insemination (IUI) treatment cycles on probability of pregnancy using a logistic regression model which considers age, basal follicle stimulating hormone (FSH) concentrations and treatment cycles. This example is for an infertile woman aged 39 years. The multivariate logistic equation used was $P = 1/(1 + e^{-\text{logit score}})$ where $P = \text{probability of pregnancy and logit} = 0.7 - (0.001 \times \text{age} \times \text{basal FSH}) - (0.51 \times \text{age}) + (0.113 \times \text{cycles})$. 

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FSH and number of treatment cycles) will influence the reproductive outcome of infertility therapy. The actual model should use data obtained from the clinic where the patient is undergoing treatment.

Discussion

The current investigation was undertaken to determine the impact of age, basal FSH concentrations and ovulation induction/IUI treatment cycles on pregnancy rates in infertile women aged ≥35 years. Previously we have reported decreased pregnancy rates in women ≥40 years undergoing ovulation induction/IUI therapy (Pearlstone et al., 1992). This study expanded our data to include women aged 35–39 years and provided a unique model which incorporated the interaction of both age and basal FSH concentrations as a predictor of pregnancy.

In this population, basal FSH concentrations could be bifurcated into two groups: patients with a favourable prognosis, with a basal FSH ≤23 mIU/ml, and those with a poor prognosis, with a basal FSH ≥24 mIU/ml. No pregnancies were observed in patients with a basal FSH >23 mIU/ml. Ebbiary et al. (1994) presented data in which an elevated FSH was reported as ≥10 mIU/ml, resulting in slower follicular growth, smaller follicle diameters, and lower luteal phase salivary progesterone concentrations. They concluded that infertile women with ‘elevated’ FSH are in their perimenopause despite having regular ovulatory cycles. Our data do not support the FSH limits imposed by their study. However, we did see a trend towards a decline in fertility when the FSH values exceeded 15 mIU/ml (Table II).

FSH concentrations may differ significantly when performed at another facility or when another assay method is employed (Scott et al., 1990; Hershlag et al., 1992). Therefore, these data must be interpreted with caution when extended to another institution. Furthermore, differences in glycosylation of the FSH molecule and the resulting various isoforms are influenced by the stage of the menstrual cycle and chronological age (Wide and Wide, 1984; Reddi et al., 1990). Recently, Seifer et al. (1993) proposed a method for converting FSH values across institutions using an equation to convert values obtained with different assay systems. We terminated our study when a different FSH standard was used by our laboratory (changed from second IRP-HMG to second IRP-78/549), thereby eliminating assay bias in the interpretation of our data. We also believe that cutoff values for clinically applicable tests should be derived from clearly recognized endpoints, which in this report is the inability to achieve a clinical pregnancy and represents an FSH value ≥24 mIU/ml.

Basal FSH measurements have been used as a marker for ovarian reserve (Scott et al., 1989; Toner et al., 1991; Pearlstone et al., 1992; Scott and Hofmann, 1995). Increasing evidence suggests that the decline in reproductive potential is related to factors within the ovary. However, it appears that the age of onset of diminished ovarian reserve and the associated decrease in reproductive capacity vary considerably. Indeed, seminal work by Sherman and Korenman (1975) has demonstrated that women in their mid-thirties frequently have subtle elevations in their circulating FSH concentrations. Subsequent reports from both fertile and infertile populations indicate that these changes in FSH secretion are initially manifested in the early follicular phase (Lenton et al., 1988). Additional screening techniques, including the clomiphene citrate challenge test and the GnRH agonist stimulation test, though more cumbersome and expensive, have been shown to be useful predictors of ovarian reserve in infertile populations (Navot et al., 1987; Scott and Hofmann, 1995; Scott et al., 1995). These tests require increased cost, time and patient compliance. We believe models can be constructed which may predict outcomes based on knowledge of the patient responses to prior therapy and her individual characteristics, such as age, basal FSH and history.

In this study, patients were classified on the basis of either initial FSH measurements or their most recent value if repeated. It is possible, indeed probable, that some patients in this report with lower FSH concentrations actually had higher values in a prior or in subsequent cycles. Our analysis would therefore underestimate the prognosis for patients with persistently favourable basal FSH concentrations. The role of serial basal FSH concentrations to facilitate the selection of an optimal cycle to initiate treatment in patients undergoing ovulation induction/IUI therapy remains unclear. Intercycle variability in patients undergoing in-vitro fertilization (IVF) treatment has been reported by Scott et al. (1990). In their analysis the patients with lower basal FSH values had minimal intercycle variability, while those with elevated basal FSH values demonstrated greater intercycle variation. Furthermore, when patients who had demonstrated both a high and a low FSH value were analysed separately, the IVF cycle characteristics were consistently those of a poor responder. Hence, patients with a greater degree of cycle variability appear to have a decline in their ovarian reserve, despite the absence of a persistently elevated FSH value. We are currently evaluating the relative effects of large variations in basal FSH concentrations on predicting pregnancies based on our logistic regression model.

It has been shown that pregnancy rates in infertile women ≥35 years undergoing ovulation induction are generally low (Navot et al., 1987; Dodson and Haney, 1991), and no patient >44 years of age achieved a clinical pregnancy. Previously, we reported that the pregnancy rates per treatment cycle (and 95% confidence intervals) at our institution were 13.6% (9.5–17.7%) for women <30 years, 9.6% (7.0–12.2%) for women 30–34 years, 7.7% (5.5–9.9%) for women 35–39 years and 3.5% (1.7–5.3%) for women aged ≥40 years, which is consistent with the pregnancy rate per cycle in patients of similar ages in this report (Pearlstone et al., 1992). Scott et al. (1995) recently reported a similar trend in pregnancy rates using life table analyses. They observed a difference in the rate of decline in pregnancy between patients with normal ovarian reserve and those with diminished ovarian reserve as a function of age in women in the age groups ≤30, 31–33, 34–36, 37–39 and ≥40 years. No specific FSH concentration was ascribed as abnormal in their report and day 3 FSH values ranged between 1.9 and 42.1 mIU/ml. In our study, we determined that, in addition to basal FSH values, chronological age was also an independent predictor of pregnancy as determined by stratified and multivariate logistic regression analyses. These
data are further strengthened by the validation of the clinical outcomes of this large cohort over time.

Our study demonstrates the importance of basal FSH concentrations on the prognosis of pregnancy with ovulation induction/IUI therapy. Patients presenting to fertility clinics will bring individual attributes which empirically should contribute to their chances for achieving pregnancy. This model allows individual patient-specific predictions of the likelihood of achieving pregnancy per treatment cycle. The data regarding FSH and age as factors affecting outcomes of ovulation induction treatments are consistent with observations made on patients undergoing assisted reproductive techniques (Scott et al., 1989; Toner et al., 1991). These studies have generally suggested that basal FSH is a superior predictor of IVF outcome than chronological age. However, our data indicate that age, number of treatment cycles and the interaction term of age \( \times \) basal FSH concentrations better predict intervention outcomes for ovulation induction/IUI patients. When counselling the infertile patient in the age group studied (\( \geq 35 \) years old), the attendant increase in both spontaneous abortion and congenital anomalies must also be considered.

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References


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