THE MOST INFLUENTIAL FACTORS FOR A SUCCESSFUL PREGNANCY AFTER IN VITRO FERTILIZATION BY MODEL OF PROBIT REGRESSION

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ABSTRACT

The issue of infertility is one of the most important topics addressed by society, especially in our current situation. The Probit regression method is one of the most important methods in this analysis which effects on the statistical tests of the significance of the estimated parameters of the regression model. In this paper, we studied the Probit regression model to determine the most important factors affecting the success of pregnancy and life birth after in-vitrofertilization (IVF), where a simple random sample of (160) infertile individuals was withdrawn, represented by the following variables; Maternal age, paternal age, Types of infertility, Number of previous treatment cycles, Who is the cause of the infertility (man or woman), Number of retrieved oocytes, Frozen embryos transfer (FET), Anti-Müllerian hormone (AMH), Follicle-stimulating hormone (FSH) and Luteinizing hormone (LH). Of these and through the statistical program SPSS, we concluded that the paternal and maternal ages, type of infertility, cause of infertility and FSH are influential factors on the success of pregnancy.

Keywords: Probit regression, variables, in-vitro fertilization, success of pregnancy


INTRODUCTION

In spite of the great development in the assisted reproductive technologies (ART) that occurs during recent years, the infertility remains a highly prevalent global condition, moreover some counties around the world are regarded to have high infertility prevalence such as Central and South Asia, Middle East and North Africa, Central and Eastern Europe(1).
The assisted reproductive technology includes many procedures; the most popular are, the intrauterine insemination (IUI) and the intracytoplasmic sperm injection (ICSI). During these procedures, the woman takes drugs in order to stimulate the development of extra oocytes (or eggs) in her ovaries then the eggs are picked up with an ultrasound-guided needle and let them to fertilize with sperm in dishes in case of IUI or injected with active sperm mechanically in case of ICSI. In laboratory, the fertilized ova(zygotes) develop into embryos within few days under controlled conditions and at proper scoring day the best developed embryo is transferred in to the mother’s uterus and the remains of developed embryos are frozen for upcoming cycles. The fertilization of ova in both conditions is called in vitro fertilization (IVF) since it occurs in the laboratory and outside the body and the baby born as a result of the IVF is called test tube baby.

The pioneers of the IVF are Sir Robert Edwards and Dr. Patrick Steptoe, and the first baby born by the IVF is Louise Brown since 1978. (2)

IVF success rate means the pregnancy and life birth will occur. As in other treatment, it depends on characteristics and lifestyle of the couples who are having the treatment. It was established that there are many variables have been described as influencing the success rate after IVF such as, the woman’s age, the length of infertility, type of infertility, the sperm count and the number of mature follicles. However, there is no agreement among various investigators about the nature and ranking of these variables. (3)(4) Human Fertilization and Embryology Authority (HFEA) published guideline variables Prediction of IVF success such as; female age, number of retrieved oocytes and transferred embryos, ovarian reserve, duration and type of infertility, number of previous treatment cycles, previous pregnancy history and body mass index (BMI). (5)

Our aim in this article is to determine the most influential factors for IVF success statistically using Probit regression model. To do so, we must study the response variable (dependent variable) which is Human chorionic gonadotropin (HCG) (pregnancy test) and independent variables that effect on the IVF success. These variables are:

Human chorionic gonadotropin (HCG)

Is a hormone secreted by placenta after implantation of the embryo during third week of gestation. It can be detected in blood and urine referring to pregnancy. It has role in promoting the maintenance of the corpus luteum during the beginning of pregnancy and for secretion of the hormone progesterone during the first trimester. (6)

Maternal age

Is very important as it reflects the ovarian reserve which determines the capacity of the ovary to produce oocytes (egg cells) that determine the chances of fertilization resulting in pregnancy. The number of oocytes will reduce with the age so that females at reproductive age have higher chances for pregnancy than females at advanced age as a result of that, there is an inverse correlation between age and female fertility. (6)

Paternal age

It is established that female fertility reaches its irreversible end with the menopause (around the age of 51 years), while in men; it is maintained for long period. But recent study shows that sperm count decreases and DNA damage increases with age. Moreover, it is published, IVF success rate decreases considerably over the age of fifty. (6)
Types of infertility

It was noticed that woman with primary infertility was significantly younger than women with secondary infertility and she had more oocytes and fewer embryos, therefore the chance of fertilization and pregnancy was less\(^7\).

Number of previous treatment cycles

Chances of a live birth after IVF procedure fall as the number of failed cycles increase\(^7\).

Who is the cause of infertility (man or woman?)

Infertility is defined as failure of conception, after a one-year period of unprotected intercourse, its causes either from paternal side or maternal side. Unexplained infertility (no identified male or female cause) accounts about 25% of the total cases. The most common causes for maternal infertility are Ovulatory disorders, polycystic ovaries, endometriosis and Tubal damage. Male infertility factors contribute to approximately 50% of all infertility cases and the most common causes are too few sperm (oligospermia) or no sperm at all (azospermia), abnormal sperm (Short lifespan or abnormal morphology) and physical or structural abnormalities\(^7\).

Number of retrieved oocytes

The higher the number of retrieved oocytes the higher the IVF success rates that the number of retrieved oocytes indicate to predict pregnancy and live birth\(^7\).

Frozen embryos transfer (FET)

Normally in IVF procedures, many oocytes are activated hormonally and are collected and fertilized in vitro in lab and the developing embryos are incubated for few days under controlled suitable environment. One or more best developed embryo are transferred into womb’s uterus. Others developing embryo are frozen for further trials of IVF. Unfortunately, transferring the frozen embryos doesn't increase the IVF success rate despite its common use as it is published recently in the Eshare conference\(^8\). Although, there is many articles propose that FET is more successful in resulting ongoing pregnancies than fresh embryos\(^9\)(\(^10\)).

Anti-Müllerian Hormone (AMH)

AMH is secreted by developing mature ovarian follicles it is helpful in measuring the level of ovarian reserve where higher the level of AMH in the bloodstream indicates the higher the number of eggs remaining in the ovaries and its low level is reflected to the low ovarian reserve as it seen normally in women who are approaching menopause\(^11\).

Luteinizing hormone (LH) and follicle-stimulating hormone (FSH)

These hormones are glycoproteins which are secreted from the anterior lobe pituitary gland and they are called gonadotroph because they stimulate the gonads (testes and ovaries in males and females respectively) and regulate many aspects of gonadal function. Normally these hormones under negative feedback control

LH stimulates secretion of sex steroids from the gonads. In females, it induces ovulation of mature follicles on the ovary. The residual cells within ovulated follicles proliferate and secrete progesterone and estradiol. Progesterone helps in maintenance of pregnancy. While FSH stimulates the maturation of ovarian...
follicles so that it uses prior to IVF procedure to develop more than usual number of developing mature follicles (superovulation). Diminished secretion of LH or FSH results in hypogonadism and infertility (failure of gonadal function)\textsuperscript{(11)}.

**MATERIALS AND METHODS**

**Probit regression model**

The study relied on some quantitative analysis techniques such as regression analysis using the probit model. This analysis is a type of regression used with the binomial response variables of the response experiment (IVF).

The idea of analyzing probit was first published in the journal Science by Chester Bliss in 1934\textsuperscript{(12)}. The Probit model is a probability model where the dependent variable is shown as a variable dummy variable ie a variable takes two values (0, 1)\textsuperscript{(13)} The econometric problem arises from the fact that the dependent variable is binary.

The model aims at estimating the probability of occurrence of a given object and specific characteristics of a category, as well as its classification as a probability of occurrence, which is a binary classification model.

This model is similar to the Logit model in the nature of the dependent variable as it is qualitative variable that takes two classes, zero and one, and is dependent on the probabilistic condensation function \( f(x_t, B) \) and the cumulative distribution function, if we have The distribution is normal (normal distribution) with an average of \( \mu = 0 \) and variance \( \sigma^2 = 1 \) the CDF, PDF format is as follows\textsuperscript{(14)}:

\[
= \exp \left(-0.5(X_t B)^2/\sqrt{2\pi}\right) \ldots \ldots \ldots (1)
\]

\[
= \frac{f(x_t B)f_t(\beta X_t \alpha F_t = F(X_t B)}{\int_{-\infty}^{X_t B}} \exp \left(-0.5(X_t B)^2/\sqrt{2\pi}\right) \ldots \ldots (2)
\]

The logarithmic probability (LLF) function of the problem model takes the following form\textsuperscript{(15)}.

If we impose the following relationship

\[
\text{LLF}(\beta) = \sum_{t=1}^{T} (Y_t \ln F(X_t \beta) + (1 - Y_t) \ln(1 - F(X_t \beta)))
\]

\[I = b_0 + b_1 X \ldots \ldots \ldots (3).\]
If I assume that I represents (1) in the event of an event and (0) if it does not occur and (x) is an independent variable and assuming that a level of I is called I * if I is higher than I * = 1, and if the distribution is normal with the same mean and variance we can estimate the coefficients of Equation 4 and are calculated as follows:\(^16\):

\[
P\left(\frac{Y}{X} = 1\right) = P(I * \leq I) = P\left(Z \leq B_0 + B_1X\right)
\]

((F(B_0 + B_1X)^\text{(4)})

1. The average probability of an event occurring when X is a given value.) \(P(Y = 1/X)\)

Z: Standard Normal Standard Variable

\(F = \) the cumulative distribution function that can be written as follows

\[
F(I_t) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{I_t} e^{-z^2/2} dz
\]

\(= \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\beta_1 + \beta_2X_t} e^{-z^2/2} dz
\)

In order to obtain the value of I (I) and the parameters \((\beta_1, \beta_2)\) we take the inverse function (4).

\[
I = F^{-1}(I)
\]

\(= F^{-1}(pt)\)

\(F^{-1}\) = the inverse of the CDF function

Note that the Probit model also eliminates the problem of heterogeneity of random error variation by adopting the cumulative probability distribution function

**RESULTS AND DISCUSSION**

A simple random sample consisting of (160) infertile infertility patients was taken from the infertility center at Kafeel Hospital in the holy governorate of Karbala. Using the statistical program SPSS, the data were analyzed statistically to study the effect of independent factors; number of previous treatment cycles, paternal and maternal ages, infertility type, who is the cause of infertility, number of retrieved...
oocytes, FET, LH, FSH on the dependent variable which is +/- of pregnancy test and in the Probit regression method as shown in the table (1).

Table 1: The values of Parameter Estimates in Probit regression

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>Std. Error</th>
<th>Z</th>
<th>Sig.</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age</td>
<td>.028</td>
<td>.008</td>
<td>3.383</td>
<td>.001</td>
<td>.012 -.045</td>
</tr>
<tr>
<td>Paternal age</td>
<td>-.038</td>
<td>.007</td>
<td>-5.161</td>
<td>.000</td>
<td>-.052 -.023</td>
</tr>
<tr>
<td>Type of the infertility</td>
<td>.094</td>
<td>.026</td>
<td>3.610</td>
<td>.000</td>
<td>.043 .145</td>
</tr>
<tr>
<td>Number of previous treatment cycles</td>
<td>.125</td>
<td>.110</td>
<td>1.136</td>
<td>.256</td>
<td>-.091 .341</td>
</tr>
<tr>
<td>Who is the cause of infertility (man or woman)</td>
<td>-.070</td>
<td>.036</td>
<td>-1.919</td>
<td>.055</td>
<td>-.141 .001</td>
</tr>
<tr>
<td>Number of retrieved oocytes</td>
<td>-.012</td>
<td>.008</td>
<td>-1.433</td>
<td>.152</td>
<td>-.028 .004</td>
</tr>
<tr>
<td>FET</td>
<td>-.112</td>
<td>.087</td>
<td>-1.293</td>
<td>.282</td>
<td>-.282 .058</td>
</tr>
<tr>
<td>AMH</td>
<td>.011</td>
<td>.006</td>
<td>1.722</td>
<td>.085</td>
<td>-.001 .023</td>
</tr>
<tr>
<td>FSH</td>
<td>-.019</td>
<td>.008</td>
<td>-2.196</td>
<td>.028</td>
<td>-.035 -.002</td>
</tr>
<tr>
<td>LH</td>
<td>.020</td>
<td>.010</td>
<td>1.931</td>
<td>.054</td>
<td>.000 .040</td>
</tr>
<tr>
<td>Intercept</td>
<td>-2.027</td>
<td>.293</td>
<td>-6.909</td>
<td>.000</td>
<td>-2.321 -.1734</td>
</tr>
</tbody>
</table>

a. PROBIT model: PROBIT(p) = Intercept + BX

We note from the above table, the values of the probability, the standard error, the probability Z values, the p_ value and the limits of confidence for each of them were found in the above table. The variables (maternal age, paternal age, infertility type, FSH) were significant, with a value of less than 0.05, (Number of attempts, infertility factor, number of withdrawn eggs, freezing, lutein (LH), and analysis of ovarian fertilization (AMH). Therefore, the model containing all the studied variables can be written as follows:

\[
P = -2.027 + 0.028X_1 - 0.038X_2 + 0.094X_3 - 0.019X_4 + 0.125X_5 + 0.07X_6 - 0.012X_7 - 0.112X_8 + 0.011X_9 + 0.20X_{10}
\]

\[
0.000.0010.0000.0000.0280.256 0.055 0.1520.196 0.0850.054
\]

It is reduced to a model with only significant variables as follows:

\[
P = -2.027 + 0.028X_1 - 0.038X_2 + 0.094X_3 - 0.019X_4 0.00,0.001,0.000,0.000,0.028
\]

To test Goodness-of-Fit (the difference between observed values and expected values), the Chi-Square test was performed and the value of p_ value was equal to 8310. It is greater than 0.05 and we accept the null hypothesis that there is a correlation between observed values and predicted values It means that the model is true and perfect.
CONCLUSION

The paternal and maternal ages, type of infertility, cause of infertility and FSH are influential factors on the success of pregnancy.

ETHICAL CLEARANCE

The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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REFERENCES


