Using Regression Model Data to Predicts the Outcomes of Pregnancies (A Case Study of Dutse General Hospital)

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Abstract
A logistic regression model has been developed previously to predict the outcome of pregnancies. This model was based on the human chorionic gonadotropin (HCG) ratio. As women present at earlier gestation to early pregnancy units (EPU) the number of women diagnosed with early pregnancy of unknown location increases. Some of these women will have an ectopic pregnancy (EP) and this group in the population poses the greatest concern. Data were gathered in a single early pregnancy unit from all women with an early pregnancy, were this data set was divided into a model building. We developed regression model with expert information using this data set to predict the outcome of pregnancies.

Keywords: chorionic gonadotropin, gestation, embryao, pregnancy.

INTRODUCTION
A pregnancy as defined by Sutton et al. (2006) is the state of carrying embryo or fetus in the uterus, in mammals pregnancy is defined as the period between in plantation of a fertilized egg (zygote) in wall of the uterus and delivery or other termination.

Condous et al. (2005) added that during each menstrual cycle on oocyte (pre-mature) develops in one of a woman’s two ovaries, As enlarges it produce hormone that signal the uterus to build up its lining and prepare itself for plantation if conception does occur.

Study was undertaken by Zayed et al. (1997) to investigate the use of human chorionic gonadotropin (HCG) concentration and other significance factors to predict the likelihood of a pregnancy progressing to detection of cardiac activity by ultrasound.

Bjercke et al. (1999) identify that the most accurate predictive model is to used a single day -14 HCG concentration and Maternal age in predicting the outcomes of pregnancies. Ongoing pregnancy rates were proportional to day-14 concentration and inversely proportional to maternal age.

Sutton et al. (2006) said, after in plantation the embryo begins the process of forming a placenta, a large organ made up of both embryonic and maternal tissue that will provide oxygen and nutrients to the developing baby through the unbiblical cord. During this time the level of hormones produces by the embryo increase and cause some of the main symptoms associated with the early pregnancy.

Moreover, Condous et al. (2004) states some sign and symptoms of pregnancy as,
The first sign of a new pregnancy is a missed menstrual period, if your monthly cycle is regular this can obvious. However many women’s commonly experience irregular period or skip periods entirely this sign can be easy to missed. other sign and symptoms of early pregnancy include:

i tender swollen breast or nipples
ii fatigue
iii slight bleeding that is lighter in color than normal menstrual blood
iv cramping
v frequent urination
vi faintness and dizziness e.t.c

An ectopic pregnancy was defined by condous et al. (2004) as the complication of pregnancy in which the pregnant in plants outside the uterine cavity. Furthermore ectopic pregnancy is dangerous for the mother. Internal bleeding being a common complication. Most ectopic pregnancy occur in the fallopian tube, but implantation can also occur in the cervix ovaries and abdomen.

An ectopic pregnancy is a potential medical emergency and if not treated properly can lead to death. Also miscarriage is the lost of a pregnancy before 20 weeks gestation. In fact it is usually occur before 12 weeks, about one in seven recognized pregnancy will miscarriage and about one in three women will experience a miscarriage during their reproductive life. As a result we now know that up to 60% of all conception.

This was a prospective non-interventional observational study, from 3rd January 2010 to 3rd February 2011 women presenting to the EPU at Dutse general hospital Jigawa state with a positive urinary pregnancy test underwent a transvaginal ultrasound examination for various reasons are six hundred and sixty two (662).

Women were classified as having a pregnancy of unknown location (PUL) if there was no evidence of an intra or extrauterine pregnancy on tranvaginal sonography. The criteria used in classification were;
i. Visualization of an intrauterine gestational sac.

ii. Identification of an adnexal mass thought to be an ectopic pregnancy.

iii. Heterogeneous tissue within the endometrial cavity.

iv. Maternal hemodynamic instability or pain.

Women classified with a PUL had blood taken to measure their human chorionic gonadotropin (HCG) and progesterone level using automated electrochemiluminescence immunodissays (ECLIAS) at presentation 0hour and 48hour later. This was based on existing strategies to predict the outcomes of PULS and their own previous experienced. If the serum HCG level increased by >66% in 48hour they generally classified PULs as probable intrauterine pregnancies. If the HCG level decreased over 48hour or the initial progesterone level was <20% they generally classified a pregnancy as a failing PUL, possible ectopic were classified on the basis of either a discriminatory of a suboptical rise of <66% over 48hour and compared with the final outcomes as well as with the predicted outcomes of the logistic regression model.

The costs of misdiagnosing an ectopic pregnancy are greater than those of misdiagnosing a failing PUL or an intrauterine pregnancy. The costs of misdiagnosing an ectopic pregnancy are greater than those of misdiagnosing a failing PUL or an intrauterine pregnancy.

The model was incorporated into a Microsoft excel package and installed on the desktop of the central EPU computer so as to provide a user friendly interface. The serum, HCG result at 0hour and 48hour were entered on to the excel. Spread sheet, giving not only on HCG ratio in real time but also probabilities for the three possible outcomes.

1. A failing PUL
2. An intrauterine pregnancy
3. An ectopic pregnancy.

These predicted outcomes were recorded for clinical management.

<table>
<thead>
<tr>
<th>Failing</th>
<th>IUP</th>
<th>Ectopic</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>300</td>
<td>90</td>
<td>272</td>
<td>66.67%</td>
</tr>
</tbody>
</table>

In the early pregnancy unit (EPU), the location of a pregnancy may be confirmed on the basis of the initial tranvaginal ultrasound examination. In 90-92% of women who present themselves with a positive urinary pregnancy test.

Diagnosis includes a failed intrauterine pregnancy, or an ectopic pregnancy, the remaining 8-10% have an empty uterus with no signs of pregnancy, and these are classified as pregnancies of unknown location (PULs).

**AIM AND OBJECTIVES**

The aims and objectives of this study was to evaluate the performance of this model in comparison with clinical management decision made by experienced nurse practitioners in the clinic.

And also to evaluate the model in an early pregnancy clinical setting. The model can be used by those with limited knowledge or understanding of the behavior of serum and in turn aid in the classification of pregnancies into those at low and those at high risk.

**MATERIALS AND METHODS**

As part of the study serum quantitative human chorionic gonadotrophin (HCG) concentration are taken on days 14 and 16 days oocyte aspiration. If the day 14 HCG test is positive, a second HCG concentration is taken 48hour later (day-16), in part to assist in predicting viable intrauterine pregnancies or to aid in evaluating for a possible ectopic pregnancy. An ultrasound was then performed at 6-7 weeks gestational age to verify cardinal activity and number of gestational sacs.

Often additional HCG concentrations were drawn according to physicians and patient desire for reassurance or to follow a falling concentration. An ongoing pregnancy for this study was defined as one which progressed at least to the point of detection of cardiac activity by ultrasound.

Pregnancies defines as not ongoing were ectopic pregnancies and those that had falling HCG concentration which ultimately become negative, an empty gestational sac on ultrasound (an embryonic) or a fetal pole with no cardiac activity visualized (missed abortion). Multiple gestations were defined by having more than one embryo with cardiac activity. Data analysis using multiple logistic regression models was performed.

Initial analysis of the data considered multiple possible prognostic and confounding factors, assessing each individually and in multiple combinations for their significance. These factors included patient age, day 14 HCG concentration, day 16 HCG concentration, the type of transfer (day-3 embryo versus blastocyst) number of embryos transferred.

Once the significance of each of these factors was determined, the fitting of several logistic regression models was performed utilizing various combinations of the significance factors. This allowed for the determination of the significance of each predictive factor individually as well as in varying combinations to predicting an ongoing pregnancy.
THE RESULT OF THE PREDICTION

Analysis of the factors thought to impact pregnancy outcome was first undertaken using the chi-square test to compare proportions and student’s t-test to compare continuous data in order to determine the significance of a factor in outcome prediction. The differences in age between the groups was strongly significant (P=0.0005), as was the differences in the day-14 and day-16 HCG concentrations (P<0.001 and P<0.001, respectively).

Table I:

<table>
<thead>
<tr>
<th>Prognostic factor</th>
<th>Pregnancies total N(=662)</th>
<th>Ongoing (n=468)</th>
<th>Not going (N=194)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>32.8 ± 4.1</td>
<td>32.5±4.0</td>
<td>33.7±4.1</td>
<td>0.0005</td>
</tr>
<tr>
<td>Day-14 HCG (ratio)</td>
<td>125.7 ± 97.4</td>
<td>153.0 ± 94.1</td>
<td>60.1 ± 70.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Type of embryo</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 3 embryo</td>
<td>517 (78.1)</td>
<td>355 (68.7)</td>
<td>162 (31-3)</td>
<td>0.03</td>
</tr>
<tr>
<td>Blastocyst</td>
<td>145 (21.9)</td>
<td>113 (77.9)</td>
<td>32 (24.0)</td>
<td></td>
</tr>
<tr>
<td>Embryos transferred</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>21 (3.2)</td>
<td>14 (66.7)</td>
<td>7 (33.3)</td>
<td>NS</td>
</tr>
<tr>
<td>2</td>
<td>260 (39.3)</td>
<td>189 (72.7)</td>
<td>71 (27.3)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>244 (36.9)</td>
<td>177 (72.5)</td>
<td>67 (27.5)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>115 (17.4)</td>
<td>75 (65.2)</td>
<td>40 (34.8)</td>
<td></td>
</tr>
<tr>
<td>&gt;5</td>
<td>22 (2.2)</td>
<td>13 (59-1)</td>
<td>9 (40.9)</td>
<td></td>
</tr>
</tbody>
</table>

The day 14 and day 16 HCG concentrations were found to be highly correlated. This relationship is shown in figure 1 ($r=0.880$, $P<0.0001$, $r^2=0.774$) with each data point representing an individual rate cycle.

Four ectopic pregnancies occurred in the 662 documented pregnancies, one with a blastocyst transfer and three with days -3 embryos, yielding an ectopic rate of 0.6%. The mean day-14 and day 16 HCG concentrations of these ectopic pregnancies were 31 and 82 MI/M respectively, with an average rise of 179% over the 2-day period.

Table II below list the comparison of the four different logistic regression models used for the prediction of an ongoing pregnancy, with odds ratio (OR) associated 95% confidence interval (CI) and P-Value. The models analyzed used varying combinations of the initial significant predictive factors, age, day-14 and day -16 HCG concentrations.
Table II

<table>
<thead>
<tr>
<th>Model</th>
<th>Age</th>
<th>Day-14 HCG</th>
<th>Day 16-HCG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age + day-14 + day-16</td>
<td>0.91 (0.87-0.96)</td>
<td>1.01 (1.00-1.02)</td>
<td>1.01 (1.00-1.01)</td>
</tr>
<tr>
<td>HCG (full model)</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age + day-14 HCG</td>
<td>0.91 (0.87-0.97)</td>
<td>1.02 (1.02-1.03)</td>
<td>NA</td>
</tr>
<tr>
<td>Age + day-16 HCG</td>
<td>0.91 (0.86-0.96)</td>
<td>NA</td>
<td>1.01 (1.00-1.02)</td>
</tr>
<tr>
<td>Day-14 + day 16+ 16 HCG</td>
<td>NA</td>
<td>1.01 (1.00-1.02)</td>
<td>1.01 (1.00-1.02)</td>
</tr>
<tr>
<td>Day-14+ day 16 HCG</td>
<td>NA</td>
<td>1.01 (1.00-1.02)</td>
<td>1.01 (1.00-1.01)</td>
</tr>
</tbody>
</table>

In each model, age has an OR of 0.91, indicating that for each increase in age of 1 year, there is a 9% decrease in the chance of a successful pregnancy outcome. Both the day-14 and day-16 HCG, components of the models show on OR of 1.01-1.02. Thus, a 1 unit increase in the day-16 HCG concentration is associated with an increase in the odds of success by a factor of 1.01 or (1%).

Out of 662 patients, the full model age + day-14+ day-16 correctly classified ongoing versus not ongoing pregnancies in 555 patients (83.8%), age + day 14 correctly classified 562 patients (84.9%), age + day 16 correctly classified 552 patients (84.9%) and day 14+day 16 correctly classified 562 patients (84.9%) the disagreement between any two of the four models ranged from only 3-9%.

![Day 14 HCG (MIU/ML)](image)

Age <30, no=136

![HCG Ratio](image)
DISCUSSION
The figures above displays the results of the data by age group. These graphs show the proportion of pregnancies progressing to the point of detection of cardiac activity based on age group and the initial day 14 HCG concentration. This was created by calculating the percentage of cycles ongoing within each HCG concentration quartile.

Each point represents the mean of the quartile group when the HCG concentrations were divided into deciles, similar graphs, were produce with larger standard errors.

As can be seen, there is a declining probability of an ongoing pregnancies with increasing age. The peak percentage of ongoing pregnancies also declines with ages, as does the percentage for a given HCG concentration. These same relationships hold true for the probability of multiple gestation as well.

The figure 2 shows a graphical representation of the chance of an ongoing pregnancy base on age group and initial day -14 HCG concentrations. Success has been shown to be related to the patient’s age with success rate decreasing with increasing age. Success rate begins to decline after age 30, with sharper rates of decline after ages 35 and 40 (CDC et al, 2006). Given these trend-points, the cut off points of 30, 35 and 40 years of age were used to stratify the data into clinically relevant groups.

As expected, ongoing pregnancy rates consistent increased across all age groups as the day 14 HCG values increased. On going pregnancies rates also declined consistently as age increased, with ongoing rates declining from 78.1% for those 40 aged 30 years or less to a low of 48.4% for those 40 years or older. As HCG values increased, the rate of multiple pregnancies increased as well.

The data presented in figure 2 will be useful for counseling patients as to chance of success during the stressful period following the result of their first HCG concentration. These data will provide patients with a reasonable estimate of their chance of having an ongoing pregnancy as well as the chance of a multiple gestation. Although, implementation of these results could reduce the expense of treatment by limiting the number of unneeded HCG concentration, it is unlikely that clinicians will abandon this routine as patient often want the concrete numbers obtained from laboratory results rather than just reassurance that the pregnancy is progressing normally.

The maternal age, day -14 HCG concentration and day-16 concentration were found to be strong predictors of successful pregnancy continuation. The difference in age between those pregnancies that were ongoing and those that were not was strongly significant (P=0.005), as was the differences within the day 14 and day 16 HCG concentration (P<0.001) this significance indicates that these variables may be predictive of implantation success.

The study centre early data confirmed these findings, however within the past 2 years, there has been a clear benefit in blastocyst transfer compared with day-3 embryo transfer resulting in ongoing pregnancy rates of...
48.9% versus 86.2% respectively (P=0.003). This benefit in blastocyst transfer has been mirrored in more recent studies (Papanikolaou 2005, 2006). This recent significance may reflect ongoing change in the culture technique of blastocyst. The development of culture media that more closely matches the needs of a developing embryo has been an area of continued research and has likely contributed to this success.

The higher pregnancy rate could also be attributed to selection bias. At this study usually only those with at least four good quality embryos on day-3 are allowed to be cultured to day -5 before being transferred, thereby, possibly selecting those with higher quality embryos or those that would be inherently more successful.

Although the differences in the number of embryos transferred were not statistically significant, there was a small but non-significant trend to have multiple pregnancies with larger number of embryos transferred. Within this study’s data, singleton pregnancies accounted for 61.3% of cycles (average 2.7 embryos transferred) twins 31.9% (average 2.8 embryos transferred), triplets 6.6% of cycles (average 3.1 embryos transferred) and a single quintuplet set accounting for 0.2% of all cycles (4 embryos transferred).

The result from these data may be criticized due to the fact that multiple embryo transfers was and still is the norm. one may theorize that, by transferring multiple embryos, there may be instances in which more than one embryo in plants, with subsequent early loss of one or more embryos.

REFERENCES
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