Original Articles

AMNIOTIC FLUID CREATININE IN NORMAL PREGNANCY—A TEST FOR FETAL MATURITY

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Abstract

The amniotic fluid creatinine is an important and useful parameter, to measure in later part of pregnancy for fetal age assessment. This is especially so when it is used in conjunction with L/S ratio. Linear regression analysis is better than pairwise "t" test analysis as better understanding of the data is obtained by this analysis. In pairwise 't' test analysis, the size of type one error cannot be controlled (JPMA 29:206, 1979).

Introduction

The amount of creatinine in amniotic fluid is similar to that found in the maternal serum in the early part of pregnancy. In the later phases of pregnancy the creatinine concentration increases abruptly, so that at term it is about twice that of maternal serum.

During the later part of pregnancy, a significant amount of the creatinine in amniotic fluid originates from fetal muscle and is excreted from the fetal serum, into the fetal urine and into the amniotic fluid. This study was conducted to assess the accuracy of this parameter for establishment of fetal maturity in disputed cases of fetal age.

Material and Methods

Between January 1975 through June 1977, 111 samples of amniotic fluid were obtained. Amniocentesis was carried out through transabdominal route, between 33-38 weeks of gestation. These patients had normal pregnancy and were admitted to the Foothills hospital in Calgary, Alberta, Canada. The indication for amniocentesis was disparity between the uterine size and expected date of confinement.

The Jaffe Alkaline picrate reaction was used to determine creatinine concentration.

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Statistical Methods

The data collected was arranged for computer analysis, and punched on the IBM Cards.

Statistical methods like Pairwise 't' test and linear regression analysis were used to analyse our data.

Two types of statistical analysis were used. The first was linear regression. The second was comparison of the mean levels of the dependent variables observed over each of the following three regions of the independent variables: $X < 35$ weeks, 35 weeks $\leq X \leq 37$ weeks. The comparison was first carried out using pairwise t-tests. Details of methods and summaries of results follow below.

Linear Regression

Two different linear regressions were carried out, one regression for each parameter and for each of the 4 dependent variables. In each case the assumed model was

$$Y_i = \alpha + \beta X_i + e_i, \quad i = 1, \ldots, N,$$

where N is the number of observations, X_i is the observed gestational age in weeks, Y_i is the corresponding observed value of the dependent variable, a and B are unknown regression parameters (to be estimated), and the e_i's are independent normally distributed random error with mean O and common unknown variance.

Least squares estimates of a and B were computed, to yield an estimated regression line

$$\hat{Y} = a + bX.$$

The null hypothesis $H_o : B = O$ was tested against the alternative $H_a : \beta/O$ at level $\alpha = 0.5$. To carry out the test, one computes

$$t = \frac{b}{S_e \sqrt{(X_i - \bar{X})^2}}$$

where

$$S_e^2 = \frac{1}{n-2} \sum \left[Y_i - (a + bX_i) \right]^2$$

and rejects H_o if (t) exceeds the upper 2.5% point of the t-distribution with n-2 degrees of freedom.

Table 1 summarizes the linear regression analyses, giving N, a, b and t, and indicating whether H_o is rejected at the .05 level. The value of the statistic r^2, which can be roughly interpreted as the percentage of the variability in the data and can be 'explained' by a linear relationship between Y and X was tabulated.

Table 1 : Linear Regression Analysis of Creatinine Values

Dependent Variable Y	*Sample Size* N	*Estimated Intercept* a	*Estimated Slope* b	*t Value for testing* $H_o : B = o$ *Vs* $H_1 : B \neq o$	*Significant at level* $\alpha = .05$	r^2
Creatinine in mg/dl	111	—1.95	0.110	6.117	Yes	0.256

Pairwise T-Test

The observed Y's were divided into 3 groups: (1) those Y's for which the corresponding $X < 35$ weeks; (2) those Y's for which 35 weeks $X \leq 37$ weeks; and those Y's for which $X > 37$ weeks. The assumed model was

$$Y_{ij} = \mu_i + e_{ij} \qquad \begin{matrix} i = 1,2,3 \\ j = 1, \ldots N_i. \end{matrix}$$

where U_1, U_2 and U_3 are the true mean values of the Y_{ij}'s in the 3 groups, N_i is the number of observations in the ith group, and the e_{ij}'s are independent normally distributed random variable with mean O and common unknown variance.

The scatter diagram of Y vs X was also considered. In those cases in which H_o is rejected, indicating a regression line with a slope "significantly", different from O, the estimated regression line $\hat{Y} = a + bX$ is plotted on the scatter diagram.

Tests of $H_0: \mu_1 = \mu_2$ against $H_a: \mu_1 \neq \mu_2$,

$H_0: \mu_1 = \mu_3$ against $H_a: \mu_1 \neq \mu_3$,

$H_0: \mu_2 = \mu_3$ against $H_a: \mu_2 \neq \mu_3$,

were carried out at the .05 level of significance. To test $H_0: U_i = U_j$ against $H_a: U_i \neq U_j$ at level $\mathcal{L} = .05$, one computes

$$t = \frac{\overline{Y_i} - \overline{Y_j}}{S\sqrt{\frac{1}{N_i} + \frac{1}{N_j}}},$$

where $$S^2 = \frac{(N_i - 1)S_1^2 + (N_j - 1)S_2^2}{N_i + N_j - 2}$$

and rejects H_0 if (t) exceed the upper .025 point of the t-distribution with $N_i + N_j - 2$ degrees of freedom.

The pairwise t-tests are summarized in Table II. An asterisk next to the value of t indicates that there is a significant difference in the group means (i.e. $H_0: U_i = U_j$ is rejected at the level $\mathcal{L} = .05$).

Table II: Pairwise "t" Test Analysis Creatinine Values

N_x	$\bar{X}$	N_y	$\bar{Y}$	t	t	d.f.	Weeks of gestation
11	1.654545	21	2.085714	0.4716279	−2.45628*	30	x: < 35wks y: 35-37wks
78	2.403846	21	2.085714	0.572519	2.260247*	97	x: ≥ 38wks y: 35-37wks
78	2.4038461	11	1.654545	0.5846319	3.97944*	87	x: ≥ 38wks y: < 35wks

* Significant at .05 level.

Results

Our results indicate that there is a significant difference in creatinine concentration in the amniotic fluid before 35 weeks of gestation, between 35-37 weeks and at 38 weeks of pregnancy.

Fig. 1 shows scattergram of the creatinine values of 111 samples, table I and II show linear regression analysis and pairwise "t" test results, respectively.

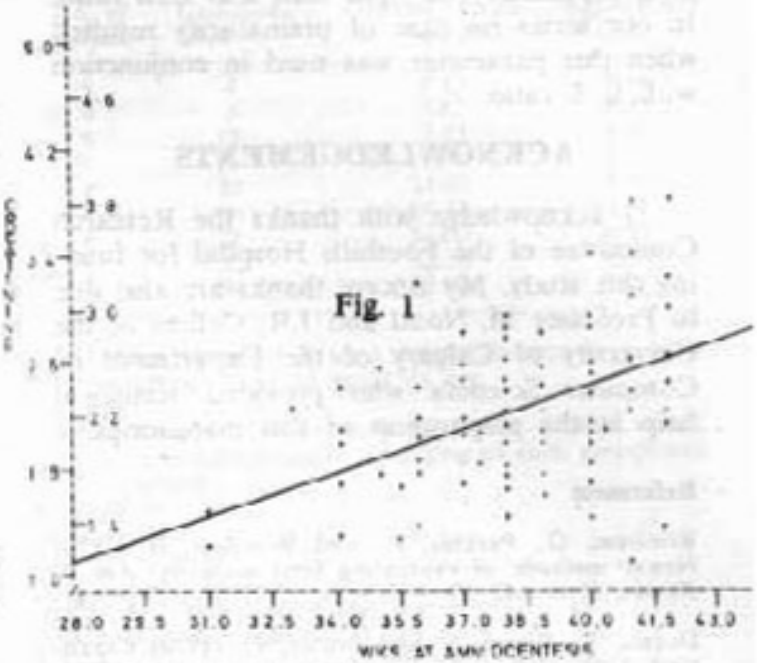

Fig. 1

We found that value of 1.8 mgm % indicated fetal maturity. There was progressive increase in the concentration of creatinine in the amniotic fluid as the pregnancy advanced. This is shown in Fig. 1 by the regression line drawn on the scattergram.

Discussion

Measurement of amniotic fluid creatinine correlates well with fetal gestational age, this has been reported previously (Bemtrem et al., 1970; Doran et al., 1970). The correlation is only with fetal age and not with fetal survival, as is often needed in high risk obstetric cases.

This parameter alone is not so helpful as it is in conjunction with other amniotic fluid parameter i.e., lipid cells and L/S ratio. In our series no case of prematurity resulted when this parameter was used in conjunction with L/S ratio.

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References

Bemtrem, G., Perkins, P. and Waxman, B. (1970) Newer methods of evaluating fetal maturity. Am. J. Obstet. Gynecol., 106:917.

Doran, T., Bjerre, S. and Porter, C. (1970) Creatinine Uric acid and electrocytes in amniotic fluid. Am. J. Obstet. Gynecol., 116: 325.