

LENGTH OF PREGNANCY IN AFRICAN AMERICANS: VALIDATION OF A NEW PREDICTIVE RULE

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This study evaluated whether a new predictive rule is more accurate for estimating the length of pregnancy in African Americans than Nägele's rule, the accepted standard. After identifying women in early pregnancy, telephone interviews were conducted to obtain information about 16 previously established determinants of gestational length. Based on these data, a linear multivariate regression model was used to predict an estimated delivery date (EDD) for each mother. In addition, the EDD was determined using Nägele's rule. Later, the actual delivery date was compared with the EDD predicted by the new rule and with the EDD predicted by Nägele's rule. Each pregnancy was assigned to its better prediction group, either the new rule's group or the Nägele's rule group.

Fifty-seven pregnancies were identified prospectively and monitored. The new rule predicted the actual delivery date more accurately in 66% (37/56) of pregnancies, Nägele's rule was a better predictor in 34% (19/56) of pregnancies, and both rules were equally accurate in predicting the delivery date for one pregnancy. The new rule was more precise than Nägele's rule ($P=.022$) when the binomial distribution was used. When using the linear regression model rule, a more accurate EDD can be determined for African-American women. Moreover, it is possible to predict the risk of preterm delivery (those occurring >3 weeks earlier than the EDD). (*J Natl Med Assoc.* 1999;91:523-527.)

Key words: pregnancy ♦ Nägele's rule

Nägele's rule, named for Franz Carl Nägele (1778-1851), is a fixed-point estimator which does not permit incorporating any variability in human gestational

length. It is based on the ancient belief¹ that the length of pregnancy is equivalent to 10 lunar cycles and not on any empirical evidence. To predict the estimated delivery date (EDD) by Nägele's rule, for all women with reliable menstrual histories—irrespective of their individual differences—nine months and seven days are added to the first day of the last menstrual period. For example, if the last menses before pregnancy began on January 1, by Nägele's rule, the EDD would be October 8. In women with uncertain menstrual histories, Nägele's rule-based ultrasound dating is used. For example, if, on March 1, an ultrasound examination of a fetus diagnosed a pregnancy of 10 weeks and three days duration, the EDD would be October 2.

Several years ago, because of our interest in factors that could influence gestational length and the risk of

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preterm delivery (defined as deliveries occurring >3 weeks earlier than the EDD), two of the authors (R.M. and M.A.W.) did a small retrospective study² among mostly first- or second-generation ethnic Celtic women. We learned that pregnancy length in mothers delivering for the first time (primiparas) is different from pregnancy length in mothers who have delivered previously (multiparas). In a second, larger study, using information obtained from 9355 pregnant women that included >1000 African-American women in the Delivery Interview Program,³ we showed there are no fewer than 16 statistically significant factors that can be used to account for approximately 21% of the variability (adjusted $R^2=.206$) in human pregnancy length.

This study evaluated whether this new rule using a linear regression model for predicting the EDD is more accurate than Nägele's rule.

MATERIALS AND METHODS

Study Population

Pregnant women at the Chicago Lying-in Hospital were prospectively selected from April 1994 to December 1995 for participation in the study. Enrollment criteria included singleton gestation, African-American ancestry as reported by the patient, a first-trimester ultrasound performed at Chicago Lying-in Hospital, a pregnancy surviving for at least 20 weeks, and an active patient telephone number to permit interviews after delivery.

After identifying gestations <13 completed weeks in length using records from the Chicago Lying-in Hospital Ultrasound Unit, patients were asked for informed consent before a telephone interview was conducted. The study was approved by the institutional review board.

To compute the EDD based on the regression model rule, questions were asked about the following previously identified determinants of gestational length:

- maternal age (a factor in which younger and older women have shorter gestational lengths; thus, the variable must be modeled as a parabola with a linear term, "age," and a squared term, "age²"),
- body mass index (based on height and prepregnancy weight),
- level of education (any college, yes or no),
- coffee consumption (number of cups consumed daily in pregnancy),
- alcohol consumption (yes or no),

- history of incompetent cervix (yes or no),
- history of previous deliveries (parity),
- in utero exposure to diethylstilbestrol (DES) (yes or no),
- number of spontaneous abortions,
- prior stillbirth (yes or no), and
- history of first-trimester vaginal bleeding (yes or no).

Because many of our patients were uncertain of their menstrual histories, the determination of the Nägele's rule EDD was based on ultrasound findings, not on last menstrual period.

Months later, follow-up telephone interviews were conducted to confirm the actual delivery date and to learn whether labor was induced. Pregnancies induced early for medical indication as well as those ended by elective repeat cesarean section were excluded from the analysis. Inductions for post-term pregnancies were included. The actual delivery date was compared with the EDD predicted by the new rule as well as the ultrasound-based Nägele's rule determination of the EDD. After exclusions and losses to follow-up, 57 women comprised the study population.

Power Analysis

For $\alpha=.05$, $\beta=.2$ (80% power), a true success rate in which the new rule was more correct than Nägele's rule for 60%, 70%, or 80% of pregnancies, the sample size was computed to be 189, 42, or 14, respectively. For example, if the new rule was more correct in identifying the actual EDD for 70% of pregnancies and conversely, Nägele's rule more correct in identifying the actual EDD for 30% of pregnancies, a total sample size of 42 evaluable pregnancies would have been required to ensure 80% power. Since prior epidemiologic information on which to base a power calculation was not available, as many patients as possible were enrolled during the study period.

RESULTS

The new rule is based on a least squares multiple linear regression model in which statistically significant variables, such as race, maternal age, parity, and others are summed to determine a point estimate for the EDD. Mathematically, this is expressed as:

$$y=\alpha+\beta_1x_1+\beta_2x_2+\dots+\beta_kx_k,$$

where y , the dependent variable, is the length of ges-

tation in days, α is the intercept, the β 's are the values of the various coefficients, and x_1, x_2, \dots, x_k are the values of the variables, such as race, parity, and educational level, among others (Table 1). For example, women who have delivered previously (parous women), deliver on average 3.1 days earlier than women who have not delivered before. Women who have not had any college education deliver on average 1.2 days earlier than those who have.

Of 57 pregnancies evaluated, the new rule predicted the actual delivery date more accurately in 66% (37/56) of pregnancies (Table 2), Nägele's rule was a better predictor of the actual delivery date in 34% (19/56), and in one pregnancy both rules were equally accurate in predicting the actual delivery date. For example, in subject number 30 (Table 2), the new rule EDD was within one day of the actual delivery date whereas the Nägele's rule EDD was within 11 days of the actual delivery date. Thus, for this pregnancy, the new rule was a better predictor.

By using the binomial distribution, the new rule was more accurate in determining the EDD than Nägele's rule ($P=.022$). In fact, the new rule was about twice as precise as Nägele's rule (66% versus 34%). In predictions by the new rule, the actual delivery date occurred within seven days of the predicted EDD in 53% (30/57) of pregnancies and within four days in 30% (17/57) of pregnancies.

DISCUSSION

In part, Nägele's rule continues to be used commonly to predict the EDD because there have been so few studies of gestational length predictors and the factors associated with preterm delivery. Among these, Kramer,⁴ in a comprehensive review of low birthweight, found only four variables to be associated with the length of pregnancy per se: prepregnancy weight, history of preterm delivery or miscarriage, exposure to DES in utero, and cigarette smoking. Factors reported by others to be important predictors of pregnancy length include race and ethnicity,^{5,6} and parity.⁷ Using data from a large study,³ we previously reported 16 statistically significant predictors of gestational length. The regression model developed from that study formed the basis for our new rule to predict the EDD and the probability of preterm delivery.

When using this new rule, a more accurate EDD and risk for preterm delivery can be determined for individual African-American women. By way of illustration, a 29-year-old primiparous African-American woman whose body mass index is 20

Table 1. Statistically Significant* Parameter Estimates for Predicting Gestational Length, in Days, for the New Rule

Variable	β -Coefficient
Variables Used in First-Trimester Predictions	
Intercept	256.447
Maternal age	1.5648
Maternal age ²	-0.0259
Race	-2.5328
Body mass index (kg/m ²)	0.1295
Educational level	-1.1956
Alcohol	1.0463
Coffee	-0.3928
Incompetent cervix	-18.8054
Parity	-3.1169
DES exposure <i>in utero</i>	-2.6281
Miscarriage	-0.6990
Stillbirth	-4.4849
Bleeding, first trimester only	-2.8788
Variables Used for Later Complications	
Bleeding, first and other trimester	-4.1633
Bleeding, second or third, or both	-10.8793
Placenta previa	-14.4468
Abruptio placentae	-18.4556
Premature rupture of membranes	-27.3494
Pregnancy-induced hypertension	-5.4884
* $\alpha \leq .05$.	

(5'5" tall with a prepregnancy weight of 120 lb) with a history of one prior miscarriage, but who has no other risk factors that shorten pregnancy, would have a predicted gestational length of 279.4 days—256.4 days (intercept, α)—2.5 days (race) $[2.5 \{\beta_1\} \times (\text{African American})]$ +23.6 days (age) $[1.5648 \{\beta_2\} \times 29 \text{ (age in years)} - 0.0259 \{\beta_3\} \times 29^2 \text{ (age in years squared)}]$ +2.6 days (body mass index) $[0.1295 \{\beta_4\} \times 20] - 0.7 \text{ days (miscarriage)} [0.7 \{\beta_5\} \times 1] = 279.4 \text{ days}$ —not the 280 days predicted by Nägele's rule. Her risk of preterm delivery would be 7.2%.

By comparison, a 20-year-old multiparous African-American woman whose body mass index is 18 (5'6" tall with a prepregnancy weight of 112 lb) with a history of first-trimester vaginal bleeding and who drinks two cups of coffee daily would have a predicted gestational length of 270.3 days—256.4 days (intercept, α)—2.5 days (race) $[2.5 \{\beta_1\} \times (\text{African American})]$ —3.1 days (parity) $[3.1 \{\beta_2\} \times (\text{multiparous})]$ +20.9 days (age) $[1.5648 \{\beta_3\} \times 20 \text{ (age in years)} - 0.0259$

Table 2. Absolute Differences* (in Days) Between Actual Delivery Date and EDD Predicted by Nägele's Rule and Between Actual Delivery Date and EDD Predicted by the New Rule

Patient No.	Nägele Δ	New Rule Δ	Patient No.	Nägele Δ	New Rule Δ
01	17	06	30	11	01
02	05	01	31	14	04
03	01	07	32	52	44
04	04	09	33	15	02
05	25	16	34	02	06
06	14	04	35	07	18
07	05	05	36	10	01
08	04	06	37	06	04
09	06	13	38	18	11
10	04	04	39	00	09
11	09	05	40	25	19
12	10	02	41	16	07
13	27	16	42	07	25
14	06	04	43	11	01
15	19	10	44	03	11
16	26	16	45	31	06
17	05	06	46	10	02
18	04	05	47	01	10
19	21	08	48	54	47
20	33	25	49	01	12
21	09	03	50	04	05
22	34	21	51	05	09
23	02	06	52	15	04
24	01	10	53	10	15
25	47	35	54	09	01
26	44	34	55	11	20
27	09	05	56	38	26
28	08	01	57	16	04
29	04	37			

*|Δ|. EDD=estimated delivery date.

$\{\beta_4\} \times 20^2$ (age in years squared)] + 2.3 days (body mass index) $[0.1295 \{\beta_5\} \times 18] - 2.9$ days (first-trimester vaginal bleeding) $[2.9 \{\beta_6\}] - 0.8$ days (coffee) $[0.4 \{\beta_7\} \times 2] = 270.3$ days. The woman in this example would have a 24% risk of preterm delivery.

Concerning limitations of the new rule, the data from the Delivery Interview Program did not include information regarding prior history of preterm delivery and cocaine abuse—now agreed-on predictors of preterm delivery. However, including this information would make the predicted EDD for women even earlier, not later. So, if anything, the new rule overpredicts gestational length. The large dataset on which the new predictive rule is based does contain information on 40 variables, 16 of which are statistically significant.

In practice, the new rule may be even more precise than what we are reporting because information captured in the model about certain pregnancy complications, eg, abruptio placentae, occur later in pregnancy than the first trimester when the EDD would be assigned for a patient. Revising the EDD when these later-in-pregnancy complications occur would permit an even more accurate prediction of the patient's delivery date (Table 1).

CONCLUSION

The predictive rule validated in this study can be used to estimate a more accurate EDD and to identify those at risk for preterm delivery. Overall, for whites in the United States, 8.5% of deliveries are preterm, while for African Americans, the risk of

preterm delivery is 17.8%,⁸ although some African-American women have a lesser risk while others have a greater risk. In the future, when the capacity to prevent preterm delivery may be improved, an important step in prevention will be identifying the mother who is at higher-than-average risk. We believe the use of this new rule will facilitate such identification.

Literature Cited

1. Saunders N, Peterson C. Can we abandon Nägele's rule? *Lancet*. 1991;337:600-601.
2. Mittendorf R, Williams MA, Berkey CS, Cotter PF. The length of uncomplicated human gestation. *Obstet Gynecol*. 1990;75:929-932.
3. Mittendorf R, Williams MA, Berkey CS, Lieberman E, Monson RR. Predictors of human gestational length. *Am J Obstet Gynecol*. 1993;168:480-484.
4. Kramer MS. Determinants of low birth weight: methodological assessment and meta analysis. *Bull World Health Organ*. 1987;65:663-737.
5. Doering GK. Normale schwangerschaft und geburt. *Geburtshilfe Frauenheilkd*. 1962;22:1191-1194.
6. Saito M, Yazawa K, Hashiguchi A, Kumasaka T, Nishi N, Kato K. Time of ovulation and prolonged pregnancy. *Am J Obstet Gynecol*. 1972;112:31-38.
7. Henderson M, Kay J. Differences in duration of pregnancy. *Arch Environ Health*. 1967;14:904-911.
8. Main DM, Main EK. Preterm birth. In: Gabbe SG, Niebyl JR, Simpson JL, eds. *Obstetrics: Normal and Problem Pregnancies*. 2nd ed. New York, NY: Churchill Livingstone; 1991:829-880.



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Anti-Human Immunodeficiency Virus Activity of Curcumin as Measured by a Decrease in PCR-RNA Levels in Human Immunodeficiency Virus-Positive Patients

Wilbert C. Jordan, Tinh Duong, David Jones, Anita Francis, Jeanne Hill, and Alberto Miranda

The charts of patients who voluntarily obtained the herb curcumin were reviewed. These patients were self-selected based on community information that curcumin was effective against human immunodeficiency virus (HIV). All patients had CD4 counts >500 and were not taking any antiretroviral medications. Of the 22 patients who participated, 15 showed improvement as measured by a drop in PCR-RNA for HIV and 16 showed improvement as measured by an increase in CD4 count. Twelve patients showed an improvement by both measurements. This herb, an alternative therapy, has anti-HIV activity, and its potential as an early preventive therapy needs further investigation.

In Vivo Production of Type 1 Cytokines in Healthy Sickle Cell Disease Patients

Stephen C. Taylor, Samuel J. Shacks, and Zengwei Qu

Interleukins (IL)-1, 2, 12 and interferon (IFN)- γ along with soluble IL-2 receptor (sIL-2R) were measured from sera obtained from healthy sickle cell disease (SCD) patients and healthy control subjects. The cytokines were assessed by ELISA in 60 SCD patients and 58 controls. Results showed no significant detectable levels of IL-1 or IL-12 in the sera of either group. Significantly elevated levels of IFN- γ were measured in 20 (33%) of 60 SCD patients and 21 (36%) of 58 controls. A large subset of 18 (41%) of 43 healthy controls and a smaller subset of 12 (21%) of 58 SCD patients demonstrated detectable levels of IL-2. The sIL-2R levels of the SCD group were significantly higher than that of the controls. The results revealed comparable circulating levels of all type 1 cytokines in both the healthy SCD and normal control subjects, with the exception of in vivo sIL-2R production. Elevated serum levels of both IL-6 and tumor necrosis factor (TNF)- α have been reported previously in a significant percentage of SCD steady-state subjects. These two cytokines are known to increase sIL-2R expression and may help explain the difference between the patient populations. Immune activation markers like sIL-2R are produced by cells that mediate host responses to infection or inflammatory stimuli. The implication of higher levels of sIL-2R in SCD is not clear, but chronic Parvovirus B19 infection, chronic polyclonal activation of B cells, and defective regulation of antibodies are possible explanations for the elevated levels in SCD.