Accuracy of gestational age estimation by means of fetal crown-rump length measurement

Salim Daya, MB, MSc
Hamilton, Ontario, Canada

OBJECTIVE: The purpose of this study was to develop a gestational age table by means of crown-rump length measurements in the first trimester in pregnancies conceived through in vitro fertilization.
STUDY DESIGN: Ninety-four infertile women with singleton intrauterine pregnancies resulting from in vitro fertilization underwent ultrasonographic examinations in the first trimester. The relationship between gestational age (calculated with the day of oocyte retrieval used as day 14) and the crown-rump length was explored with regression analysis.
RESULTS: A quadratic model demonstrated the best fit to the data, indicating a curvilinear relationship between crown-rump length and gestational age. Estimates of gestational age with crown-rump length measurements between 40 and 60 mm were observed to be similar to published tables, but outside this range the tables either overestimate or underestimate the true gestational age.
CONCLUSION: A more accurate equation for gestational age estimation with crown-rump length measurements in early pregnancy has been developed with in vitro fertilization pregnancy data. (Am J Obstet Gynecol 1993;168:903-8.)

Key words: Gestational age, crown-rump length, ultrasonography, in vitro fertilization, early pregnancy

Precise knowledge of the gestational age of the fetus is very important in the successful management of pregnancy, especially when obstetric complications develop. It is also of vital importance in the evaluation of fetal growth so that appropriate decisions can be made in the presence of intrauterine growth retardation. For a variety of reasons, the gestational age is often unknown or may be inaccurate.

In women with regular menstrual cycles the reliance on the first day of the last menstrual period (LMP) as a reference point to determine duration of pregnancy is generally accepted. However, the follicular phase has a skewed distribution,[1] and many factors may affect the time interval from LMP to ovulation, even in women with regular cycles. In fact, wide variation (−6 days to +4 days) has been reported between the expected time of ovulation predicted by the LMP and the actual time observed by ultrasonographic monitoring of follicular growth and collapse.[2, 3] This variation is further emphasized by the observation that in 15% of normal pregnancies neonatal age assessment differed markedly from that assigned by certain menstrual dates.[4] Similarly, menstrual history was considered reliable in only 18% of women in a large study that attempted to identify clinical estimators of gestational age.[5]

Ultrasonographic measurement of the fetal crown-rump length introduced more objective criteria for estimation of gestational age. However, the "gold" standard used was the LMP[6, 7] and, more recently, date of ovulation on the basis of basal body temperature graphs and timing of insemination with donor sperm or ultrasonographic demonstration of follicle collapse.[8, 9] Both these parameters have significant variability and are a potential source of error in estimating gestational age.

Pregnancies resulting from in vitro fertilization (IVF) have made it possible to study fetal growth without the uncertainties of time of ovulation and conception. The prupose of this study was to develop a gestational age table on the basis of crown-rump length measurements in the first trimester in IVF pregnancies and to compare the predictability of existing tables[6-9] with those generated from these data.

Material and methods

The study population consisted of 94 infertile women with singleton intrauterine pregnancies resulting from treatment in the IVF program at Chedoke-McMaster Hospitals, Hamilton, Ontario, Canada. Embryos were transferred into the uterus 2 days after the day of oocyte retrieval, which was assigned day 14 of gestation. The

From the Department of Obstetrics and Gynaecology, McMaster University.
S.D. is Career Scientist of Ontario Ministry of Health.
Received for publication February 14, 1992; revised July 15, 1992; accepted September 22, 1992.
Reprint requests: Salim Daya, MB, MSc, Department of Obstetrics and Gynaecology, McMaster University, 1200 Main St., W., Hamilton, Ontario, Canada L8N 3Z5.

0002-9378/93 $1.00 + .20 6/1/42806

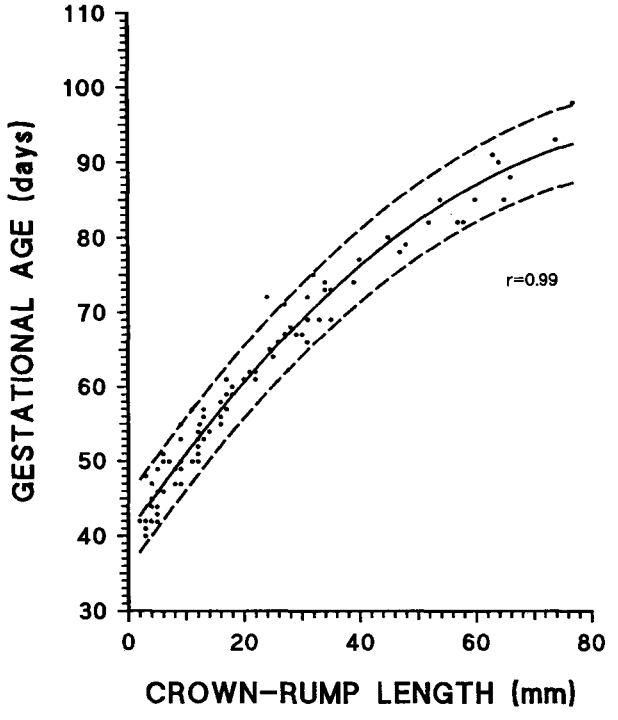

Fig. 1. Relationship between fetal crown-rump length and gestational age. Quadratic regression equation is as follows: Gestational age = 40.447 + 1.125(crown-rump length) − 0.0058 (crown-rump length)^2. 95% Prediction interval is also shown.

validity of this assumption has previously been tested by means of human chorionic gonadotropin normal curve, the curve from IVF pregnancies plotted either on this normal curve or parallel to it with a variability of ± 1 day.[10, 11] All pregnancies were confirmed with rising serum titers of human chorionic gonadotropin and are presently continuing or have already delivered normal infants.

Ultrasonographic examinations were performed with the Aloka SSD-650 scanner with convex sector probes (Omnium, Richmond Hill, Ontario, Canada). The 5 MHz probe with 60-degree scanning angle was used for transvaginal scanning and the 3.5 MHz probe with 60-degree scanning angle was used for transabdominal scanning. The crown-rump length was measured along the longest axis with the fetus in an extended position if possible. All measurements (in millimeters) were made directly on the frozen screen by means of calipers applied to the outer margins of the head and the trunk. The averge of two to three measurements was taken.

Statistical analysis. Patients had one to three ultrasonographic examinations in the first trimester. For data analysis the examination selected for patients having more than one scan was done randomly. The relationship between gestational age (calculated with the day of oocyte retrieval as day 14) and crown-rump length was explored by means of polynomial regression analysis to identify the model that provided the best fit to the data. The 95% confidence interval and prediction interval were also calculated.

Table I. Polynomial regression analysis of ultrasonographic measurements of crown-rump length with respect to gestational age

Regression models	*F Values*		
	Overall regression	*Lack of fit*	*Improved predictive power with higher-order model*
Straight-line	1669 ($p < 0.001$)	2.78 ($p < 0.001$)	–
Quadratic	1561 ($p < 0.001$)	1.03 ($p = 0.46$)	76.95 ($p < 0.001$)
Cubic	1159 ($p < 0.001$)	0.82 ($p = 0.75$)	10.91 ($p = 0.001$)
Quaternary	871 ($p < 0.001$)	0.81 ($p = 0.75$)	1.15 ($p = 0.29$)

Results

Fig. 1 represents a scattergram of crown-rump length plotted against gestational age showing a curvilinear relationship between the two variables. To determine which regression model would best fit the data, the following were tested: straight line, quadratic, cubic, and quaternary. Table I shows that all models demonstrate a significant overall regression. However, when lack of fit for each model is tested, the simple linear model is not appropriate ($F_{44,48} = 2.78$, $p < 0.001$), and the quadratic model provides significantly more predictive power (partial $F_{1,91} = 76.95$, $p < 0.001$). Although the higher-order cubic model improved the predictive power of the quadratic model (partial $F_{1,90} = 10.91$, $p = 0.001$), it is not a suitable model to use because it is computationally more tedious and the regression coefficient for the third-order variable was only 3.94×10^{-5}, thus making an insignificant contribution to gestational age calculation. The residuals plotted against crown-rump length for the straight line, quadratic, and cubic models confirmed the superiority of the quadratic model over the simple linear one and no apparent benefit from using the cubic model (plots not shown). The quadratic regression line is shown in Fig. 1 and confirms that the rate of growth of the fetus is not linear as has previously been suggested.[3] By means of this equation the gestational age for various crown-rump length measurements has been calculated (Tables II and III).

Table IV shows the differences between the true gestational age (from IVF pregnancies) and those pre-

Table II. Gestational age in days as determined by crown-rump length measurements

Crown-rump length (mm)	*Gestational age (days)*
2	42.7
3	43.8
4	44.9
5	45.9
6	47.0
7	48.0
8	49.1
9	50.1
10	51.1
11	52.1
12	53.1
13	54.1
14	55.0
15	56.0
16	56.9
17	57.9
18	58.8
19	59.7
20	60.6
21	61.5
22	62.4
23	63.2
24	64.1
25	64.9
26	65.7
27	66.6
28	67.4
29	68.2
30	68.9
31	69.7
32	70.5
33	71.2
34	71.9
35	72.7
36	73.4
37	74.1
38	74.8
39	75.4
40	76.1
41	76.8
42	77.4
43	78.0
44	78.6
45	78.6
46	79.8
47	80.4
48	81.0
49	81.6
50	82.1
51	82.6
52	83.2
53	83.7
54	84.2
55	84.7
56	85.1
57	85.6
58	86.1
59	86.5
60	86.9
61	87.3
62	87.8
63	88.2
64	88.5
65	88.9
66	89.3
67	89.6
68	90.0
69	90.3
70	90.6
71	90.9
72	91.2
73	91.5
74	91.7
75	92.0
76	92.2
77	92.5
78	92.7
79	92.9
80	93.1

dicted with crown-rump length dating curves from four different reports. Marked differences were seen between IVF data and gestational age predicted by day of ovulation[8, 9] or menstrual dates.[6, 7] With the ovulation-timed equations it is apparent that gestational age is consistently overestimated (mean 2.4 to 3.9 days). The error is most obvious during the early gestational period when the fetus is <40 mm long and later in pregnancy when the fetal length is >60 mm (Figs. 2 and 3). The discrepancy when menstrual data are used is surprisingly less and in general tends to underestimate gestational age (mean of 1.9 days) (Fig. 4). By means of equations described by Robinson and Fleming[6] and Drumm et al.,[7] underestimation occurred early in pregnancy, but toward the end of the first trimester increasing overestimation was observed (Fig. 5). All equations produced similar estimates of gestational age with crown-rump length measurements between 40 and 60 mm, but outside this range the curves either overestimated or underestimated the true gestational age.

Comment

The results confirm that in early pregnancy a curvilinear relationship exists between gestational age and fetal crown-rump length. With growth curves for patients who underwent two ultrasonographic examinations Rossavik et al.[12] stressed that crown-rump length growth should be described by a linear function rather than by a second-order polynomial. As the data show, the simple linear model does provide a significant overall regression but does not fit the data properly. A better fit is obtained by the higher-order model, suggesting that crown-rump length–based gestational age tables should be used with a quadratic equation as shown in Tables II and III. This will allow more precise estimation of gestational age when first trimester ultra-

Table III. Gestational age in weeks as determined by crown-rump length measurements

Crown-rump length (mm)	Gestational age (wk)		
	Fitted value	95% Confidence interval	95% Prediction interval
2	6.1	6.0-6.2	5.4-6.8
3	6.3	6.1-6.4	5.6-6.9
4	6.4	6.3-6.5	5.7-7.1
5	6.6	6.4-6.7	5.9-7.3
6	6.7	6.6-6.8	6.0-7.4
7	6.9	6.8-7.0	6.2-7.6
8	7.0	6.9-7.1	6.3-7.7
9	7.2	7.1-7.3	6.5-7.8
10	7.3	7.2-7.4	6.6-8.0
11	7.4	7.3-7.5	6.8-8.1
12	7.6	7.5-7.7	6.9-8.3
13	7.7	7.6-7.8	7.0-8.4
14	7.9	7.8-8.0	7.2-8.6
15	8.0	7.9-8.1	7.3-8.7
16	8.1	8.0-8.2	7.4-8.8
17	8.3	8.2-8.4	7.6-9.0
18	8.4	8.3-8.5	7.7-9.1
19	8.5	8.4-8.6	7.8-9.2
20	8.7	8.6-8.8	8.0-9.3
21	8.8	8.7-8.9	8.1-9.5
22	8.9	8.8-9.0	8.2-9.6
23	9.0	8.9-9.1	8.3-9.7
24	9.2	9.1-9.2	8.5-9.8
25	9.3	9.2-9.4	8.6-10.0
26	9.4	9.3-9.5	8.7-10.1
27	9.5	9.4-9.6	8.8-10.2
28	9.6	9.5-9.7	8.9-10.3
29	9.7	9.6-9.8	9.0-10.4
30	9.9	9.8-9.9	9.2-10.5
31	10.0	9.9-10.1	9.3-10.6
32	10.1	10.0--10.2	9.4-10.8
33	10.2	10.1-10.3	9.5-10.9
34	10.3	10.2-10.4	9.6-11.0
35	10.4	10.3-10.5	9.7-11.1
36	10.5	10.4-10.6	9.8-11.2
37	10.6	10.5-10.7	9.9-11.3
38	10.7	10.6-10.8	10.0-11.4
39	10.8	10.7-10.9	10.1-11.5
40	10.9	10.8-11.0	10.2-11.6
41	11.0	10.9-11.1	10.3-11.7
42	11.1	10.9-11.2	10.4-11.8
43	11.2	11.0-11.3	10.5-11.8
44	11.2	11.1-11.4	10.5-11.9
45	11.3	11.2-11.5	10.6-12.0
46	11.4	11.3-11.5	10.7-12.1
47	11.5	11.4-11.6	10.8-12.2
48	11.6	11.4-11.7	10.9-12.3
49	11.7	11.5-11.8	11.0-12.4
50	11.7	11.6-11.9	11.0-12.4
51	11.8	11.7-12.0	11.1-12.5
52	11.9	11.7-12.0	11.2-12.6
53	12.0	11.8-12.1	11.2-12.7
54	12.0	11.9-12.2	11.3-12.7
55	12.1	11.9-12.3	11.4-12.8
56	12.2	12.0-12.3	11.5-12.9
57	12.2	12.1-12.4	11.5-12.9
58	12.3	12.1-12.5	11.6-13.0
59	12.4	12.2-12.6	11.6-13.1
60	12.4	12.2-12.6	11.7-13.1
61	12.5	12.3-12.7	11.8-13.2
62	12.6	12.3-12.8	11.8-13.3
63	12.6	12.4-12.8	11.9-13.3
64	12.7	12.4-12.9	11.9-13.4
65	12.7	12.5-12.9	12.0-13.4
66	12.8	12.5-13.0	12.0-13.5
67	12.8	12.6-13.0	12.1-13.5
68	12.9	12.6-13.1	12.1-13.6
69	12.9	12.7-13.2	12.2-13.6
70	13.0	12.7-13.2	12.2-13.7
71	13.0	12.7-13.3	12.3-13.7
72	13.1	12.8-13.3	12.3-13.8
73	13.1	12.8-13.4	12.3-13.8
74	13.1	12.8-13.4	12.4-13.8
75	13.2	12.9-13.4	12.4-13.9
76	13.2	12.9-13.5	12.4-13.9
77	13.2	12.9-13.5	12.5-14.0
78	13.3	12.9-13.6	12.5-14.0
79	13.3	13.0-13.6	12.5-14.0
80	13.3	13.0-13.6	12.6-14.0

Table III—Cont'd

sonographic scanning is performed and will allow assessment of fetal growth during this period of gestation. Such information may prove to be useful in understanding the problem of recurrent pregnancy loss, especially if early fetal growth retardation is observed before fetal death. The outcome of pregnancies resulting from IVF has been the subject of several studies. Although the frequency of multiple pregnancy is increased compared with the general population, the outcome in singleton pregnancies indicates that fetal growth is normal.[13, 14] Thus the information obtained from this study will be very useful for gestational age assessment in the first trimester.

Crown-rump length dating curves based on menstrual history or date of ovulation are less accurate than those generated by means IVF pregnancies in which the date of conception is known. The use of LMP as a reference point for pregnancy dating has been well established. However, the precision of the estimate of gestational age is poor. In a prospective study 28% of patients had uncertain dates, and an additional 15% were later determined to have provided inaccurate dates.[4] In some retrospective studies 22% to 40% of patients were believed to have had suspicious LMP dates.[15, 16] Saito et al.[17] have shown that by using LMP dates a delay in ovulation, as indicated by basal body temperature graphs, is the major contributing cause for apparent prolongation of pregnancy over 295 days. It has been estimated, by measuring the midcycle luteinizing hormone surge, that normal ovulation may occur within a range of −4 days to +6 days from the midpoint of the cycle.[18] Similarly, a wide variation (−6 days to +4 days) has been reported when LMP dates were used to predict ovulation compared with ovulation time observed in women undergoing follicular growth monitoring with ultrasonography.[2, 3]

Before the availability of ultrasonographic monitor-

Table IV. Comparison of gestational age prediction by means of formula in literature with that generated from IVF data

	Mean difference (days)	*Range*	*SD*
Menstrual dating			
Robinson and Fleming[6]	−1.9	−9.9-5.6	2.78
Drumm et al.[7]	−1.9	−10.0-7.5	3.25
Ovulation dating			
MacGregor et al.[8]	+2.4	−6.9-8.5	2.82
Selbing and Fjallbrant[9] (timing of insemination with donor sperm)	+3.9	−5.5-11.4	3.40
Selbing and Fjallbrant[9] (basal body temperature)	+3.8	−4.8-9.9	2.88

Minus sign, Underestimation of gestational age with respect to IVF data; *plus sign,* overestimation.

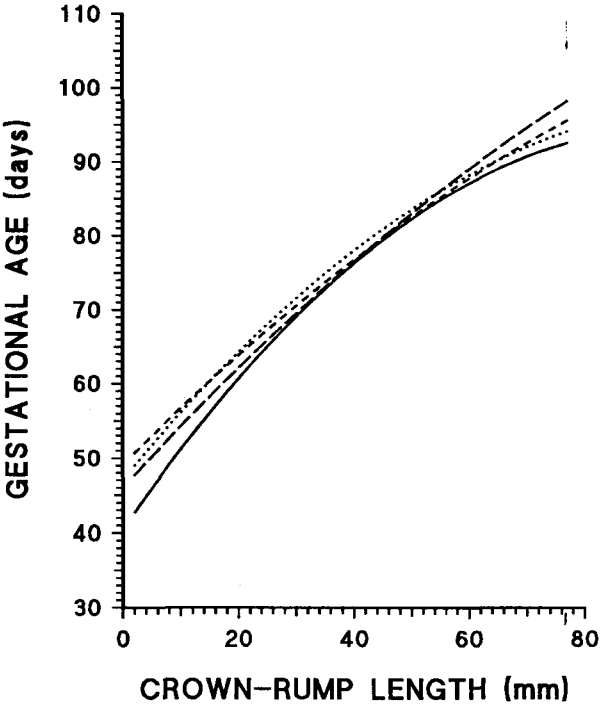

Fig. 2. Relationship between fetal crown-rump length and gestational age by means of IVF data and compared with ovulation-based data. —, IVF pregnancy data; – –, equation described by MacGregor et al.[8]; - - - -, equation described by Selbing and Fjallbrant[9] with insemination date with donor sperm and basal body temperature graphs (·····).

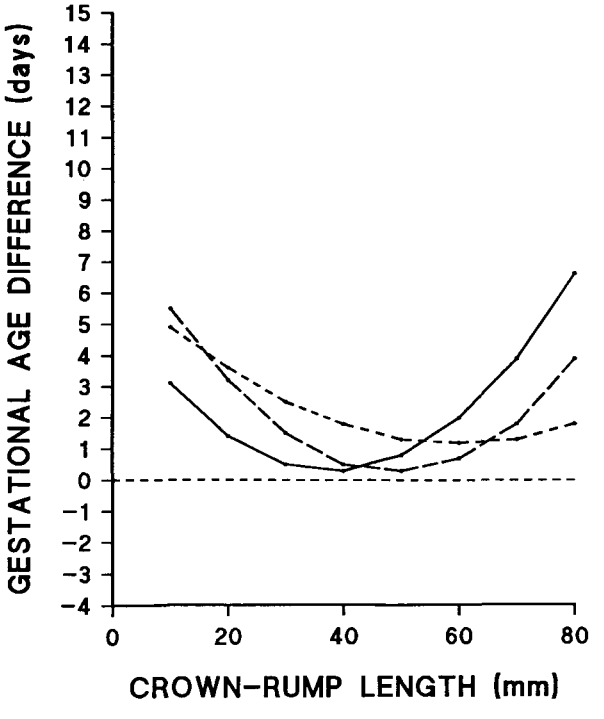

Fig. 3. Discrepancy in gestational age between equation generated from IVF-based crown-rump length measurements and equations based on ovulation day. —, Equation described by MacGregor et al.[8]; – –, equation described by Selbing and Fjallbrant[9] with insemination date with donor sperm and basal body temperature graphs (- - - -).

ing for follicular growth, information about conception was obtained from basal body temperature graphs and insemination records that allowed one to estimate the time of ovulation and hence of conception. Now that IVF therapy has enabled conception dating to be more precise, it is possible to study fetal growth without the uncertainties inherent in using ovulation-based or menstrual dates. Nevertheless, some variability still exists because of measurement errors. These errors can be reduced by using higher frequency transvaginal transducers that produce a better image quality because of the increased resolution. Errors caused by variability in the conception-to-implantation interval may also be present. However, the implantation window in humans is quite narrow, making it unlikely that this factor will cause significant variability. Transfer of embryos into the uterus in which the endometrium was histologically at day 17 to 19 resulted in pregnancy, whereas on day 20 or later no pregnancy occurred.[19] This observation suggests that the endometrium is optimally prepared to allow implantation for only a very short period of time after conception. A third potential source of error is the biologic variability in fetal growth rate between individuals. However, it is unlikely that large differences will be seen when measuring growth in early pregnancy, because the fetus is still quite small and is relatively easy to measure. Small differences in growth may be imperceptible with current technology and should not pose much of a problem in estimating fetal growth.

In conclusion, the data for gestational age by means of IVF pregnancies indicate that the previously published crown-rump length–based growth curves either underestimate or overestimate the true gestational age. It is possible that such variances may not be clinically important. However, when several scans are performed,

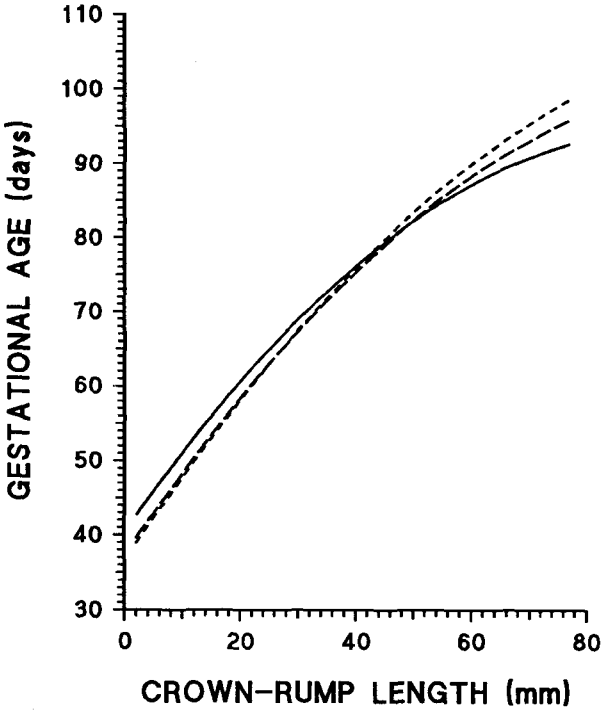

Fig. 4. Relationship between fetal crown-rump length and gestational age by means of IVF data and compared with menstrual history data. —, IVF pregnancy data; – –, equation described by Robinson and Fleming[6]; - - - -, equation described by Drumm et al.[7].

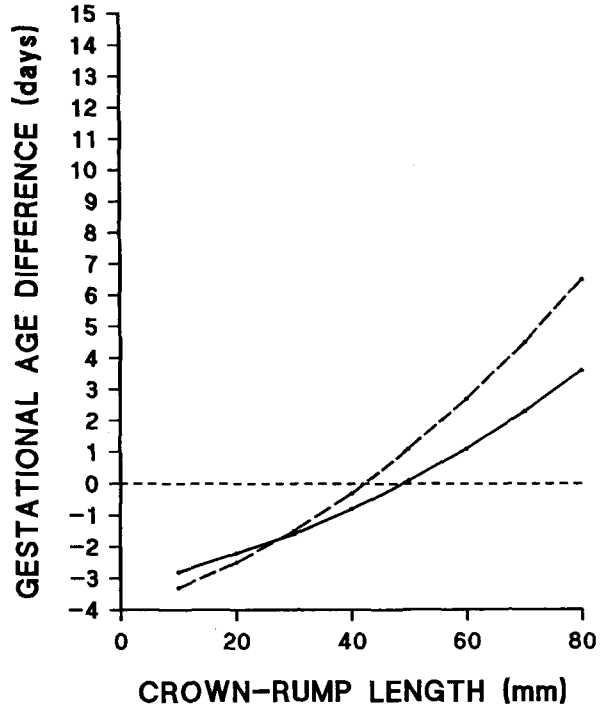

Fig. 5. Discrepancy in gestational age between equation generated from IVF-based crown-rump length measurements and equations based on menstrual history. —, Equation described by Robinson and Fleming[6]; – –, equation described by Drumm et al.[7]

these errors may become magnified. Obstetric decisions often depend on knowledge of the gestational age, and if this can be precise then management becomes clearer. Furthermore, it may be possible to better define the limits of normality for antenatal diagnostic tests such as α-fetoprotein measurement, which has a wide variance, probably because of imprecision in gestational age estimation. This hypothesis awaits further testing with the gestational age equation described in this study.

REFERENCES

1. Sharpe PJH, Nordheim AW. Distribution model of human ovulatory cycles. J Theor Biol 1980;83:663-73.
2. Queenan JT, O'Brien GD, Bains LM, et al. Ultrasound scanning of ovaries to detect ovulation in women. Fertil Steril 1980;34(2):99-105.
3. Rossavik IK, Gibbons WE. Variability of ovarian follicular growth in natural menstrual cycles. Fertil Steril 1985;44: 195-9.
4. Sabbagha RE. In: Spellacy WN, ed. Management of the high-risk pregnancy. Baltimore: University Park Press, 1976.
5. Hertz RH, Sokol RJ, Knoke JD, Rosen MG, Chik L, Hirsch VJ. Clinical estimation of gestational age: rules for avoiding preterm delivery. Am J Obstet Gynecol 1978;131:395-402.
6. Robinson HP, Fleming JEE. A critical evaluation of sonar "crown-rump length" measurements. Br J Obstet Gynaecol 1979;82:702-10.
7. Drumm JE, Clinch J, MacKenzie G. The ultrasonic measurement of fetal crown-rump length as a method of assessing gestational age. Br J Obstet Gynaecol 1976;83: 417-21.
8. MacGregor SN, Tamura RK, Sabbagha RE, Minogue JP, Gibson ME, Hoffman DI. Underestimation of gestational age by conventional crown-rump length dating curves. Obstet Gynecol 1987;70:344-8.
9. Selbing A, Fjallbrant B. Accuracy of conceptual age estimation from fetal crown-rump length. JCU 1984;12: 343-6.
10. Daya S. Human chorionic gonadotropin increase in normal early pregnancy. Am J Obstet Gynecol 1987;156:286-90.
11. Daya S. Determination of gestational age by measuring human chorionic gonadotropin levels. In: Boutaleb Y, Gzouli A, eds. Recent developments in fertility and sterility series. Volume 2: the study of ovulation and early pregnancy. Carnforth: Parthenon, 1990.
12. Rossavik IK, Torjusen GD, Gibbons WE. Conceptual age and ultrasound measurements of gestational sac and crown-rump length in in-vitro fertilization pregnancies. Fertil Steril 1988;49;1012-7.
13. Cohen J. The efficiency and efficacy of IVF and GIFT. Hum Reprod 1991;6:613-8.
14. Lancaster PAL. In: Wood C, Trounson A, eds. Clinical in vitro fertilization. Berlin: Springer-Verlag, 1989:81-94.
15. Campbell S. The assessment of fetal development by diagnostic ultrasound. Clin Perinatol 1974;1:507-25.
16. Dewhurst DJ, Beazley JM, Campbell S. Assessment of fetal maturity and dysmaturity. Am J Obstet Gynecol 1972;113: 141-9.
17. Saito M, Yazawa K, Hashiguchi A. Time of ovulation and prolonged pregnancy. Am J Obstet Gynecol 1972;112: 31-8.
18. Bell ET, Loraine JA. Time of ovulation in relation to cycle length. Lancet 1965;1:1029-30.
19. Rosenwaks Z, Navot D, Veeck L, et al. Oocyte donation. The Norfolk Program. Ann N Y Acad Sci 1988;541:728-41.