Total body water in pregnancy: assessment by using bioelectrical impedance[1-3]

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ABSTRACT Determinations of total body water (TBW) calculated from deuterium dilution spaces and bioelectrical-impedance measurements were made serially in a group of 15 women before, during, and after pregnancy. Similar measurements were made once in a group of 50 nonpregnant women and intermittently in another group of 10 women during pregnancy and postpartum. TBW increased significantly during pregnancy, then decreased postpartum. Estimates of TBW in pregnancy and postpartum calculated with models derived from nonpregnant and pregnant women were similar to measured values. Changes in reactance and resistance explained more of the variance in predicting changes in TBW than did body weight, abdominal circumference, or hematocrit (50–75% vs 4–50%, respectively). Changes in TBW estimated with the nonpregnancy impedance model were significantly different than either the measured changes or changes predicted with the pregnancy impedance model. These findings indicate that the impedance method is a practical and valid method for determining longitudinal changes in TBW. *Am J Clin Nutr* 1994;59:578–85.

KEY WORDS Total body water, bioelectrical impedance, pregnancy

Introduction

It is widely accepted that maternal weight gain during pregnancy is necessary for proper gestational development of the fetus (1). The development of standards for optimal maternal weight gain during pregnancy, however, has been limited by the recognition that the changes in the relative contribution of the components of weight gain are not well defined. These components include the products of conception (fetus, placenta, and amniotic fluid), uterine and breast tissue, body water (intracellular and extracellular water), and maternal fat. They change in variable amounts among women during pregnancy, thereby distinctly affecting the interpretation of individual weight gain.

The topic of changes in maternal body composition during pregnancy in healthy women has been reviewed (2). Because of the limited available information, it was concluded that there remains a need to determine the effects of changes in body composition on the outcome of pregnancy. Although limitations exist regarding the use of available methods to assess body fat content of pregnant women, determination of total body water (TBW) can be performed safely by using isotope dilution methods with deuterium or oxygen-18. Investigations of TBW during pregnancy and postpartum have been limited generally to cross-sectional studies with an emphasis on the final weeks of pregnancy (3–8) without determinations of TBW made before pregnancy. Furthermore, different experimental methods and biological fluids were used in the determination of isotope dilution volumes.

One approach that may facilitate large-scale studies of TBW in pregnant women is tetrapolar bioelectrical impedance analysis (BIA). This method relies on the conduction of a single-frequency, constant electrical current to determine total conductor volume of the body (9). Because water and electrolytes are the dominant factors affecting electrical conduction in the body, TBW is easily assessed by tetrapolar BIA (10). Previous research demonstrated the validity of this approach to estimate TBW in adults and children (11–16). The application of this method in conditions of changing fluid status is limited (17–19).

Assessment of TBW in human pregnancy represents a challenge for any noninvasive conductivity technique. In addition to changes in water volume and distribution, body geometry and hematocrit values also change (1). Each of these factors has been reported to influence the conduction of an applied electrical current (20, 21).

The purpose of the present study was to determine longitudinal changes in TBW in a series of women before conception, periodically throughout pregnancy, and in the postpartum period. A second objective was to develop and validate a model by using BIA variables to predict TBW during pregnancy. This study demonstrates the practicality and validity of using BIA to monitor longitudinal changes in TBW.

Methods

Subjects

Initially, 40 women volunteered to participate in the longitudinal pregnancy study. Because of difficulty in becoming pregnant, an inability to meet testing schedules, and personal consid-

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[2] Mention of a trademark or proprietary product does not constitute a guarantee or warranty of the product by the US Department of Agriculture and does not imply its approval to the exclusion of other products that may also be suitable.

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erations, only 15 women completed all aspects of the study. All subjects gave written informed consent before participation in the study, which was approved by the University of North Dakota Institutional Review Board and the US Department of Agriculture Human Study Committee.

Fifteen women, 11 primigravidae and 4 multigravidae, aged 21–37 y, participated in the longitudinal study. They were recruited while they were planning to become pregnant. All of these women had normal full-term pregnancies and delivered single healthy infants without complications. This group is termed the longitudinal, cross-validation sample.

Fifty additional women, aged 22–35 y, who were healthy and not pregnant were studied to develop a model for the prediction of TBW by using BIA variables. This sample is referred to as the nonpregnant model-development group.

Another group of 10 primigravidae, aged 22–35 y, was studied before pregnancy and cross-sectionally during their pregnancies and postpartum. The TBW and BIA data were used to develop a pregnancy-specific impedance model for TBW assessment.

Design

After volunteering to participate in this study, the women in the longitudinal study were scheduled for baseline testing that was repeated every 90 d unless a woman missed a menstrual period. The testing included determination of deuterium dilution space (DDS), anthropometry, and BIA measurements.

All of the women reported their usual menstrual activity to be a 26–40-d cycle. If a woman failed to menstruate within the expected time based on her usual experience, she underwent a pregnancy test. If the test was positive, the woman was scheduled to repeat the baseline testing approximately every 90 d. Pregnancy was documented with a positive plasma human chorionic gonatropin test. On average, there was a 14–16-wk period between the time of the last prepregnancy and first trimester body composition evaluation. In general, in addition to measurements made before pregnancy, the women were studied at ≈14, 26, and 36–38 wk of gestation.

The women were scheduled for postpartum testing at 8 wk after delivery. Each woman received medical clearance before testing was performed. Two women were tested at 10 wk postpartum because of scheduling conflicts. All of the women were lactating when the postpartum testing occurred.

Because some women were unable to attend all testing dates during their pregnancies and postpartum, their cross-sectional data were used to develop a pregnancy-specific model to predict TBW. The distribution of observations was five at 12 wk, eight at 24 wk, eight at ≈36 wk gestation, and nine at 8–10 wk postpartum. All of the 10 women underwent prepregnancy body composition assessment.

Protocol

After an overnight fast the women came to the laboratory where standing height and body weight were determined with a stadiometer and a calibrated scale, respectively. Abdominal circumference, measured with a steel tape, was defined as the horizontal distance around the abdomen at the umbilicus (22). Determinations of DDS and BIA were made after the anthropometric measurements on the same day.

Total body water

DDS was determined as described (13). Each woman received orally 10–12 g D_2O (99.8% purity; Cambridge Isotope Laboratory, Cambridge, MA) mixed with 300 mL distilled-deionized water. Venous blood samples were obtained before and 4 h after ingestion of the deuterium mixture. Confirmation of equilibration of plasma deuterium concentration was tested in a subsample of women ($n = 5$) from whom plasma samples were obtained hourly for 4 h after ingestion of the tracer. All urine excreted during the equilibration period was analyzed for deuterium concentration. After vacuum sublimation, plasma and urine water were analyzed for deuterium concentrations by fixed-filter infrared spectroscopy (23). The analytical precision and accuracy were 2.5% (23). DDS (in L) was calculated by using the retained deuterium dose(ing) and the 4-h plasma deuterium concentration (in g/L):

$$\text{DDS} = \frac{(D_2O \text{ dose given} - D_2O \text{ in urine})}{(\text{4-h plasma } D_2O)}$$

TBW (in L) was calculated from DDS by assuming a 4% overestimation of TBW from DDS because of deuterium-hydrogen exchange (24):

$$\text{TBW} = \text{DDS}/1.04$$

Clinical chemistry

Plasma sodium concentration and hematocrit value were determined by using an aliquot of the fasting venous blood obtained before the deuterium ingestion. Plasma sodium was assayed by using flame photometry (model 443; Instrumentation Laboratory, Inc, Lexington, MA). Hematocrit value was determined by a standard method and instrumentation (Coulter model S; Coulter Electronics, Hialeah, FL).

Bioelectrical impedance

Determinations of resistance (R) and reactance (Xc) were made with a tetrapolar impedance plethysmograph (model 101; RJL Systems, Mt Clemens, MI) as described elsewhere (11). Each woman, clothed but without shoes or socks, was supine on a table made of nonconductive materials. Aluminum foil spot electrodes (no. M6001; Contact Products, Dallas) were positioned in the middle of the dorsal surfaces of the hands and feet proximal to the metacarpal-phalangeal and metatarsal-phalangeal joints, respectively, and also medially between the distal prominences of the radius and the ulna and between the medial and lateral malleoli at the ankle. Specifically, the proximal edge of one detector electrode was in line with the proximal edge of the ulnar tubercle at the wrist, and the proximal edge of the other detecting electrode was in line with the medial malleolus of the ankle. The current-introducing electrodes were placed a minimum distance of the diameter of the wrist or ankle beyond the paired detector electrode. A thin layer of electrolyte gel was applied to each electrode before application to the skin. An excitation current of 800 μA, AC, at 50 kHz was introduced into the volunteer at the distal electrodes of the hand and foot; the voltage drop across the patient was detected with the proximal electrodes. Measurements of R and Xc were made by placing electrodes on the right hand and foot, 3–4 h after ingestion of deuterium. The variability of repeated R and Xc measurements determined on the same day was $< 1\ \Omega$.

Statistical analyses

Data are expressed as mean ± SE. Models using impedance variables and physical characteristics to predict TBW were de-

TABLE 1
Prepregnancy physical, hematologic, and bioelectrical characteristics of the women in the model groups and the longitudinal validation sample*

	Model groups		Validation group (n = 15)
	Nonpregnant (n = 50)	Pregnant (n = 10)	
Age (y)	29.3 ± 0.5	28.7 ± 0.7	28.5 ± 0.9
Height (cm)	168.2 ± 1.4	167.4 ± 2.0	167.4 ± 1.8
Weight (kg)	62.9 ± 1.7	63.8 ± 1.5	63.0 ± 3.0
Body mass index†	22.3 ± 1.2	22.7 ± 1.33	22.4 ± 1.2
Body water (kg)	31.5 ± 0.7	30.3 ± 1.2	31.8 ± 1.0
Water wt/body weight (%)	50.4 ± 0.9	50.2 ± 1.7	50.4 ± 1.9
Hematocrit (l)	0.43 ± 0.03	0.42 ± 0.01	0.41 ± 0.02
Plasma sodium (mmol/L)	140 ± 2	141 ± 2	140 ± 2
Resistance (Ω)	578 ± 12	586 ± 8	594 ± 15
Reactance (Ω)	64 ± 4	66 ± 2	71 ± 2

* $\bar{x}$ ± SE.
† In kg/m^2.

rived by stepwise-multiple-regression analysis with the maximum R^2 method (25) in the nonpregnant and pregnant women.

These models were evaluated in the longitudinal study group to determine the validity of the nonpregnancy and pregnancy BIA models to predict measured TBW (26). Measured and predicted TBW values determined longitudinally were compared by using analysis of variance with a repeated-measures design (25). Comparisons of physical characteristics were done with a one-way analysis of variance (25). When the main effect was significant, post hoc Tukey's contrasts were used to identify significant differences (25). The method of Bland and Altman (27) was used to determine bias in the prediction of TBW and changes in TBW with impedance measurements.

Results

The prepregnancy characteristics of the women in each model and validation sample are summarized in **Table 1.** There are no marked differences in the physical or bioelectrical impedance characteristics among the groups.

Isotope equilibration

Table 2 shows the plasma deuterium concentrations and changes relative to the preadministration values during the deuterium equilibration tests before, during, and after pregnancy. In general plasma deuterium concentration reached a plateau, defined as a significant increase in the change in deuterium concentration relative to the baseline or predose deuterium concentration data, during the remainder of the equilibration test, at 2 h. This pattern did not change until the third trimester when the plateau was established at ≈3 h. Equilibration occurred at 2 h in the postpartum period.

Longitudinal changes during pregnancy

A general pattern was observed for the physical, biochemical, and impedance characteristics measured longitudinally during pregnancy (**Table 3**). Body weight and abdominal circumference increased significantly after the first trimester and did not return to prepregnancy status in the postpartum period. Body mass index increased significantly during the second and third trimesters. Body water increased significantly, whereas R and Xc decreased significantly during pregnancy; TBW decreased, R and Xc increased significantly postpartum, returning to control values. Hematocrit value decreased significantly during pregnancy then returned to prepregnancy values in the postpartum period. There was no significant change in TBW expressed as a fraction of body weight during pregnancy and postpartum.

Predictors of total body water

Some physical and impedance variables were correlated significantly with TBW in the nonpregnant women and the women

TABLE 2
Plasma deuterium oxide (D_2O) concentrations and changes during deuterium equilibration test and by pregnancy status*

	Time after oral D_2O dose				
	0 h	1 h†	2 h	3 h	4 h
			g/L		
Prepregnancy‡	0.03 ± 0.01	2.33 ± 0.12	3.51 ± 0.16	3.52 ± 0.15	3.50 ± 0.15
Δ§		76 ± 4	116 ± 5	116 ± 5	116 ± 5
First trimester	0.04 ± 0.01	2.33 ± 0.14	3.48 ± 0.13	3.46 ± 0.14	3.46 ± 0.13
Δ		57 ± 3	86 ± 4	86 ± 3	86 ± 3
Second trimester	0.03 ± 0.01	2.11 ± 0.13	3.11 ± 0.13	3.12 ± 0.12	3.11 ± 0.13
Δ		69 ± 4	99 ± 5	103 ± 4	99 ± 5
Third trimester	0.03 ± 0.01	2.06 ± 0.15	2.52 ± 0.14	2.80 ± 0.13	2.81 ± 0.14
Δ		68 ± 5‖	83 ± 5¶	92 ± 4	93 ± 5
Postpartum	0.03 ± 0.01	2.30 ± 0.14	3.40 ± 0.12	3.41 ± 0.12	3.40 ± 0.13
Δ		76 ± 5	112 ± 4	113 ± 4	112 ± 4

* $\bar{x}$ ± SE; n = 5.
† Change significantly different at 1 h than at other times, $P < 0.05$ (Tukey's contrasts).
‡ Prepregnancy significantly different from other time periods, $P < 0.001$.
§ Calculated as ratio of timed postdose concentration to baseline (0 h) D_2O concentration.
‖ Significantly different from 2-, 3-, and 4-h concentration for third trimester, $P < 0.05$.
¶ Significantly different from 3- and 4-h concentration for third trimester, $P < 0.05$.

TABLE 3
Characteristics of 15 women before, during, and after pregnancy*

	Prepregnancy	First trimester	Second trimester	Third trimester	Postpartum
Weight (kg)	63.0 ± 3.0[a]	64.0 ± 2.9[a]	71.6 ± 2.9[b]	77.3 ± 3.2[c]	68.1 ± 2.9[d]
Body mass index†	22.4 ± 1.2[a]	22.9 ± 1.2[a]	25.6 ± 1.2[b]	27.6 ± 1.3[b]	23.6 ± 0.9[a]
C_{abd} (cm)‡	76.1 ± 2.9[a]	80.7 ± 2.7[a]	94.5 ± 2.6[b]	102.9 ± 2.5[c]	90.0 ± 2.2[b]
Hematocrit (l)	0.41 ± 0.02[ab]	0.37 ± 0.06[abc]	0.35 ± 0.08[c]	0.36 ± 0.08[c]	0.40 ± 0.08[a]
Plasma sodium (mmol/L)	140 ± 2	140 ± 2	141 ± 2	142 ± 2	141 ± 2
Resistance (Ω)	594 ± 15[a]	589 ± 16[a]	551 ± 18[b]	521 ± 24[c]	573 ± 19[a,b]
Reactance (Ω)	71 ± 2[a]	69 ± 2[a,b]	63 ± 2[b,c]	59 ± 2[c]	67 ± 2[a,b]
Body water (kg)	31.8 ± 1.0[a]	32.5 ± 1.0[a]	35.1 ± 1.0[b]	39.6 ± 1.6[c]	34.2 ± 1.2[a,b]
Water wt/body wt (%)	50.4 ± 1.9	51.1 ± 1.5	49.5 ± 1.6	50.0 ± 1.4	50.3 ± 1.5

* $\bar{x}$ ± SE. Values in the same row with different superscripts are significantly different, $P < 0.05$ (Tukey's contrasts).
† In kg/m^2.
‡ Abdominal circumference.

studied longitudinally during pregnancy and postpartum (**Table 4**). Standing height was a relatively weak, though significant, predictor of TBW. Regardless of status, R was the best single predictor of TBW, accounting for 67–79% of the variance in predicting TBW. Xc, hematocrit value, and abdominal circumference explained more of the variance in predicting TBW in the pregnant than in the nonpregnant women (61%, 24%, and 16% in comparison with 12%, 10%, and < 1%, respectively).

Prediction model

The multiple-regression equations derived separately for the estimation of TBW in the 50 nonpregnant women and the 10 women studied cross-sectionally during pregnancy are presented in **Table 5.** The independent variables are ht^2/R and body weight in the nonpregnant women.

The predictors of TBW in the pregnant women include ht^2/R, abdominal circumference, body weight, hematocrit value, and Xc.

Prediction of TBW by using BIA

Use of the prediction models derived in nonpregnant and pregnant women (Table 5) yielded mean TBW values that were similar to those determined by using isotope dilution (**Table 6**).

Analyses of the relationships among measured and predicted TBW values indicated linear relationships. By using the nonpregnancy model, predicted TBW was correlated significantly (R^2 = 0.893, SEE = 1.46, $P < 0.0001$) with measured TBW. The regression equation relating measured and predicted TBW values, $y = 0.958x + 1.15$, has a slope similar to 1 and an intercept not different from 0. Similarly, the pregnancy model predicted TBW values that were significantly related (R^2 = 0.918, SEE = 1.15, $P < 0.0001$) to the measured values. The regression equation $y = 0.990x + 0.42$ has a slope not different from 1 and an intercept similar to 0.

Examination of the relationships among the differences between measured and predicted TBW values (eg, residual values) and the mean of the measured and predicted TBW values indicated no significant relationships with either prediction model. With the nonpregnancy model, the residual scores were not significantly correlated (R^2 = 0.028) with mean TBW values. Also, the differences between the measured and predicted TBW values derived from the pregnancy model were weakly correlated (R^2 = 0.020, P = 0.36) with the average TBW values.

Predictors of change in TBW

The measured R and Xc were good predictors of TBW throughout pregnancy (**Table 7**). They explained more (≈60%) of the variance in estimating TBW than did weight, abdominal circumference, or hematocrit value (49%, 27%, and 8%, respectively). The best predictor of longitudinal determinations of TBW was ht^2/R, which accounted for 90% of the variance in predicting TBW.

A similar pattern was observed in estimating longitudinal changes in TBW from changes in these variables. Changes in ht^2/R were the best predictors of change in TBW from prepregnancy values. Changes in R, body weight, and Xc were better predictors of change in TBW than were abdominal circumference and he-

TABLE 4
Predictors of total body water in 50 nonpregnant women and 15 women studied throughout pregnancy and postpartum

	Height	Weight	Resistance	Reactance	Hematocrit	C_{abd}*
Nonpregnant	0.331†	0.580‡	−0.889§	−0.349†	0.308†	0.028
Pregnant‖	0.250†	0.614‡	−0.821§	−0.778§	0.490†	−0.396†

* Abdominal circumference.
† $P < 0.05$.
‡ $P < 0.0005$.
§ $P < 0.0001$.
‖ Univariate correlations adjusted for repeated measures.

TABLE 5
Multiple-regression equations to predict total body water (TBW) by using bioelectrical impedance, anthropometric, and biochemical measures of 50 nonpregnant women and 10 women studied intermittently during pregnancy and postpartum*

Independent variable	R^2	SEE
Nonpregnancy model: TBW = 0.610 X1 + 0.063 X2 + 0.06		
X1, height^2/res	0.963	1.18
X2, weight	0.980	0.97
Pregnancy model: TBW = 0.700 X1 + 0.051 X2 − 0.069 X3 − 0.029 X4 − 0.043 X5 + 2.833		
X1, height^2/res	0.901	1.42
X2, C_{abd}	0.920	1.30
X3, weight	0.932	1.20
X4, Xc	0.949	1.07
X5, hematocrit	0.960	0.92

* Res, resistance; Xc, reactance; C_{abd}, abdominal circumference.

matocrit values (86%, 72%, and 69% as compared with 63% and 20%, respectively).

The nonpregnancy model significantly underestimated the changes in TBW during pregnancy and lactation (**Table 8**). In contrast, the pregnancy model yielded estimates of change in TBW that were similar to the measured changes in TBW.

This observation is confirmed with the analysis of the relationships between measured and predicted changes in TBW during pregnancy and postpartum. With the nonpregnancy model the linear relationship between measured and predicted change in TBW ($y = 1.038x + 0.881$) has an intercept that is significantly different ($P < 0.006$) from 0. In contrast, the pregnancy model estimated changes in TBW that were linearly related to the measured changes in TBW ($y = 0.998x + 0.393$); the slope and intercept of this relationship were similar to the line of identity.

Differences between measured and predicted changes in TBW determined with the nonpregnancy model were correlated significantly ($R^2 = 0.10$, $P < 0.05$) with the average TBW values. The residual scores from the measured and predicted changes calculated with the pregnancy model, however, were not related ($R^2 = 0.03$, $P = 0.21$) to the mean TBW values assessed during pregnancy and postpartum.

TABLE 6
Comparisons among measured and predicted total body water values in 15 women studied serially before pregnancy, during each trimester of pregnancy, and postpartum*

	Measured	Predicted total body water: Nonpregnancy model	Predicted total body water: Pregnancy model
	L	*L*	*L*
Prepregnancy	31.7 ± 1.0	32.2 ± 1.0	31.9 ± 1.0
First trimester	32.2 ± 1.0	32.8 ± 1.0	32.4 ± 1.0
Second trimester	35.1 ± 1.0	35.3 ± 1.1	35.3 ± 1.0
Third trimester	38.6 ± 1.6	38.1 ± 1.7	38.9 ± 1.6
Postpartum	34.0 ± 1.1	34.0 ± 1.0	33.6 ± 1.0

* $\bar{x}$ ± SE. Significant effect of time period, $P < 0.0001$.

TABLE 7
Relationship among impedance, anthropometric, biochemical measurements, and total body water (TBW), and changes in these variables before, during, and after pregnancy in 15 women

	TBW		ΔTBW	
	r*	SEE	r*	SEE
Resistance	0.789	2.5	0.860	1.7
Reactance	0.755	2.7	0.694	2.4
Height^2/Resistance	0.950	1.2	0.910	1.3
Weight	0.701	3.1	0.725	2.3
C_{abd}†	0.520	3.8	0.635	2.8
Hematocrit	0.282	4.3	0.200	3.5

* Univariate correlations adjusted for repeated measures.
† Abdominal circumference.

The relationship between residual scores (deuterium dilution minus impedance predictions based on the impedance pregnancy model) for individual changes in TBW as a function of mean change in TBW (deuterium dilution and by predicted impedance) is shown in **Figure 1.** The slope of this line is similar to 0 ($t = 0.051$; $P = 0.96$) and the intercept is not different from 0 ($t = 1.07$; $P = 0.21$).

Discussion

The use of tetrapolar BIA technology to assess TBW is not new (28). Early investigations established that tetrapolar bioelectrical conductance, expressed as 1/R and normalized for conductor length or stature, was a significant predictor of TBW in healthy adults and children (10). Subsequent studies showed that BIA is a valid method to predict acute changes in TBW, either in response to saline infusion or dehydration (19, 29). The findings of the present study indicate that BIA is a valid approach to determine longitudinal changes in TBW, particularly in human pregnancy.

An important observation is that changes in body geometry and regional fluid accumulation significantly influence the ability of BIA to estimate changes in conductor volume. Comparisons among measured TBW and TBW predicted with models devel-

TABLE 8
Comparison of measured and predicted changes in total body water during pregnancy and lactation in 15 women*

	Changes in total body water: Measured	Changes in total body water: Nonpregnancy model	Changes in total body water: Pregnancy model
		kg	
First trimester	0.5 ± 0.4	0.1 ± 0.3	0.6 ± 0.4
Second trimester	3.5 ± 0.6	1.7 ± 0.3†	3.4 ± 0.5
Third trimester	7.1 ± 1.1	5.4 ± 1.1†	6.2 ± 1.0
Postpartum	2.3 ± 0.6	1.2 ± 0.4†	1.9 ± 0.5

* $\bar{x}$ ± SE. Change measured relative to prepregnancy values. Significant effect of both method and time period, $P < 0.0001$ (ANOVA).
† Significantly different from pregnancy model and measured values, $P < 0.05$ (Tukey's contrasts).

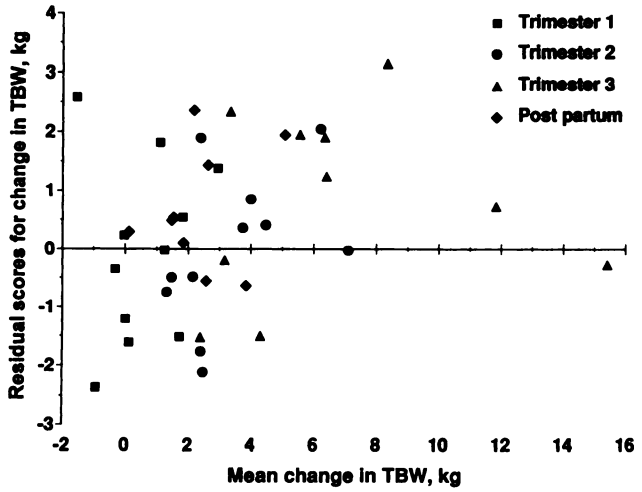

FIG 1. Plot of the individual changes in total body water (TBW) during pregnancy and postpartum calculated from the estimates made by deuterium dilution minus the corresponding change predicted with the pregnancy impedance model as related to the mean change in TBW calculated by using data from deuterium dilution and the pregnancy impedance model. The equation describing the data is $y = 0.101x + 0.017$; $R^2 = 0.03$, SEE = 1.28 kg.

oped in nonpregnant and pregnant subjects indicated no differences among the mean estimates. This observation indicates that a generalized model (eg, either a nonpregnancy or pregnancy model) is capable of adequately estimating mean changes in TBW. However, comparisons of changes in TBW from the prepregnancy values to those observed throughout pregnancy and postpartum demonstrated that only the pregnancy-specific prediction model estimated changes in TBW similar to the measured values. Therefore, the pregnancy-specific model offers the sensitivity to monitor within-subject increases in TBW. Analyses of differences between measured and predicted changes in TBW derived from the nonpregnancy model indicated a bias or a tendency to underestimate longitudinal changes in TBW during pregnancy and postpartum.

This limitation of BIA also has been reported in attempts to monitor changes in regional fluid accumulation. In patients with cirrhosis estimates of change in TBW derived from whole-body BIA measurements and models derived in healthy adults without altered fluid status have been shown to underestimate fluid loss after paracentesis (30, 31). It has been suggested that regional BIA measurements, specifically of the trunk or abdomen, may improve the sensitivity of the BIA method to assess changes in regional fluid retention (31). Whether regional BIA measurements will enhance estimates of TBW in pregnancy remains to be demonstrated.

One specific predictor in the pregnancy-dependent model was abdominal circumference, which is an index, in addition to height of body geometry. The inclusion of measures of body geometry in BIA models was previously suggested (21) but not implemented and validated until the present study.

Another specific predictor of TBW in pregnancy was hematocrit value. The hypothesis that hematocrit value could be an important predictor of TBW is based on the findings that the resistivity of blood, determined with a bipolar electrode system, is dependent on the packed cell volume or hematocrit value (20, 32). Recently, a significant positive relationship was demonstrated between packed cell volume and impedance determined by using a tetrapolar system (33). Because changes in resistivity affect impedance measurements, factors such as hematocrit value may be important variables in predicting electrical conductor volume and hence TBW.

It has been shown that human pregnancy is associated with an increase in blood volume and a disproportionate increase in plasma volume relative to red cell mass (34). Because plasma volume expansion directly influences extracellular water, and thus TBW, it is reasonable to suggest that BIA variables may be unique predictors of TBW and its distribution. Studies in nonobese and obese adults identified R and Xc as significant predictors of TBW (13, 35). Importantly, Xc was shown to be a unique predictor of extracellular water. As shown in the present study, Xc explained more of the variance in predicting TBW in pregnant than in nonpregnant women (61% vs 12%, respectively), which suggests that Xc was indexing the increase in extracellular water characteristic of late pregnancy.

The changes in body weight and TBW observed in the present study are consistent with those reported in cross-sectional studies of human pregnancy. The reported maternal weight gain in four studies (3, 6–8) ranged from 9.2 to 11.2 kg in women studied intermittently during pregnancy. If these data are normalized to 40-wk gestation, the range of weight gain is 9.2–13 kg (2). The estimated gestational changes in TBW in these studies ranged from 6.3 to 8.5 L. The relative contribution of water to the observed weight gain was calculated to be ≈70%. Corresponding data from the present study are an average increase of 7.2 L in TBW and 14.3 kg in body weight with the change in TBW representing 50% of the weight gain.

It is important to note that the values provided for TBW were actually DDS in these studies (3, 6–8). If TBW is calculated from DDS, assuming a 4% deuterium-labile hydrogen exchange (24), the TBW estimates range about from 6 to 8 L, which represent > 60% of the gestational weight gain.

In addition to the present study, there is only one report of changes in body weight and TBW before conception, during pregnancy, and postpartum. Forsum et al (36) reported longitudinal changes in body composition of a group of 22 healthy Swedish women who had similar ages (28.7 ± 0.9 y) and weight before pregnancy (61.0 ± 2.0 kg) as the women in the present study. The observed average gestational change in weight was 11.7 kg, which is similar to the 14 kg shown in the present study. The mean change in TBW, however, was 5.7 L in comparison with the 7.2 L found in the present study. Interestingly, the relative contribution of TBW to the weight gain reported in the Swedish study is similar to that observed in the present study (49% vs 50%).

There are two important methodologic differences between the discussed cross-sectional and longitudinal studies. In contrast to the present study and other studies (3–8), Forsum et al (36) used oxygen-18 labeled water and sampled saliva rather than blood to monitor the dilution of the isotopically labeled water. Although it is recognized that deuterium exchanges to a small degree with nonaqueous hydrogen (24), no appropriate correction apparently was made in the calculation of TBW from DDS in the previous studies (3, 6–8). Furthermore, it has been shown that salivary concentrations of oxygen-18 and deuterium are similar to those measured in the blood (23, 37). Thus, it seems unlikely that these factors completely explain the reported differences in TBW val-

ues among the studies of TBW and gestation. It is more likely, however, that the inconsistency among the longitudinal studies and the cross-sectional observations reflects differences in experimental design.

One complication of the use of deuterium dilution to assess TBW in pregnancy is the lack of demonstration of isotopic equilibration in any of the previous publications. In an early study, Seitchik (4) administered deuterium orally and collected urine for isotope analysis during the ensuing 24–30 h. An equilibration period of 10 h in nonpregnant women and more than 17 h in pregnant women was reported. The observed change in calculated DDS was only 10% (32 vs 35 L) at 37–40 wk of pregnancy. The small increase in estimated TBW during pregnancy was interpreted by Seitchik (4) to represent either a redistribution of deuterium or a failure of true isotopic equilibration. The latter point is perhaps the appropriate explanation because pregnant women have larger residual urine volumes after urination as compared with nonpregnant women. In addition, pregnant women urinate smaller volumes more frequently so that each urine specimen may be contaminated with urine remaining in the bladder from prior voidings. These circumstances may result in the failure to reach a true isotopic equilibration when urine specimens are used to determine DDS in human pregnancy.

Information about the equilibration of deuterium during pregnancy is not available in the literature. The present study describes the time course of plasma deuterium concentration after ingestion of deuterium during pregnancy (Table 2). Although subtle, the equilibration of deuterium is affected by duration of gestation. Relative to control, the stabilization of plasma deuterium concentration is delayed from 2 to 3 h in the last trimester of pregnancy. This finding suggests that previous studies of deuterium dilution in pregnant women that used a 3–4-h equilibration period for the determination of DDS probably achieved isotopic equilibration in the blood (3, 6–8).

It should be noted that the pregnant women in this study did not suffer from any significant disruption of electrolyte homeostasis as would be seen in conditions such as edema or preeclampsia. This distinction is noteworthy because an inverse relationship between plasma sodium and R has been observed in vivo and in vitro (20, 38). It would be expected, therefore, that the influence of significant alterations in plasma sodium concentration on the estimation of TBW in human pregnancy should be investigated in a subsequent study.

In summary, the present study demonstrates that the significant increase in TBW during pregnancy in humans can be accurately assessed with tetrapolar BIA. This assessment requires a model that includes BIA variables and anthropometric measurements required to correct for changes in body geometry associated with pregnancy. The BIA variables reflect longitudinal changes in TBW as it increases and decreases during pregnancy and postpartum better than anthropometric or biochemical measurements. It is concluded that BIA is a practical and useful method for estimating longitudinal changes in TBW. ■

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