Body composition analysis with bioelectric impedance in adult Indians with ESRD: Comparison with healthy population

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Evaluation of body composition provides clinically useful information in several diseases including chronic kidney disease. Bioimpedance analysis (BIA) is a simple, cheap, and noninvasive tool for monitoring body composition. We performed BIA in 451 healthy adults and 162 end-stage renal disease (ESRD) patients. Resistance (*R*) and reactance (Xc) values were obtained at 50-kHz frequency using a tetrapolar impedance meter. Body compartments were derived using population-specific regression equations. Phase angles (arctan Xc/*R*) were calculated and impedance vector distribution was determined using the RXc graph method. Compared to healthy population, ESRD patients had similar post-dialysis resistance with lower reactance and phase angle, indicating decreased soft tissue mass and inadequate ultrafiltration. BIA equations estimated decreased fat mass index and intracellular water, whereas the total body and extracellular water percentages were increased. Sex-specific reference *R*Xc plots with 95, 75, and 50% tolerance ellipses were drawn for the healthy population. A significant difference was noted in the vector positions and 95% confidence ellipses of the two sexes and body mass indices of $\leqslant$25 and $>$25. In conclusion, we present the reference BIA parameters for Indian population. ESRD patients show significant body compartment alterations. The *R*Xc score graph can differentiate ESRD patient from normal controls and can be used to monitor nutrition and hydration status.

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Body composition analysis is useful for assessing nutritional status and predicting clinical outcomes.[1] Composition is altered in chronic kidney disease patients because of protein-energy malnutrition, altered micronutrient status, and variable fluid homeostasis.[2–4] Techniques used to evaluate body compartments include isotope dilution, hydrodensitometry, dual-energy X-ray absorptiometry, magnetic resonance imaging, computerized tomography, neutron activation analysis and bioelectric impedance analysis (BIA).[5–9] BIA is quick, simple, noninvasive, cheap, safe, can be done anywhere using a small handheld equipment, and thus suitable for large-scale studies. Modern nutritional surveys such as 3rd US National Health and Nutrition Examination Survey (NHANES III) have collected BIA data.[10]

BIA is based on the principle that tissues are full of electrolyte-containing fluids and conduct an electric current. Current flow is affected by resistance (*R*, the opposition to flow through intra- and extracellular ionic solutions) and reactance (Xc, additional opposition from the capacitant effect of cell membranes and tissue interfaces). Impedance (*Z*), the frequency-dependant opposition of the flow of current, is a composite of *R* and Xc. The relationship between Xc and *R* in circuits is given by phase angle (PA), arctangent of Xc/*R*. Lower PA is associated with cell loss,[11] whereas high PA indicates increased body cell mass.

BIA data have been reported from Caucasians, African Americans, and Hispanic populations.[12–15] South Asians form an ethnically distinct population and are expected to have significantly different body composition because of genetic variations and differences in dietary habits and body habitus. A vast majority of individuals in India are vegetarians and the incidence of central obesity is higher.

We collected BIA data in healthy adults and developed population reference parameters to serve as standard for future comparison. Data were also collected in patients of end-stage kidney disease (ESRD). This is the first report on BIA parameters from India.

RESULTS

A total of 613 adults (age 39.3$\pm$13.1 years, 63% males) comprising of 162 ESRD patients (age 42.6$\pm$16 years, 74%

males) and 451 healthy controls (age 38±11.7 years, 61.4% males) were studied. The demographic characteristics of the population are shown in Table 1. The ESRD patients had been on dialysis for 6.6±3.4 months, and the interdialytic weight gain in hemodialysis (HD) patients was 1.8±1.1 kg. ESRD patients were older, shorter, and lighter than the control population. The body mass index (BMI) was significantly more in the control population. The causes of ESRD were diabetic nephropathy (50), chronic glomerulonephritis (34), chronic interstitial nephritis (23), hypertensive nephrosclerosis (eight), hereditary kidney disease (seven), others (nine), and unknown (31). A total of 17 male and two female subjects gave history of smoking.

The normalized body composition parameters are shown in Table 2. Among the controls, female subjects exhibited higher *R*, *R*/height (*H*), Xc, and Xc/*H* and lower PA than male subjects. Comparison between healthy population and those with ESRD showed a significantly lower Xc/*H* and PA in both sexes in the latter group.

The derived body compartment values are shown in Table 3. In both sexes, ESRD patients exhibited a significantly lower fat mass percentage (18.3±11.1 vs 25.6±10.3, $P<0.0001$) and fat mass index (4.4±3.8 vs 6.7±3.7 kg/m^2, $P<0.001$). The total body water was lower in ESRD patients (33.6±3.9 l vs 36.5±3.7 l, $P<0.001$) but the total body water percentage was significantly increased (60.3±7.7 vs 54.4±5.6, $P<0.0001$). The extracellular water (ECW) percentage (54.9±11.6 vs 42.2±4.3), ECW/intracellular water (ICW) ratio (1.5±1.4 vs 0.74±0.16), and the plasma water (3.9±1.2 vs 3.3±0.6 l) were also higher in the ESRD group.

The results of the bioimpedance vector analysis (BIVA) are presented in Figures 1–3. Figure 1 shows the *R*Xc graph with the mean vector length and the 50, 75, and 95% tolerance ellipses for the healthy Indian population. The vector was longer and shifted downwards in female compared to male subjects. The separate 95% confidence ellipses of the two sexes confirm the significant difference between the two populations ($P<0.05$, Hotelling's T^2 test). Female subjects showed bigger ellipses, signifying a greater heterogeneity in the BIA characteristics. We examined the effect of BMI on the vector. In both sexes, a clear shortening ($P<0.05$) was noted in individuals with higher BMI. Older individuals (age >45 years) exhibited a statistically insignificant vector shortening. On comparison with healthy controls, the ESRD population showed a clear vector displacement in both sexes, because

Table 1 | Demographic characteristics of the study population

Characteristic	ESRD	Controls	*P*-value
Male subjects	*n*=120	*n*=277	
Age (years)	43±17	39±12	<0.05
Height (cm)	166.5±7.5	170.4±6.8	<0.01
Weight (kg)	57.6±13.6	70.9±13.0	<0.01
BMI	20.7±4.4	24.4±4.1	<0.01
Female subjects	*n*=42	*n*=174	
Age (years)	43±15	37±12	<0.05
Height (cm)	153.7±5.6	157.5±6.2	<0.01
Weight (kg)	54.4±13.6	62.4±12.4	<0.01
BMI	23.0±5.7	25.1±5.0	<0.05

ESRD, end-stage renal disease; BMI, body mass index.

Table 2 | Bioimpedance parameters in ESRD patients and healthy controls

Characteristic	ESRD	Control	*P*-value
R/H (Ohm/m)			
Male subjects	334±82	320±42	0.055
Female subjects	394±82	400±58	0.554
Xc/*H (Ohm/m)*			
Male subjects	27±12	37±8	<0.01
Female subjects	32±13	42±0.01	<0.01
Phase angle (°)			
Male subjects	4.54±1.3	6.6±0.96	<0.01
Female subjects	4.5±1.4	5.9±0.94	<0.01

ESRD, end-stage renal disease; Xc, reactance; R, resistance; H, height (m).

Table 3 | Derived body compartments values in ESRD and control population

Characteristic	ESRD	Control	*P*-value
Male subjects	*n*=120	*n*=277	
Fat mass (%)	15.4±8.3	21.6±7.98	<0.0001
Fat mass index (kg/m^2)	3.45±2.8	5.57±2.9	<0.0001
Body cell mass (%)	41.2±4.0	43.2±3.1	<0.0001
Muscle mass (%)	39.3±4.2	39.1±3.1	0.6
Total body water (%)	61.3±6.1	56.5±3.6	<0.0001
ECW (%)	35.3±10.4	23.3±4.0	<0.0001
ICW (%)	26.2±5.6	32.2±1.4	<0.0001
ECW/ICW[a]	1.6±1.4	0.76±0.15	<0.0001
Plasma water (l)	4.2±1.1	3.6±0.5	<0.0001
Female subjects	*n*=42	*n*=174	
Fat mass (%)	26±13	32.0±10.6	<0.007
Fat mass index (kg/m^2)	6.85±4.8	8.6±4.1	0.03
Body cell mass (%)	38.9±6.1	38.5±4.3	0.72
Muscle mass (%)	31.2±5.3	31.3±4.1	0.9
Total body water (%)	57.5±10.7	51.1±6.5	0.0006
ECW (%)	29.7±12.9	21.2±4.7	0.0001
ICW (%)	27.9±5.6	29.8±3.1	0.04
ECW/ICW[a]	1.3±1.5	0.72±0.19	<0.0001
Plasma water (l)	3.2±1.0	2.7±0.8	0.004

[a]ECW, extracellular water; ICW, intracellular water; ESRD, end-stage renal disease.

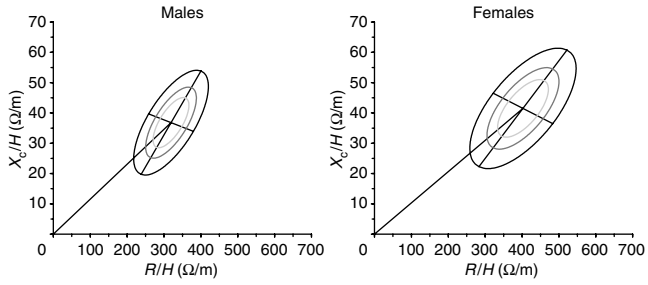

Figure 1 | The *R*Xc graph with the mean bioimpedance vector and 50, 75, and 95% tolerance ellipses for Indian reference population.

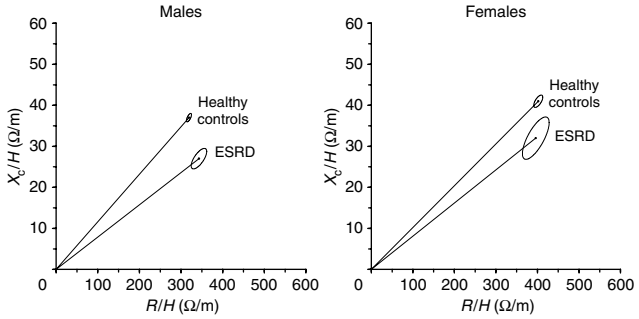

Figure 2 | The bioimpedance vector and 95% confidence ellipses for Indian ESRD patients and control population. The lack of overlap of the confidence ellipses indicates statistically significant difference in vector distribution ($P<0.05$, Hotelling's T^2 test), because of a smaller Xc/*H* component with a comparable *R/H* component (Table 2).

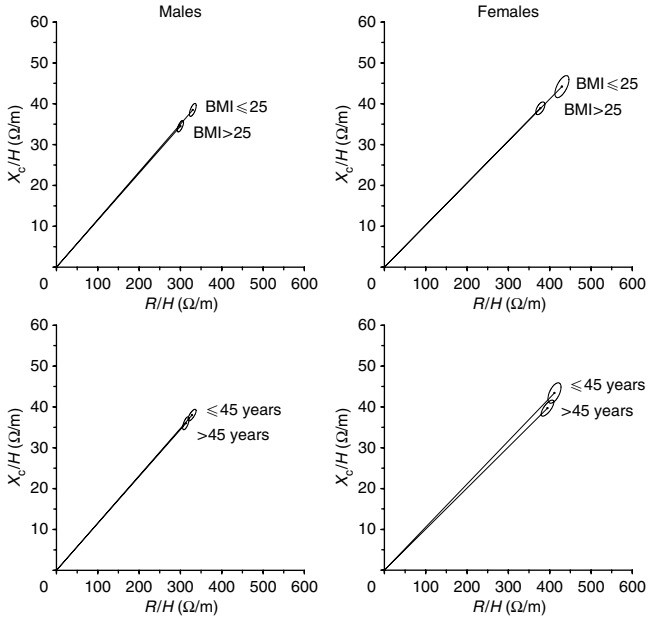

Figure 3 | Bioimpedance vectors and 95% confidence ellipses in healthy controls divided according to BMI ⩽25 and >25 (upper panel) and age ⩽45 years and >45 years in male subjects (left) and female subjects (right). The difference between the two groups depicted in the upper panel is significant ($P<0.05$, Hotelling's T^2 test).

of a decreased Xc/*H* component with a comparable *R/H* component ($P<0.05$).

We calculated the axis lengths for a reference *R*Xc score graph that can be utilized for vector comparison with populations other than Indians. The dimensionless values for the major axis were: 50% = 1.52, 75% = 2.16, and 95% = 3.18 and for the minor axis, 50% = 0.67, 75% = 0.96, and 95% = 1.41 (slopes 45° and −45°). The correlation coefficient between *R/H* and Xc/*H* was 0.672.

DISCUSSION

This study describes new body composition data using whole-body impedance at 50 kHz, and establishes BIA standards in a specific ethnic group not studied previously. We found a clear influence of sex and BMI on impedance vector components in the healthy population. These findings are consistent with reports in healthy adults from Europe[12] and the United States.[16] Sex, race, BMI, and age-influenced BIA parameters of healthy adults were evaluated in the NHANES III.[13] The less marked effect of age in the present study is likely due to a narrow age range and the confounding effect of BMI increases with age.

The estimated body compartment values in healthy individuals were close to the white NHANES III population.[10] ESRD patients exhibited a pronounced loss of fat compartment without loss of body cell mass (BCM) and muscle mass. This inconsistency may be because of the application of prediction equations for calculation of body composition in ESRD. Also, as the incidence of central obesity is high in Indians,[17] limitation of caloric intake with the onset of uremia could lead to depletion of fat mass before other compartments get affected. In American ESRD patients, fat mass was reduced in white and black female and white male subjects, but was increased in black males.[10] As expected, the percentage of total body water, ECW, and plasma fluid was increased in ESRD, more so than those reported in American ESRD patients. As our patients were receiving only 8 h/week HD, this finding was not surprising. In addition, male ESRD patients also showed a significant decrease in the ICW, which contributed to the high ECW/ICW ratio. Dumler and Kilates[10] found the ICW to be lower in white as well as black female subjects with ESRD, whereas in males, the ICW was decreased in white subjects but increased in black subjects. Compartment analysis using equations can result in errors because assumptions must be made about electrical properties of the human body, particularly of soft tissue hydration and the mathematical model, as well as biological variability of patients.[18] In particular, estimates of plasma water and muscle mass are based on several physiological assumptions in healthy individuals. Hence, such data can at best be considered approximate, and changes smaller than 1–2 kg can be hard to detect.[19] Because of these limitations, derived body compartment values have not been used for following up individual patients.

PA in healthy individuals was lower than that reported in the NHANES III with a different analyzer. Women had smaller PA, but no difference was noted between different age or BMI groups within the same sex. Piccoli *et al.*[13] found the phase angle to be lower in women as well as elderly. As noted before, ESRD patients had a much lower PA compared to sex-matched controls. PA decreases with increasing dialysis duration, and is a better predictor of survival than the usual nutritional parameters.[20–23] In one study,[24] low PA conferred a 20-fold increased risk of cardiovascular death in HD patients after controlling for inflammatory parameters. PA is decreased in sepsis,[18] human immunodeficiency virus wasting syndrome,[25] solid tumors,[26,27] burns,[28] and sickle-cell

disease.[29] On the other hand, PA increased after fluid removal with dialysis[14,16,30] and decreased in patients with edema.[14–16,31] Finally, shorter and more downsloping vectors in HD patients were associated with a higher risk of death. The risk was independent of age, gender, race, diabetes, dialysis duration, albumin, creatinine, hemoglobin, ferritin, and phase angle.[32] PA thus indicates a combined dimension of nutritional status and it should only be considered in groups with comparable hydration (similar *R* values).[14,16]

BIVA is the graphical depiction of impedance as a vector with a magnitude and an angle which are driven to vary by body composition within their 50, 75, and 95% tolerance ellipses (*R*Xc graph). The upper and lower poles of the 75% tolerance ellipse represent bioelectrical thresholds for dehydration and fluid overload, respectively.[13–16,31] For an individual, this graph can provide information whether prediction equations would be reliable in derivation of body compartment values. Data from a patient whose vector that falls outside the 75% tolerance ellipse is unlikely to yield accurate results.[12,13]

BIVA confirmed difference in body composition of the two sexes. The smaller vector size in males and individuals with higher BMI suggests less fat mass and the smaller ellipses in men indicate uniformity of body composition. Other studies have noted similar heterogeneity in women[12–14,33,34]. Garnett *et al.*[35] found the high body fat and lower total body mineral content in girls to be associated with higher insulin-like growth factor-I, estradiol, testosterone, and leptin concentrations. Fluxes in sex hormones secondary to pregnancies and/or menopause also contribute. Subcutaneous adipocytes increase to support the demands of pregnancy and lactation and disappear with menopause. The total amount as well as distribution of adipose tissue in perimenopausal women is affected by testosterone, estrogen, and sex-hormone binding globulin levels.[36] These differences together with a different geometry of limbs and trunk are likely to get reflected in the vector magnitude and angle.

Bioimpedance vector displacement has been documented in renal disease, cirrhosis, and cardiac surgery. Both malnutrition and overhydration are associated with reduced PA, but can be differentiated with the help of BIVA.[14] Vector shortening and narrow PA indicate a state of overhydration, whereas vector lengthening and narrow PA indicate loss of soft tissue mass and malnutrition.[14–16,31,37–40] BIVA can be thus used to assess ultrafiltration adequacy during HD and hydration in peritoneal dialysis patients.[15,16]

BIVA can also help to follow body composition at the individual level using tolerance ellipses. Vectors for a patient taken at different time points can be plotted on the *R*Xc graph to follow their progress (*R*Xc path graph).[30,31] Dialysis prescription can be evaluated in feedback with the direction of vector displacement. However, the place of BIVA as a standalone tool for serial assessment of patients with kidney diseases needs to be established in prospective studies.

*R*Xc score graph allows comparison of BIVA data obtained in subjects with different sex and races, and using differently calibrated instruments by plotting standardized deviates of vectors so that the score intervals are no longer bound to a particular setting.[13] Owing to a comparable correlation coefficient between *R* and Xc values, the axis lengths of the tolerance ellipses for the reference *R*Xc score graph for our population were found to be close to those described for the Americans,[13] and hence it is possible to use the same *R*Xc score graph for comparison of patient data.

Subjects in this study were derived from north Indian states, reflecting the geographic location of our Institute. Populations of different geographic regions in India exhibit ethnic diversity; people of the north are mainly Indo-Aryan, in the south they are mostly Dravidian. Some of the tribal populations are of Tibeto-Burmese and proto-Australoid extract. The generalizability of the body composition data to these other groups needs to be verified.

In summary, we present reference BIA data for healthy population from India and show that sex and BMI influence the pattern of bioimpedance vector distribution. ESRD patients showed significant body compartment alterations with displacement of impedance vector indicating inadequate ultrafiltration and malnutrition. The prognostic significance of these parameters needs to be validated in prospective studies.

MATERIALS AND METHODS

The study was conducted at the Postgraduate Institute of Medical Education and Research, a large tertiary care referral hospital in north India. Study subjects were healthy adults and ESRD patients of either sex. The exclusion criteria were: age less than 18 years, acute illness in the last 3 months, recent change in dialysis modality, post transplant status, limb amputation, or presence of arteriovenous fistula in both arms. To ensure homogeneity between the control and ESRD population, healthy individuals were selected from the friends and relatives accompanying the ESRD patients. General physical examination, urinalysis, and blood sugar and creatinine estimation were carried out to establish the healthy nature of controls. Informed consent was obtained from all subjects.

Weight in light clothing was recorded on a digital scale in the fasting state. Height was measured using a wall-mounted stadiometer. BIA was performed with a single 50 kHz frequency system with tetrapolar electrodes (Maltron Bioscan v 916, Rayleigh, UK) by one of two operators (AJ and MCS) according to the manufacturer's instructions. Subjects were asked to pass urine and placed in supine position with arms lying parallel and away from the trunk and legs separated so that they were not touching each other. Two pairs of disposable, pre-gelled electrodes were used; the first was placed on the dorsum of the hand over the third metacarpoplalangeal joint and the wrist and the second over the ipsilateral third metatarsophalangeal and ankle joints. HD was performed twice a week in 4-h sessions using low-flux polysulfone dilayzers and bicarbonate bath. Preliminary work showed that *R* and Xc became stable 15 min after the end of HD session (data not shown), and hence the study was carried out 15–60 min after the end of an HD session. Electrodes were placed on the arm opposite the access site. Peritoneal dialysis patients emptied the peritoneal cavity before measurements. Average of two readings was obtained in all. Measurements were repeated thrice on different days in 30 subjects (20 controls and 10 ESRD), and the intraindividual variability was found to be $<2\%$.

BIVA was conducted using *R* and Xc, the components of the *Z* vector. Raw values were normalized by the subject heights (*R/H* and Xc/*H*) and represented in the *R*Xc plot constructed using BIVA software (Piccoli A, Pastori G, available at E-mail: apiccoli@unipd.it). The normal interval of the reference population was expressed in percentiles (50th, 75th, and 95th) of the Gaussian bivariate probabilistic graph.[12,31] Finally, we calculated the parameters required to generate the dimensionless *R*Xc score graph for Indian population using the formula described earlier.[13]

Data are expressed as mean $\pm$ s.d. Derived values like fat-free mass, fat mass, body cell mass, muscle mass, and body water compartments were normalized for body weight and expressed as percentages. Fat mass and fat-free mass indices were derived by dividing the masses by the square of height. Compartments were estimated using the analyzer's software for body composition. Groups were compared using unpaired Student's *t*-test. *Z/H* vectors were compared using Hotelling's T^2 test. Male and female subjects were analyzed separately. Subgroup analysis was carried out in the controls grouped according to the BMI ($\leqslant 25$ and >25) and age ($\leqslant 45$ and >45 years).

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