Relationship between total body water and microvascular complications in patients with type 2 diabetes mellitus

Relación entre el agua corporal total y las complicaciones microvasculares en pacientes con diabetes mellitus tipo 2

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Abstract

The study analyzed the relationship between total body water (TBW), extracellular fluid (ECF), and intracellular fluid (ICF) with microvascular complications in patients with type 2 diabetes (T2DM) in Tungurahua, Ecuador, in 2023. One hundred and twenty-one patients with T2DM from diabetes clubs, selected by non-probability convenience sampling, were included. Demographic data and data on neuropathy, retinopathy, and nephropathy were collected employing surveys. Body composition was measured with electrical bioimpedance. As for the results, 69.9 % of patients had neuropathy, 42.1 % retinopathy, and 9.1 % nephropathy. The Mann-Whitney test showed significant differences in body water levels in neuropathy (TBW: p = 0.018, ICF: p = 0.022, ECF: p = 0.014), while in retinopathy (TBW: p = 0.883, ICF: p = 0.910, ECF: p = 0.885) and nephropathy (TBW: p = 0.975, ICF: p = 0.868, ECF: p = 0.857) no differences were found. A negative correlation was observed between age and TBW, ICF and ECF reduction. Males presented higher water volumes than females. TBW, ICF, and ECF are associated with diabetic neuropathy, whereas their relationship with other microvascular complications was not significant. Adequate hydration could play a key role in the management of diabetic neuropathy.

Keywords: **Body Water, Extracellular Fluid, Intracellular Fluid, Diabetes Mellitus.**

Resumen

El estudio analiza la relación entre el agua corporal total (ACT), el líquido extracelular (LEC) y el líquido intracelular (ICF) con las complicaciones microvasculares en pacientes con diabetes tipo 2 (DMT2) en Tungurahua, Ecuador, durante 2023. Se incluyeron 121 pacientes con DMT2 de clubes de diabetes, seleccionados por muestreo no probabilístico por conveniencia. Se recopilaron datos demográficos y sobre neuropatía, retinopatía y nefropatía mediante encuestas. La composición corporal se midió con bioimpedancia eléctrica. En cuanto a los resultados el 69,9 % de los pacientes presentaron neuropatía, el 42,1 % retinopatía y el 9,1 % nefropatía. La prueba de Mann-Whitney mostró diferencias significativas en los niveles de agua corporal en la neuropatía (ACT: p = 0,018, ICF: p = 0,022, LEC: p = 0,014), mientras que en la retinopatía (ACT: p = 0,883, ICF: p = 0,910, LEC: p = 0,885) y nefropatía (ACT: p = 0,975, ICF: p = 0,868, LEC: p = 0,857) no se hallaron diferencias. Se observó una correlación negativa entre la edad y la reducción de ACT, ICF y LEC. Los hombres presentaron mayores volúmenes de agua que las mujeres. El ACT, ICF y LEC están asociados con

la neuropatía diabética, mientras que su relación con otras complicaciones microvasculares no fue significativa. La hidratación adecuada podría desempeñar un papel clave en el manejo de la neuropatía diabética.

Palabras clave: **agua corporal, líquido extracelular, liquido intracelular, diabetes mellitus.**

INTRODUCTION

Water, an essential component of the human body, plays a fundamental role in multiple physiological processes, such as regulating body temperature, transporting nutrients and oxygen, eliminating waste through urine, and maintaining acid-base balance. (1) The human body is composed, on average, of 60% water, (2) a proportion that varies according to age, sex, and individual body composition. (3)

This total body water (TBW) is distributed between different compartments of the body: the extracellular fluid (ECF) and the intracellular fluid (ICF). (4,5) Both compartments are essential for life, but their functions and locations differ. (6) The ECF, representing approximately one-third of TBW, is outside the cells. (7) Its main functions include regulating electrolytes, transporting oxygen to cells, and removing metabolic waste products. (8)

On the other hand, the ICF, which constitutes the remaining two-thirds of the TBW, (7) is located within cells. Its functions are crucial for cellular processes, facilitating the transport of substances and maintaining cellular homeostasis. (8)

Since water plays a crucial role in regulating blood glucose, (9) Adequate hydration is essential for diabetes management. Maintaining optimal hydration levels helps stabilize glucose and reduces the risk of developing type 2 diabetes (T2DM). (10) While dehydration can compromise glycemic control and increase diabetic complications. (11)

This close relationship between hydration and glycemic control becomes even more relevant when we consider the complications associated with T2DM. Moreover , T2DM is a chronic disease characterized by hyperglycemia (12,13) that affects millions of people worldwide and is a major cause of morbidity and mortality. (14) In Ecuador, this condition has a prevalence of approximately 1 in 10 individuals. (15)

Small vascular involvementIt is a frequent consequence of poorly controlled T2DM. (16,17) This complication manifests as diabetic retinopathy, nephropathy and neuropathy, (18,19,20) negatively impacting quality of life. (21)

Pla's study (22) collected evidence on the impact of dehydration in diabetic patients, suggesting that it may influence the development and progression of microvascular complications. However, the relationship between body water distribution and these complications is still not fully understood. Considering the fundamental role of water in vascular health, it is of utmost importance to assess the hydration status of these patients to prevent or mitigate these types of complications.

This research aimed to determine the relationship between total body water, extracellular and intracellular water, and microvascular complications in patients with type 2 diabetes mellitus.

MATERIALS AND METHODS

An observational, descriptive, cross-sectional study was conducted to determine the association between total body water, extracellular water, and intracellular water levels and microvascular complications in patients with type 2 diabetes mellitus who attended diabetes clubs at health centers in the Province of Tungurahua in 2023.

The population consisted of 121 subjects, selected using non-probability convenience sampling, as this selection was based on the accessibility and willingness of participants. Although participation was voluntary and the ethical principles of informed consent were respected, it is recognized as a limitation that the results may not represent all diabetic patients in the province.

The inclusion criteria were as follows: patients over 18 years of age with a confirmed diagnosis of type 2 diabetes mellitus who actively participated in diabetes clubs in the province of Tungurahua. Participants were also required to be willing to participate voluntarily and sign informed consent. Those included were those without serious illnesses that could interfere with body composition measurement, such as terminal or acute conditions unrelated to diabetes, and who were in stable condition for bioimpedance measurement. Patients diagnosed with gestational diabetes, those menstruating at the time of the assessment, and patients who did not attend body composition analysis on an empty stomach were excluded. Data were collected through a structured survey based on validated instruments for patients with diabetes, such as the American Diabetes Association (ADA) Diabetes Risk Test. This survey obtained demographic data on age and sex, as well as the presence of microvascular complications, such as retinopathy, nephropathy, and neuropathy.

To perform the bioelectrical impedance measurement, the participant had to meet certain requirements such as: fasting, wearing light and comfortable clothing, not wearing shoes or socks, and women not being menstrual. The participant was positioned on a non- conductive base with their arms and legs slightly separated, approximately 20 cm apart, to avoid errors in the reading. Four electrodes were placed on the back of the hands and on the front of the feet.

Before electrode placement, the subject was required to remain recumbent for at least 15 minutes to ensure even fluid distribution. The measurement was conducted in a controlled environment, with a room temperature of 22 to 24°C to prevent thermal fluctuations from affecting the results. Furthermore, participants were ensured to be adequately hydrated in the 24 hours prior to the measurement, as hydration influences the accuracy of body composition measurements.

To assess extracellular and intracellular TBW, a multi-frequency bioelectrical impedance analyzer [23,24] from theInBody ® brand, model S10, was used. Prior to using the analyzer, the height and weight of each participant were recorded, following the standardized techniques of the International Society of Biotechnology (ISBM) protocol for the Advancement of Kinanthropometry (ISAK). [25]

Height was measured using a Seca 213 portable stadiometer, the device has a measuring range of 20 to 205 cm with an accuracy of 1 mm, ensuring precise measurements, is easily disassembled and assembled quickly. While weight was measured using a SENSSUN digital scale model IF1011AR, with a maximum capacity of 180 kg and an accuracy of 50 g. The scale allows conversions between kg, pounds and stones, and has a 74 x 35.6 mm LCD display for easy reading of the results.

The data were recorded in a database created with Microsoft Excel 2019 and exported to the statistical software SPSS version 21. This allowed statistical processing to be carried out using frequency tables and descriptive statistical tests, in addition to non-parametric tests (Mann-Whitney U test) and non-parametric correlations using the Spearman scale.

The study was approved by the Bioethics Committee for Research in Human Beings of the Technical University of Ambato, approved under Resolution UTA-CONIN-2023-0347-R. Thus guaranteeing respect for the principles of beneficence, non-maleficence, autonomy and justice, as established in the Declaration of Helsinki. [26] The corresponding authority granted the necessary permission to access the study population. The researchers agreed to respect the anonymity of the participants, who signed the informed consent to participate in the research.

RESULTS

In the demographic analysis according to sex, it was found that 75% were female and 25% were male.

According to age, the age range was 37 to 99 years, with a mean of 68.46 years and a standard deviation of 11.720, indicating a diverse population in terms of age.

Among microvascular complications, diabetic neuropathy was observed in 69.9% of cases, diabetic retinopathy in 42.1% of cases, and diabetic nephropathy in 9.1%. It should be noted that these percentages do not add up to 100%, as some patients presented with more than one complication simultaneously (Table 1).

Table 1. Frequency of microvascular complications in patients with T2DM

Table 1

Frequency of microvascular complications in patients with T2DM

	Diabetic Neuropathy		Diabetic Retinopathy		Diabetic Nephropathy	
	Frequency	%	Frequency	%	Frequency	%
Suffering from illness	81	66.9	51	42.1	11	9.1
Does not suffer from any disease	40	33.1	70	57.9	110	90.9
Total	121	100.0	121	100.0	121	100.0

Descriptive analysis of the sample, consisting of 121 patients, revealed considerable variability in TBW measurements and age. TBW levels ranged from 16.3 to 46.4 liters, with a mean of 29.005 liters and a standard deviation of 5.7576, reflecting considerable dispersion in TBW levels. ICF values ranged from 9.7 to 28.8 liters, with a mean of 17.669 liters and a standard deviation of 3.6319, indicating significant variation in this compartment. ECF ranged from 6.6 to 18.0 liters, with a mean of 11.336 liters (Table 2).

Table 2. Descriptive statistics of the sample

Table 2

Descriptive statistics of the sample

	Minimum	Maximum	Average		Typ . dev.
			Statistical	Typical error	Statistical
Total Body Water (TBW)	16.3	46.4	29,005	0.5234	5,7576
Intracellular Fluid	9.7	28.8	17,669	0.3302	3,6319
Extracellular Fluid	6.6	18.0	11,336	0.1963	2,1591
Patient's age	37	99	68.46	1,065	11,720

The Mann-Whitney U test showed significant differences in the distribution of TBW, ICF, and ECF between patients with and without diabetic neuropathy. The significance level for TBW was 0.018, leading to rejection of the null hypothesis, suggesting that ACT levels differed significantly between the two groups. Similarly, the ICF yielded a value of 0.022, indicating a significant difference. The ECF also showed a difference, with a value of 0.014. These results suggest that TBW, ICF, and ECF may play an important role in the development of diabetic neuropathy (Table 3).

In diabetic retinopathy, the significance levels were 0.883, 0.910, and 0.885 for TBW, ICF, or ECF; therefore, no significant differences were found in levels between patients with and without this complication,

respectively. Since all values were greater than 0.05, the null hypotheses were retained, suggesting that body water is not significantly related to the presence of diabetic retinopathy in this population (Table 3).

In the analysis of diabetic nephropathy, the values obtained were 0.975 for TBW, 0.868 for ICF, and 0.857 for ECF. There were no significant differences in the aforementioned distributions, due to an upper threshold of 0.05. Consequently, the null hypotheses were retained, indicating that body water in its different compartments is not significantly related to diabetic nephropathy in this sample (Table 3).

Table 3. Mann-Whitney U test to assess non-parametric tests (Asymptotic Sig.) relationship between microvascular complications and TBW, ICF and ECF

Table 3

Mann-Whitney U test to assess non-parametric tests (Asymptotic Sig.) relationship between microvascular complications and TBW, ICF and ECF

	Diabetic Neuropathy	Diabetic Retinopathy	Diabetic Retinopathy
Total Body Water	0.018	0.883	0.975
Intracellular fluid	0.022	0.910	0.868
Extracellular fluid	0.014	0.885	0.857

Spearman's correlation test showed a significant negative association between age and TBW compartments, indicating that as patients age, TBW (Rho = -0.502, p < 0.001), ICF (Rho = -0.552, p < 0.001), and ECF (Rho = -0.403, p < 0.001) volumes decrease. Regarding microvascular complications, only diabetic nephropathy showed a weak negative correlation with age (Rho = -0.176, p = 0.027), suggesting a lower prevalence in older patients, while neuropathy and retinopathy did not show significant associations. Demonstrating a relationship between aging and reduced body water, which could influence the management of type 2 diabetes (Table 4).

Table 4. Spearman correlation with demographic data (Age)

Table 4

Spearman correlation with demographic data (Age)

Variable	Spearman's Rho	*p*-value (Sig.)
Diabetic Neuropathy vs Age	0.011	0.452
Diabetic Retinopathy vs Age	-0.053	0.281
Diabetic Nephropathy vs Age	-0.176	0.027
TBW vs Age	-0.502	0.001
ICF vs Age	-0.552	0.001
ECF vs Age	-0.403	0.001

In the Mann-Whitney U test, significant differences were found in the distribution of TBW, ICF and ECF between men and women. Men presented larger volumes in these compartments, with higher average ranges compared to women. In the TBW, men had an average range of 95.83 and women 49.52 (U = 2,410,000, p = 0.001); in the ICF, the values were 94.82 in men and 49.85 in women (U = 2,379,500, p = 0.001); and in the ECF, men reached an average range of 97.58, while women 48.94 (U = 2,462,500, p = 0.001). These results indicate that men have higher volumes of water in all compartments evaluated compared to women, suggesting a significant difference in the distribution of total body water according to sex in the population studied (Table 5).

Table 5. Mann-Whitney U test to evaluate the difference in body water compartments between men and women in the studied population

Table 5

Mann-Whitney U test to evaluate the difference in body water compartments between men and women in the studied population

Variable	Sex	Average range	Ranks	U-value	p-value (Sig.)
Total Body Water	Men	95.83	2,874.9	2,410,000	0.001
	Women	49.52	4,506.32	2,410,000	0.001
Intracellular Fluid	Men	94.82	2,844.6	2,379,500	0.001
	Women	49.85	4,536.35	2,379,500	0.001
Extracellular Fluid	Men	97.58	2,927.4	2,462,500	0.001
	Women	48.94	4,453.54	2,462,500	0.001

DISCUSSION

Compared with the study conducted at the General Hospital of Zone 2 in Salina Cruz, Oaxaca, the results of the current investigation show notable differences in the prevalence of microvascular complications. In the study by Sadai et al. (2024), diabetic neuropathy had a prevalence of 3.9%, nephropathy 29.2%, and retinopathy 14.4%, with 31.7% of patients presenting at least one micro- or macrovascular complication. In contrast, in our sample of 121 participants, the rates of neuropathy (69.9%), retinopathy (42.1%), and nephropathy (9.1%) were considerably higher, which could indicate differences in the severity of diabetes in the study populations or variations in diagnostic methods. Furthermore, as in the study by Sadai et al, some patients were observed to have more than one complication at the same time, which underlines the complexity of managing patients with type 2 diabetes mellitus and the high burden of complications associated with this disease. (27)

Similar results to a study between chronic kidney disease water in type 2 diabetes, in which, ECF and TBW ratios have a significant impact on the risk of chronic kidney disease (CKD) progression, as it was observed that ECF and TBW ratios were associated with a 45 % and 78% increase in the risk of CKD progression. This is in contrast to our findings, where no significant correlations were found between TBW and microvascular complications in patients with type 2 diabetes. (28)

However, in the research conducted in patients with T2DM in older adults, a prevalence of 14 % of this disease is revealed, with a higher prevalence in women and in adults over 74 years of age. This coincides with our findings, where we observed that age is negatively correlated with TBW and ICF levels, suggesting that older patients may be at greater risk of dehydration, which could further complicate their clinical management. Regarding complications, arterial hypertension and dyslipidemia were reported to be the most common in the study population, while, in our analysis, diabetic neuropathy was the predominant complication. (29)

The results of our study showed significant differences in the distribution of TBW, ICF and ECF between patients with diabetic neuropathy ($p = 0.018$, $p = 0.022$, $p = 0.014$, respectively), suggesting that altered hydration may play a key role in the development of this complication. These findings are consistent with those reported in which subjects with diabetes were found to have lower hydration in the skin of the sole of the foot, the center of the big toe and the heel, with significance values of $p = 5.90 \times 10^{-4}$, $p = 4.30 \times 10^{-4}$ and

$p = 8.70 \times 10^{-6}$, respectively. In both studies, the relationship between hydration status and the presence of diabetic complications is evident, which reinforces the hypothesis that dehydration can affect tissue homeostasis, microcirculation and peripheral nerve function. (30)

The results of this study showed no significant differences in the distribution of TBW, ICF, and ECF in patients with diabetic nephropathy, with significance values of 0.975, 0.868, and 0.857, respectively. This contrasts with previous research in renal patients with 56.3% of the population, where an abnormally high ECF/ICF ratio was observed due to a constant state of overhydration, associated with hypoalbuminemia. The lack of significance could be due to factors such as the stage of the disease, the sample size, or external variables such as hypertension or the use of diuretics, which could have masked possible associations. (31)

Likewise the results of the significant association between elevated serum osmolality and increased risk of diabetic retinopathy in US adults (OR: 1.371, 95% CI: 1.001–1.876), in our research no significant differences were observed in the levels of TBW, ICF and ECF among patients with diabetic retinopathy. The p values for these compartments were 0.883, 0.910 and 0.885, respectively, all greater than 0.05, suggesting that body hydration is not significantly related to the presence of diabetic retinopathy in our sample. This discrepancy could be due to differences in the characteristics of the studied populations, as our sample may have different socioeconomic, environmental, or clinical factors compared to the American population analyzed in that study. (32)

Similarly, an investigation conducted in Chile evaluated 284 women, reporting a predominance of arterial hypertension (70.4%), hypercholesterolemia (48.2%), and T2DM (36.3%), along with a body composition characterized by an average body mass index of 29.7±4.8, where 71.8% were overweight. Significant differences were found in the amount of body fat and extracellular water (ECW) according to age, showing higher values in women aged 75 years or older. In our research, focused on patients with type 2 diabetes mellitus, the analyses revealed significant differences in the TBW compartments between patients with and without diabetic neuropathy, with lower TBW, ICF, and ECF in those with this complication. Furthermore, a negative correlation was identified between age and the levels of TBW, ICF, and ECF, indicating a progressive reduction in these volumes with aging. These results underline how body water composition and distribution are influenced by age and health complications, both in older women and in patients with T2DM. (33)

In the previous results of this article, the correlation is strong and significant (Rho = -0.502, p = 0.000), indicating that as age increases, TBW, as well as ICF and ECF, decrease. This is compared to the study by Tirado (2023) where, in diabetic men, the correlation is moderate and negative (Rho = -0.601), while in non-diabetic men it is lower (Rho = -0.237). In women, the correlation is weak, especially in non-diabetics (Rho = -0.056), suggesting that the relationship between age and body water varies by sex and T2DM complications. Both studies show a negative correlation between age and TBW. (34)

Limitations: This study found significant associations between body water compartments and diabetic neuropathy, but not with other microvascular complications. Although convenience sampling provided access to a relevant population for the study, it may limit the generalizability of the results. Furthermore, the sample size and unequal sex distribution could have influenced the observed associations.

Despite these limitations, the findings highlight the importance of considering TBW, ICF, and ECF in the evaluation of complications in patients with T2DM. Additional studies are needed to confirm these results and further explore their impact on microvascular complications.

CONCLUSIONS

This study found a significant association between TBW, ICF, and ECF and diabetic neuropathy in patients with T2DM. The results indicate that patients with neuropathy present significantly different levels

of TBW, ICF, and ECF, suggesting that adequate hydration may play an important role in preventing this complication. However, no significant differences were observed in the levels of these water compartments in relation to diabetic retinopathy and nephropathy, indicating that, at least in this sample, body water status is not directly related to these microvascular complications. These findings open the door to future studies that delve deeper into the role of body water in the development of complications associated with diabetes.

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Declaration of contribution:

Anderson Jordán Villacrés Benavides: Writing, editing, methodology.

Tannia Elizabeth Quiroga Torres: Validation Supervision Formal Analysis.

Efraín Marcelo Pilamunga Poveda: Statistics and analysis of results.

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