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Sex related Differences in the Distribution of Adipose Connective Tissue in Bulgarian Patients Suffering from type 2 Diabetes Mellitus

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Abstract

Aim: to compare the distribution of adipose connective tissue between 40-60 year old Bulgarian male and female patients with T2DM. Subjects: 217 patients, divided into two groups by sex. Control group: 80 healthy men and women divided into the same groups. Anthropometric parameters: weight, 9 skinfolds, Bioelectrical Impedance Analysis. Calculated indices: BMI, sfTrunk/sfLimbs ratio, skinfolds upper half of body/skinfolds lower half of body ratio, fat mass and subcutaneous fat mass.
Results: The mean values of BMI, % body fat tissue, fat mass and subcutaneous fat mass in female patients were significantly higher than in male patients, but the mean value of visceral fat tissue was significantly higher in male patients. The value of sfTrunk/sfLimbs ratio was greater in male patients than in female patients. These results are a reason for assessing the anthropological status of male patients as worse than that of female patients for the prognostic of disease.

Key words: type 2 Diabetes Mellitus, connective fat tissue, sex related comparison

Introduction

Type 2 Diabetes Mellitus (T2DM) is a long-term metabolic disorder that is characterized by high blood sugar, insulin resistance, and relative lack of insulin. It is really a social problem due to the rapidly growing number of people affected by the disease

worldwide. As of 2015, the estimated 415 million people had diabetes worldwide, with type 2 DM it makes about 90% of the cases. This represents 8.3% of the adult population, with equal rates in both women and men. According to the International Diabetes Federation, the number of diabetes mellitus patients in Europe is expected to increase from 52 millions in 2014 to 68.9 millions by 2035, mostly due to increases in overweight and obesity, unhealthy diet and physical inactivity [7]. Eastern Europe is significantly affected by the disease: Serbia – 13,4%, Bosnia and Herzegovina – 12,6%, Turkey and Romania – 12,5%, Northern Macedonia – 12,1%, Albania – 11,9%. Around 8-9% of the Bulgarian population suffers from this disease.

Conducted surveys were focused exclusively on clarifying the etiology, pathogenesis, clinical course and treatment of the disease. Limited number of studies aimed to clarify the relationship between anthropological parameters determining humans' body constitution, and the differences between both sexes. The fat accumulation in the body of patients with type 2 Diabetes Mellitus occurs primarily in two locations: in the abdomen (central, abdominal, visceral) and subcutaneously (peripheral). Fat accumulation in the abdominal area is commonly associated with increased risk for T2DM [8, 12, 13, 18]. Not many studies have been performed for the sex related distribution of adipose connective tissue. The aim of this study was to compare the distribution of adipose connective tissue between 40-60 year old Bulgarian male and female patients with T2DM.

Materials and Methods

Subjects. Totally of 165 patients aged 40-60 years suffering from type 2 Diabetes Mellitus were involved in the study. They were divided into two groups by sex: 1st group: 40-60 years of age – 92 female patients (mean 52.87±0.56 yrs), 2nd group: 73 male patients (mean 52.29±0.79 yrs). They were diagnosed by a diabetes specialist and recruited from the Clinic of Endocrinology of St. George University Hospital at the Medical University of Plovdiv, Bulgaria. The study period was 2009-2015.

The inclusion criteria were: Bulgarian ethnicity, duration of the disease of not less five years, clinically compensated diabetes at the time of the study. The exclusion criteria were: previous or existing metabolic, oncological and other disorder that could compromise the anthropological study: thyroid related diseases, adrenal glands related diseases, carcinoma, etc.

In the study were involved 80 healthy Bulgarian subjects. The control groups included 40 men at the same age range (51.33±0.93 yrs) and 40 women at the same age range (50.80±1.08 yrs).

An ethical approval was taken for this study. Informed consents were taken from all patients involved in the study.

Methods

Directly measured parameters: body weight, skinfold (sf) thicknesses were measured at 9 locations – sfTriceps, sfBiceps (brachii), sfForearm, sfSubscapular, sfXrib, sfAbdomen, sfSuprailiaca, sfThigh, and sfCalf, using Harpenden Skinfold Calipers (British Indicators Ltd) at standard sites on the right side of the body.

Bioelectrical Impedance analysis (BIA): % body fat tissue and visceral fat tissue were measured with a Body Composition Monitor Tanita BC-532.

Calculated indices: Body mass index (BMI), sfTrunk/sfLimbs ratio, skinfolds upper half of body/skinfolds lower half of body ratio, fat mass and subcutaneous fat mass.

Statistical analysis. Data were analyzed using statistical software SPSS version 15 (SPSS Inc., Chicago, IL). Independent Samples t-Test was used to compare the means of two independent anthropologic parameters in order to determine whether there was statistical evidence that the means were significantly different. The one-way analysis of variance (ANOVA) was used to determine whether there were any significant differences between the means of three or more independent parameters. $P<0.05$ (two tailed) was considered statistically significant.

Results

I. Distribution of adipose connective tissue between female patients and healthy controls.

Significant difference was found between the means of **weight** in the present study. The mean value of female patients was higher than the controls ($p<0.001$). The thicknesses of **sfTriceps, sfThigh and sfCalf** were significantly greater in the healthy controls than in female patients suffering from type 2 Diabetes Mellitus ($p<0.05$), but **sfXrib** was significantly greater in the patients ($p<0.01$), demonstrated in **Table 1**.

Table 1. Anthropological parameters of Bulgarian patients aged 40-60 years with type 2 Diabetes Mellitus compared to healthy controls at the same age.

	Female			**Male**		
Parameters	T2DM mean±sem	Controls mean±sem	P	T2DM mean±sem	Controls mean±sem	P
Weight (kg)	79.65±1.25	69.95±1.83	**<0.001***	84.47±1.38	78.47±1.78	**<0.001***
sf Triceps(mm)	21.94±1.59	28.46±1.85	**<0.05***	10.91±0.60	11.20±0.96	>0.05
sfSubscapular(mm)	28.98±1.42	26.35±1.74	>0.05	23.85±1.42	20.24±1.51	>0.05
sf X rib(mm)	28.68±1.35	22.51±1.50	**<0.01***	22.92±1.26	16.98±1.34	**<0.05***
sfSuprailiaca(mm)	21.68±1.14	23.17±1.62	>0.05	17.83±1.37	20.86±1.60	>0.05
sfAbdomen(mm)	32.06±1.40	34.60±2.03	>0.05	28.68±1.70	33.21±2.10	>0.05
sfBiceps(mm)	12.85±0.76	15.61±1.22	>0.05	7.71±0.47	6.57±0.53	>0.05
sfForearm (mm)	11.59±0.66	12.00±1.19	>0.05	8.20±0.51	7.48±0.60	>0.05
sfThigh(mm)	24.49±1.96	42.47±2.01	**<0.001***	15.08±1.04	20.21±1.89	**<0.05***
sfCalf(mm)	20.21±1.33	27.32±1.59	**<0.01***	10.51±0.86	11.39±0.91	>0.05

sf = skinfold, * statistical significance

Body composition parameters' results, investigated by Bioelectrical Impedance analysis

The values of three parameters: **% body fat tissue, visceral fat tissue and fat mass** were significantly higher in female patients than the healthy controls ($p<0.05$), demonstrated in **Table 2.**

Table 2. Body composition of Bulgarian patients aged 40-60 years with type 2 Diabetes Mellitus.

Parameters	T2DM-female mean±sem	Controls-female mean±sem	P	T2DM-male mean±sem	Controls-male mean±sem	P
BMI	29.04±0.49	26.34±0.51	**<0.001***	31.77±0.51	27.31±0.70	**<0.001***
% body fat tissue	28.71±1.11	24.75±0.86	**<0.05***	42.07±0.99	37.66±0.99	**<0.01***
Visceral fat tissue (kg)	13.79±0.72	11.00±0.55	**<0.05***	11.26±0.40	7.80±0.45	**<0.001***
Fat mass (kg)	24.02±1.30	19.83±1.07	**<0.05***	37.97±1.73	27.48±1.40	**<0.001***
Subcutaneous fat mass (kg)	15.75±0.26	15.65±0.45	>0.05	17.18±0.27	18.68±0.40	**<0.05 ***

* statistical significance

II. Distribution of adipose connective tissue between male patients and healthy controls.

A significant difference was found between the means of **weight,** too. The mean value of male patients with diabetes was significantly higher than the controls ($p<0.001$). The thickness of **sfXrib** in diabetic male patients was significantly higher than the healthy controls ($p<0.05$). The thickness of **sfThigh** in male patients was significantly lower than the controls ($p<0.05$). These results are demonstrated in **Table 1**.

Body composition parameters' results, investigated by Bioelectrical Impedance analysis.

The values of the **% body fat tissue, visceral fat tissue, fat mass** and **subcutaneous fat mass** in male patients with diabetes were significantly higher than the controls ($p<0.05$), demonstrated in **Table 2**.

III. Comparison of some anthropological parameters between female and male Bulgarian patients.

Many statistically significant differences were detected between the measured anthropological parameters in both sexes, demonstrated in **Table 3**.

Table 3. Comparison of some anthropological parameters between female and male Bulgarian patents aged 40-60 years with type 2 Diabetes Mellitus.

	females				males				
Parameters	N	Mean	SEM	SD	N	Mean	SEM	SD	**P**
Weight (kg)	92	79.65	1.25	11.99	73	84.47	1.38	9.49	**<0.01***
sfTriceps(mm)	92	21.94	1.59	15.25	73	10.91	0.60	4.04	**<0.001***
sfSubscapular(mm)	92	28.98	1.42	13.62	73	23.85	1.42	9.62	**<0.01***
sf X rib(mm)	92	28.68	1.35	12.95	73	22.92	1.26	8.52	**<0.01***
sfSuprailiaca (mm)	92	21.68	1.14	10.93	73	17.83	1.37	9.32	**<0.05***
sfAbdomen(mm)	92	32.06	1.40	13.43	73	28.68	1.70	11.51	>0.05
sfBiceps(mm)	92	12.85	0.76	7.29	73	7.71	0.47	3.21	**<0.001***
sfForearm (mm)	92	11.59	0.66	6.33	73	8.20	0.51	3.47	**<0.001***
sfThigh(mm)	92	24.49	1.96	18.80	73	15.08	1.04	7.07	**<0.001***
sfCalf(mm)	92	20.21	1.33	12.76	73	10.51	0.86	5.87	**<0.001***

sf = skinfold, * statistical significance

The mean value of weight in male patients was significantly higher than in female patients ($p<0.01$). The mean values of measured skinfolds were significantly greater in female patients than in male patients, except sf Abdomen. There wasn't detected a significant difference between the compared values ($p>0.05$).

The mean values of **% body fat tissue, fat mass and subcutaneous fat mass** in female patients were significantly higher than in male patients, but the mean value of **visceral fat tissue** was significantly higher in male patients ($p<0.001$), demonstrated in **Table 4**.

IV. Comparison of some indices between female and male patients with type 2 DM.

The **BMI** of male and female patients suffering from diabetes were significantly higher than that of the healthy controls ($p<0.001$), demonstrated in **Table 2**. The mean value of BMI in female patients was significantly higher than in male patients ($p<0.001$), demonstrated in **Table 4**. The values of the **sfTrunk/sfLimbs ratio** and **skinfolds upper half of body/skinfolds lower half of body ratio** were greater in the patients of both sexes compared to healthy controls. The value of **sfTrunk/sfLimbs ratio** was higher in male patients in comparison to female patients. The value of **skinfolds upper half of body/skinfolds lower half of body ratio** in female patients was higher than in male patients, demonstrated in **Table 5.**

Table 4. Comparison of some body composition's parameters between female and male Bulgarian patients aged 40-60 years with type 2 Diabetes Mellitus.

	female				**male**				
Parameters	N	Mean	SEM	SD	N	Mean	SEM	SD	**P**
BMI	92	31.77	0.51	4.89	73	29.04	0.49	3.34	**<0.001***
% body fat tissue	92	42.07	0.99	9.50	73	28.71	1.11	5.97	**<0.001***
Visceral fat tissue (kg)	92	11.26	0.40	3.84	73	13.79	0.72	3.87	**<0.001** *
Fat mass (kg)	92	37.97	1.73	16.59	73	24.02	1.30	6.88	**<0.001** *
Subcutaneous fat mass(kg)	92	17,18	0.27	2.59	73	15.75	0.26	2.85	**<0.001***

* statistical significance

Table 5. Comparison of some indices between female and male patients aged 40-60 years with type 2 Diabetes mellitus.

	females		**males**	
	T2DM	controls	T2DM	controls
sf trunk/sf limbs	1.34	0.85	1.79	1.67
sf upper half of the body/ sf lower half of the body	1.09	0.83	1.07	0.75

Discussion

Analysis of distribution of subcutaneous adipose connective tissue

The mean value of weight was significantly higher in the patients of both sexes than in healthy controls. The differences were very well expressed ($p<0.001$).

Attention should be paid to the distribution of subcutaneous adipose tissue in female patients with T2DM. It was found that in the female patients with T2DM the accumulation of subcutaneous adipose tissue was mostly in torso and less in the limbs. Moreover, the accumulation of adipose tissue consisted predominantly in the upper part of the body compared to the lower, the so-called "apple shaped" body. The thicknesses of sf Triceps, sfThigh and sfCalf were significantly greater in the controls than in female patients [21], but the thickness of sfXrib was significantly greater in female patients. These patients have a worse anthropological status, which would lead to a more severe clinical course of the disease.

Similar tendencies were found by the assessment of distribution of subcutaneous adipose connective tissue in male patients. The thickness of sfXrib was significantly greater in male patients than in controls, but sfThigh was significantly thicker in the controls than in male patients. Attention should be paid that there were found two significant differences only. The body shape constitution "apple" is closely associated with a poor prognostic of the disease [4]. The deposition of adipose connective tissue in the controls of both sexes was predominantly in the limbs and mainly in the lower part of the body, the so-called "pear shaped" body (**table 1 and table 5**).

The mean value of body weight in male patients was significantly greater than in female patients. It can be explained with the sexual dimorphism. Attention should be paid by the comparison of skinfolds between both sexes. The mean values of all 8 measured skinfolds were significantly higher in female patients than in male patients. The exception was sf Abdomen. There wasn't found a significant difference between the mean values of male and female patients ($p>0.05$). Only a tendency was registered, that the value of sfAbdomen in female patients was higher in comparison to male patients (**table 3**). These results defined an unfavourable distribution of subcutaneous adipose connective tissue in female patients compared to the male patients.

Analysis of Body composition parameters' results, investigated by BIA.

It has been found that abdominal obesity, also known as central or visceral obesity, was more closely related to T2DM than the general obesity. The visceral fat was more metabolically active and produced more insulin resistance [5, 16, 19].

Many significant differences were found in the parameters: BMI, % body fat tissue, visceral fat tissue and fat mass. They were significantly greater in female patients with T2DM than in healthy controls. The exception was the accumulation of subcutaneous fat mass. There wasn't detected a significant difference ($p>0.05$). The mean values of above described parameters were significantly greater in male patients than in the healthy controls at the same age, including the parameter subcutaneous fat mass. We have found that the values of following parameters: BMI, %body fat, fat mass and subcutaneous fat mass were significantly higher in female patients than in male patients to comparison between both sexes. Opposite, the mean value of visceral fat tissue was significantly greater in male patients than in female patients at the same age. This parameter is more important than the others, because it is closely related to the insulin resistance [11]. The greater values of visceral fat tissue in male patients determine a worse anthropological status in comparison to female patients.

Analysis of the calculated indices in both sexes patients suffering from type 2 DM.

The mean value of BMI in male and female patients was significantly higher than in healthy controls at the same age and sex ($p<0.05$). The levels of BMI in female patients were significantly higher compared to the male patients ($p<0.001$), (table 2 and table 4). This index demonstrates a total deposition of adipose connective tissue into the human body, but these values had less importance for the prognosis of disease compared to above described parameters [2, 9].

The accumulation of subcutaneous adipose tissue in the patients of both sexes suffering from type 2 Diabetes Mellitus was higher in the torso, than in the limbs. In contrast, the controls exhibited the opposite distribution. The accumulation of subcutaneous adipose tissue was larger in the upper half of the body, than in the lower half. It defined the model of patients' body shape as so-called "apple shaped". The controls exhibited the opposite distribution (**table 5**). The value of the ratio sf trunk/sf limbs was greater in male patients than in female patients. The value of the ratio sf upper half of the body/sf lower half of the body was greater in the female patients than in male patients, but the difference is too thin. These results demonstrated more uneven distribution of adipose connective tissue in male patients than in female patients. The accumulation of fat mass more in the trunk and less in the limbs is significantly and positively associated with a worse glucose metabolism [1, 3, 14, 17]. According to these facts the anthropological status of male patients is defined as worse than that of the female patients. Some researchers confirmed our results and described the importance of intramuscular adipose tissue [15] in patients suffering from T2DM. It is very important to investigate the relationship between the body fat distribution and the complications of the disease too [6, 10, 20].

Conclusion

The values of BMI, % body fat tissue, fat mass and subcutaneous fat mass were significantly greater in female patients than in male patients, but the value of visceral fat tissue was significantly greater in male patients. These data demonstrated the accumulation of connective adipose tissue more subcutaneously, but less viscerally in female patients. It is opposite in the male patients: the accumulation of connective fat tissue is more viscerally, but less subcutaneously. The subcutaneous adipose connective tissue was accumulated predominantly in the torso than in the peripheral part of the body (arms, thighs and lower legs) in the male patients compared to the female.

These results are a reason to assess the anthropological status of male patients as worse than that of female patients for the prognostic of disease. The complex study including anthropometry of adipose connective tissue in patients suffering from T2DM would support the evaluation of the prognosis of the disease.

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