

Hypertension in type 1 diabetic patients-the influence of body composition and body mass index: an observational study

Tip 1 diyabetli hastalarda hipertansiyon-vücut yapısı ve vücut kitle indeksinin etkisi: Gözlemsel bir çalışma

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ABSTRACT

Objective: To estimate the influence of body composition and body mass index on blood pressure in type 1 diabetic patients.

Methods: This cross-sectional, observational study included 45 type 1 diabetic patients and 30 age and sex matched healthy volunteers. Blood pressure, anthropometric measurements, and body composition by dual X-ray absorptiometry (DXA) were done for all patients and controls. T-test, one way ANOVA and multiple regressions were used for statistical analyses.

Results: Twenty diabetic patients (44.4%) had hypertension. Hypertensive diabetic patients had the highest total fat mass %, soft tissue fat mass %, abdomen fat % and fat/lean ratio followed by non hypertensives and the least was the controls (p=0.0001). Abdominal fat % was the only parameter significantly associated with mean arterial blood pressure (β -5.8, 95% CI: 3.7-8.0, p=0.0001) and systolic blood pressure (β -8.6, 95% CI: 5.4-11.9, p=0.0001) by stepwise multiple regression analysis in the diabetic patients. In the contrary, abdominal fat % (β -2.7, 95% CI: 0.9-4.5, p=0.006), duration of diabetes (β -2.5, 95% CI: 1.4-3.5, p=0.0001) and fat/ lean ratio (β -11.7, 95% CI: 1.5-21.9, p=0.03) were related to diastolic blood pressure.

Conclusion: Diabetes is associated with an increase in body fat especially abdominal, which leads to an increase in insulin resistance and decrease in lean mass. In type 1 diabetic patients, blood pressure depends on body mass index SDS and fat mass. Abdominal fat is the only factor related to mean arterial blood pressure and systolic blood pressure. (*Anadolu Kardiyol Derg 2012; 12: 60-4*)

Key words: Blood pressure, diabetes, body composition, regression analysis

ÖZET

Amaç: Tip 1 diyabetli hastalarda kan basıncına vücut yapısının ve kitle indeksinin etkisini tahmin etmektir.

Yöntemler: Bu kesitsel gözlemsel çalışmaya Tip 1 diyabetli 45 hasta, sağlıklı yaş ve cinsiyeti eşleştirilmiş, 30 gönüllü dahil edildi. Bütün hastalar ve kontroller için kan basıncı antropometrik ölçümler ve vücut bileşimi için de çift X-ray absorpsiyometri (DXA) yapıldı. İstatistiksel analiz için t-testi, tek yön ANOVA ve çoklu regresyon analizleri kullanıldı.

Bulgular: Yirmi diyabetli hastanın (%44.4) hipertansiyonu vardı. Hipertansif diyabetik hastalarda önemli derecede daha yüksek toplam yağ kitle-si yüzdesi, yumuşak doku yağ kütle yüzdesi, karın yağı yüzdeleri, yağlı/yağsız oranını hipertansif olmayanlar izledi, en azı da kontrollerde idi (p=0.0001). Diyabetli hastalarda çoklu regresyon analizi, abdominal yağ yüzdesinin, ortalama arteryel kan basıncı (β -5.8, %95 GA: 3.7-8.0, p=0.0001) ve sistolik kan basıncı (β -8.6, %95 GA: 5.4-11.9, p=0.0001) ile ilişkili tek parametre olduğunu gösterdi. Aksine, abdominal yağ oranı yüzdesi (β -2.7, %95 GA: 0.9-4.5, p=0.006), diyabetin süresi (β -2.5, %95 GA: 1.4-3.5, p=0.0001), yağlı/yağsız oranı (β -11.7, %95 GA: 1.5-21.9, p=0.03) diyastolik kan basıncı ile ilişkili idi.

Sonuç: Diyabet özellikle vücutta abdominal yağda artışa yol açar. Bu da insülin direncinin artmasına ve yağsız kitlenin azalmasına neden olur. Tip 1 diyabetli hastalarda kan basıncı vücut kitle indeksi, standart sapma puanına ve yağ kütlelerine bağlıdır. Abdominal yağ dokusu, ortalama arteryel ve sistolik kan basıncı ile ilgili tek faktördür. (*Anadolu Kardiyol Derg 2012; 12: 60-4*)

Anahtar kelimeler: Kan basıncı, diyabet, vücut yapısı, regresyon analizi

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Introduction

Hypertension and diabetes are the most common diseases that often occur together. High blood pressure, occurring in about half of diabetic patients, has a worse prognosis and is an important risk factor of their early death (1). Studies in type 1 children and adolescents have showed that the increase in blood pressure values can precede microalbuminuria and appreciated marker of diabetic renal disease (2).

Among healthy children, a significant positive correlation between body fat and blood pressure values was found (3-5). The fat tissue may influence by its pressor mechanisms such as hemodynamic disturbances, insulin resistance and hyperinsulinemia, activation of sympathetic system, sodium retention and biologically active adiposities products (6).

Body mass index is widely used as an indicator of overweight and obesity. However, it does not let to assess body composition (fat and lean mass). It could be gained with the use of bioimpedance (bioimpedance analysis-BIA) or dual energy X-ray absorptiometry (DEXA), a non-invasive, easy method that lets to assess body fat mass (7, 8). El Dayem et al. (9), reported that type 1 diabetic patients had a significant lower lean body mass and higher total fat mass, abdomen fat %, soft tissue fat mass % and fat / lean ratio compared to matched controls. No significant correlation was found between body composition and HbA1c or insulin dose.

There are relatively few studies about the impact of body fat on blood pressure values in type 1 diabetic patients in the developmental age.

We are aiming to estimate the influence of body composition and body mass index on blood pressure in type 1 diabetic patients.

Methods

Study design and patients

It is a cross sectional, observational study done after obtaining approval by the ethical committee of the National Research Centre. Written informed consent was obtained from all patients and their parents after full discussion about the whole procedures.

The study included 45 patients with type1 diabetes and 30 age and sex matched healthy control group.

All participants of the study were observed regularly at the diabetes outpatient clinic of the National Research Center.

Inclusion criteria: 1) First diagnosis of type 1 diabetes made before 18 years of age; 2) No evidence of diabetic retinopathy, neuropathy or nephropathy or any other chronic microangiopathic complication; 3) No intake of medications, hormones, vitamins or calcium preparation in the preceding 6 months aside from insulin and if necessary, thyroid hormones; 4) No chronic disease apart from celiac disease or thyroiditis under control; 5) No hospitalization or ketoacidosis in the preceding 6 months; 6) No restriction of physical activity; and 7) height of diabetic patients is more than-2 SDS.

Study protocol

Protocol determinations, all were carried out on the same day for patients and controls in the Diabetes and Endocrine Clinic, National Research Centre. It included: thorough history taking including age of patients, age at diagnosis and age of onset of diabetes and insulin regimen.

Assessment of blood pressure

Blood pressure was measured three times after 5-minute rest in the sitting position on both upper limbs with the use of automatic manometer (Omron M4 Plus, Omron Healthcare Europe, Hoofddorp, Holland). The mean value of the second and the third measurement was calculated. The measurements taken on the dominant limb were analyzed. Hypertension was considered if systolic (SBP) or diastolic (DBP) blood pressure were above the 95th percentile for age and gender in children (10).

Anthropometric measurements

Height was measured twice at the same time during the day and neared to the next millimeter using the Harpenden Stadiometer (Holtain, Ltd, Crymmych, Wales, U.K.) by the same observer. Patients' weight in decimal of kilograms using electronic balances was recorded and then plotted on the growth charts (11). Body mass index (BMI) (kg/m²) was calculated as the weight in kg divided by the height squared (m²). BMI were expressed in z scores. Child with BMI >85th - <95th percentile (corresponding to 1.03 z score) is considered as overweight, while child with BMI >95th percentile (corresponding to 1.6 z score) is considered as obese (12, 13).

All auxological data were expressed in standard deviation score (SDS). Where SDS=(Variable-Mean)/SD. The data were analyzed by the software program Growth Vision.2 provided by Novo-Nordisk, Denmark.

Assessment of puberty

Puberty was assessed by rating breast development in girls (14) and genital development in boys (15) and also pubic and axillary development for both.

The patients were subdivided according to puberty into prepubertal (n=17, 5 of them had delayed puberty) and pubertal (n=28) subgroups. On the other hand, 14 of the control group were prepubertal and the remaining 16 was pubertal.

Assessment of body composition

Lean body mass %, total fat mass %, soft tissue fat mass %, fat / lean ratio, abdomen fat % and trunk fat % were assessed by Dual energy X-ray absorptiometry (DEXA) (Norland-XR- 46, USA) were performed at the Medical Services' Centre, National Research Center.

Measurement of glycosylated hemoglobin

Diabetic control was monitored by measurements of hemoglobin A1c (HbA1c) levels at 3-months intervals. The HbA1c level was measured by DCA 2000 (Bayer AG, Leverkusen, Germany),

based on specific inhibition of latex immunoagglutination. An average HbA1c was calculated for each patient, and the mean of 4 measurements during the previous 12 months was taken.

Statistical analysis

Statistical Package for Social Sciences (SPSS) program version 12.0 (Chicago, Illinois, USA) was used for analysis of data. T- test for independent samples was used for analysis of quantitative data and non parametric (Mann-Whitney U) test was used, when data was not symmetrically distributed. Chi-square test was used for analysis of qualitative data. One-way ANOVA test was done for comparison of more than 2 groups followed by LSD post hoc test for comparison of 2 groups. Stepwise multiple regression analysis was also performed to find an association of SBP, DBP and mean arterial blood pressure (MBP) with demographic and body composition data which had p value ≤ 0.05 in simple Pearson's correlation analysis.

Results

Baseline characteristics

The study included 45 patients with type 1 diabetes, their mean age was 13.5 ± 3.1 years (8.0-18.0 years), mean age of onset of diabetes was 6.9 ± 3.6 years (1-13.3 years) and mean duration of diabetes was 6.3 ± 3.0 years (1-14 years), mean insulin dose/ kg was 1.4 ± 0.5 U/kg (0.5-2.7 U/kg), mean HbA1c was $8.8 \pm 2.1\%$ (6.0-13.0 %), mean SBP was 117.7 ± 18.0 mmHg (90.0-160.0 mmHg) and mean DBP was 79.8 ± 11.2 mmHg (60.0-100 mmHg). Height SDS of diabetic patients was -0.7 ± 1.0 (-2.0-1.3) and weight SDS was -0.04 ± 1.3 (-2.0-4.5).

According to classification of BMI, 15 (33.3%) patients had BMI $< 85^{\text{th}}$ percentile, 13 (28.9%) were overweight and the remaining 17 (37.8%) patients were obese.

Twenty diabetic patients (44.4%) had hypertension. Hypertension is significantly higher in obese children [11 patients (55 %)] followed by overweight [7 patients (35%)] and less in children with BMI $< 85^{\text{th}}$ percentile [2 patients (10%)] ($p=0.002$).

Body composition

Hypertensive diabetic patients had significantly the highest total fat mass %, soft tissue fat mass %, abdomen fat % and fat/lean ratio followed by the non hypertensive patients and the least was the controls ($p=0.0001$ for all) (Table 1). In addition, BMI SDS was significantly higher in hypertensive diabetic patients.

On the other hand, no significant difference was found in BMI and body composition assessed by DEXA in relation to puberty.

Relation between blood pressure and body composition

Abdominal fat % was the only parameter related to mean arterial blood pressure ($\beta=5.8$, 95% CI: 3.7-8.0, $p=0.0001$) and SBP ($\beta=8.6$, 95% CI: 5.4-11.9, $p=0.0001$) by stepwise multiple regression analysis in the diabetic patients (Tables 2, 3). In the contrary, abdominal fat % ($\beta=2.7$, 95% CI: 0.9-4.5, $p=0.006$), duration of diabetes ($\beta=2.5$, 95% CI: 1.4-3.5, $p=0.0001$) and fat/lean ratio ($\beta=11.7$, 95% CI: 1.5-21.9, $p=0.03$) were related to DBP (Table 4).

Table 1. Comparison between demographic data, body mass index, and body composition of hypertensive and non-hypertensive diabetic patients and controls

Variables	No hypertension (n=25)	Hypertension (n=20)	Controls (n=30)	t*/F**	p
Duration of disease, years	6.8±2.1	8.1±3.3	--	1.5	0.2
Age of onset of disease, years	6.8±4.0	8.1±3.1	---	-1.0	0.3
HbA1c, %	8.4±2.0	9.0±2.2	--	2.2	0.5
Insulin dose, U/kg	1.2±0.3	1.4±0.6	--	2.2	0.1
BMI, kg/m ²	20.1±3.1	25.0±7.4	--	0.9	0.009
BMI, SDS	0.8±0.8	2.1±1.0	--	4.9	0.0001
Total fat mass, %	34.6±8.7 ^a	43.7±4.1 ^b	22.5±5.6 ^c	35.0	0.0001
Fat / lean ratio	0.6±0.2 ^a	0.8±0.1 ^b	0.3±0.1 ^c	43.4	0.0001
Soft tissue fat, %	35.9±8.9 ^a	45.2±4.1 ^b	23.9±5.6 ^c	43.4	0.0001
Abdominal fat, %	16.9±2.5 ^a	18.8±1.4 ^b	13.0±5.1 ^c	14.4	0.0001
Trunk fat, %	24.1±4.4	25.6±3.5	21.6±8.3	2.2	0.1

Data are presented as mean±SD
*unpaired t test and **one way ANOVA test, LSD posthoc test: a, b, c (Different symbol means significance) - $p<0.05$ for comparison of two groups
BMI - body mass index, HbA1c - glycosylated hemoglobin, SD - standard deviation, SDS - standard deviation score

Table 2. Stepwise multiple regression analysis of mean arterial pressure in relation to demographic data, body mass index, and body composition of diabetic patients

Variables	β	95% Confidence interval	p
Constant	-5.9	-42.6-30.8	0.7
Abdominal fat percent	5.8	3.7-8.0	0.0001

R²= 0.76 SEM=8.0 R²: Coefficient of determination
SEM-standard error of mean Dependent variables: mean blood pressure Independent variables: duration of disease, BMI, total fat mass, fat / lean ratio, soft tissue fat and abdominal fat
BMI-body mass index

Table 3. Stepwise multiple regression analysis of systolic blood pressure in relation to demographic data, body mass index, and body composition of diabetic patients

Variables	β	95% Confidence interval	p
Constant	-28.7	-84.5-27.1	0.3
Abdominal fat percent	8.6	5.4-11.9	0.0001

R²= 0.75 SEM=12.1 R²: Coefficient of determination
SEM- standard error of mean Dependent variables: mean blood pressure Independent variables: duration of disease, BMI, total fat mass, fat / lean ratio, soft tissue fat and abdominal fat
BMI - body mass index

Discussion

Excessive total body mass along with an increased amount of fat mass are characteristic for overweight and obesity. Nowadays it is known that body fat is not only an energy stock but also a very active secreting organ. Fat tissue produces adi-

Table 4. Stepwise multiple regression analysis of diastolic blood pressure in relation to demographic data, body mass index, and body composition of diabetic patients

Variables	β	95% Confidence interval	p
Constant	9.1	-18.0-36.2	0.5
Abdominal fat percent	2.7	0.9-4.5	0.006
Duration of disease	2.5	1.4-3.5	0.0001
Fat/lean ratio	11.7	1.5-21.9	0.03

R²=0.76 SEM = 8.0 R²: Coefficient of determination
SEM- standard error of mean Dependent variable: Diastolic blood pressure Independent variables: duration of disease, HbA1c, BMI, total fat mass, fat / lean ratio, soft tissue fat and abdominal fat
BMI-body mass index, HbA1c-glycosylated hemoglobin

pokines most of which take part in the regulation of insulin sensitivity (16). Insulin resistance together with hyperglycemia, dyslipidemia and hypertension induces arteriosclerosis leading to develop cardiovascular disease.

In the current study, twenty diabetic patients (44.4%) had hypertension. Hypertension is significantly higher in obese children followed by overweight and less in children with BMI <85th percentile (p=0.002).

Overweight and obese children and adolescents had higher blood pressure values and, as proved in the literature, hypertension and prehypertension occurred among them more often in comparison with subjects with normal weight (3, 17-19). According to Guimaraes et al. (3) systolic and DBP were increased (>90 percentile) respectively in 46.5% and 42% obese boys and 39.3% and 44% obese girls. The increase in BMI for 1 unit caused 1.198 mmHg increase in SBP. McCarthy et al. (19) showed that more than a half of adolescents (11-14 years old) with hypertension or prehypertension is overweight.

In our study, 20 diabetic patients (44.4%) had hypertension. Hypertensive diabetic patients had significantly the highest total fat mass %, soft tissue fat mass %, abdomen fat % and fat/lean ratio followed by non hypertensive and the least was the controls (p=0.0001). In addition, DMI SDS was significantly higher in hypertensive diabetic patients.

Hypertension occurs in diabetic patients 2-3 times more often than in the general population. Higher blood pressure leads to diabetic macro- and microangiopathy. Type 1 diabetic children and adolescents have higher blood pressure values and they have hypertension or prehypertension more often in comparison with their healthy peers (20, 21). The relation of pathogenesis of diabetes and hypertension is still a subject of many researches.

Pietrzak et al. (22), reported a relation between BMI and body fat mass and blood pressure values in type 1 diabetic children and adolescents.

BMI is commonly accepted as easily available indicator of overweight and obesity. It is used as a relative body fat marker because the increase in body fat is accompanied by the increase in BMI. It should be remembered that BMI depends directly on body mass that consists of not only fat but also muscle mass. In children and adolescents proportion in fat and fat free mass

depends on sex and is changing with age and puberty phase (7, 23). In the current study no significant difference was found in BMI and body composition in relation to puberty.

In adolescents with normal BMI, the increase in fat mass was accompanied by SBP increase (4). Authors pointed out the need of simultaneous measurement of a few anthropometric parameters and use of other than BMI fat mass estimation. The cited studies prove their own observation showing coexistence of higher blood pressure values and excessive body mass, especially increased fat mass. More common overweight and hypertension occurrence in type 1 diabetic children and adolescents and adverse influence of fat mass and higher blood pressure on chronic diabetes complications should stimulate to perform studies concerning the pathogenetic relation between blood pressure and fat mass.

In our study, abdominal fat % was the only parameter independently associated with MBP and SBP by stepwise multiple regression analysis. In the contrary, abdominal fat %, duration of diabetes and fat/lean ratio were independent determinants of DBP.

Abdominal obesity is considered to be an indicator of insulin resistance, which is a risk factor of cardiovascular disease. In adults, the component of abdominal obesity, expressed as waist circumference, occurs in most metabolic syndrome definitions. However, there is no documented cut off points for the waist circumference in children (24).

According to all mentioned limitations, some authors consider waist/height Rate (WHtR) as a good indicator of abdominal obesity. Central obesity can be diagnosed if WHtR is higher than 0.5 and this value does not depend on age and sex (24).

Measurement of anthropometric indices of abdominal obesity seems to be important, as they could be easily available and cheap parameters evaluating the risk of cardiovascular disease. Savva et al. (25) and Bitsorri et al. (26), proved that waist circumference and WHtR are better than BMI in predicting cardiovascular disease. Brambilla et al. (27), reported that by estimating visceral fat mass in children and adolescents at the age of 7-17 years with the use of magnetic resonance, proved that waist circumference and WHtR can be much more sensitive than BMI in identification of children at risk of metabolic disorders development.

Study limitations

1. Dual-energy X-ray absorptiometry- DXA is a more technically advanced radiological method, but it is expensive, this is why we cannot do in a large number of patients.
2. Assessment of abdominal fat by waist and waist to hip ratio was not done in order to compare it with DEXA.
3. No cut off level of waist circumference is available for children and adolescence.

Conclusion

We conclude that, in type 1 diabetic children and adolescents, blood pressure values depend on BMI and fat mass. Abdominal fat is the only factor correlated to MBP and SBP.

As daily exercise is associated with substantial reductions in visceral adipose tissue and insulin resistance. Therefore, exercise should be promoted in type 1 diabetic patients.

Conflict of interest: None declared

Authors contributions: Concept - S.M.D; Design - A.A.B and S.M.D, Supervision - S.M.D and A.A.B; Material - S.M.D; Data collection &/or processing - S.M.D and A.A.B ; Analysis &/or interpretation - S.M.D; Literature search - S.M.D and A.A.B; Writing - S.M.D and A.A.B ; Critical review - A.A.B and S.M.D

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