Original article

The frequency of metabolic syndrome in patients with acrochordons

Kurtipek GS[1], Duran C[2], Kutlu O[3], Ataseven A[4], Akyürek FT[5], Kurku H[6], Elmas H[7]

Abstract:

Objective: To investigate the frequency of metabolic syndrome (MetS) in patients with acrochordons. ***Materials and Methods***: 102 patients with acrochordons and 76 controls were enrolled into the study. The presence of MetS was evaluated under the criteria NCEP-ATP III. ***Results and Discussion***: Waist circumference ($p<0.001$), body mass index ($p<0.001$), systolic ($p=0.014$) and diastolic blood pressure ($p<0.001$), insulin ($p<0.001$) and triglyceride (TG) levels ($p<0.001$) were higher in the group with acrochordons. The presence of MetS was found as 71.6% in patients with acrochordon and 40.8% in controls ($p<0.001$). ***Conclusions***: Patients with acrochordons should be evaluated in terms of the presence of MetS and its components.

Keywords: Skin tag; Acrochordon; Metabolic syndrome; Hypertension; Diabetes Mellitus.

Bangladesh Journal of Medical Science Vol. 16 No. 01 January'17. Page : 35-41

Introduction:

Also known as skin tags, acrochordons are the most common fibro-epithelial benign skin lesions and observed in the major flexor and natural folds surface of the body, such as neck, axillary and inguinal regions, and breast[1]. They may also be seen on the face and eyelids. The prevalence of acrochordons has been reported up to 46% in the general population. Acrochordons are more commonly seen in the obese and women, as well as rarely being witnessed in patients with polycystic ovary syndrome, acromegaly and Birt-Hogg-Bube syndrome[2]. Acrochordons are in the form of flesh colored to brown, soft, dermal papillomas-pedinculated lesions with smooth or irregular appearance[1]. Microscopically, a fibro-vascular core, sometimes with fat cells, covered by an unremarkable epidermis can be seen.

Metabolic syndrome (MetS), the most common endocrinopathy, is defined as the co-occurrence of metabolic risk factors in the development of both type 2 diabetes mellitus (DM) and coronary artery disease. Abdominal obesity, insulin resistance (IR), impaired glucose tolerance (IGT) or DM, dyslipidemia and hypertension are commonly seen in patients with MetS.[3] Several definitions have been described for MetS, and those defined by National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III)[4] and International

1. Gulcan Saylam Kurtipek, Department of Dermatology
2. Cevdet Duran, Division of Endocrinology and Internal Medicine
   Konya Health Application and Research Center, University of Health Sciences, Konya, Turkey
3. Orkide Kutlu, Okmeydani Training and Research Hospital, Department of Internal Medicine, Istanbul, Turkey
4. Arzu Ataseven, Necmettin Erbakan University, Meram Medical Faculty, Department of Dermatology, Konya, Turkey
5. Fatma Tuncez Akyürek, Selcuk University, Medical Faculty, Department of Dermatology, Konya, Turkey
6. Huseyin Kurku, Department of Biochemistry
7. Halis Elmas, Division of Endocrinology and Internal Medicine
   Konya Health Application and Research Center, University of Health Sciences, Konya, Turkey.

Correspondence to: Cevdet Duran, Assoc. Prof. The Division of Endocrinology and Internal Medicine, Konya Health Application and Research Center, University of Health Sciences, Meram Yeniyol, Meram, 42100, Konya, Turkey, e-Mail: drcduran@gmail.com

Diabetes Federation (IDF)[5] are commonly used. Insulin resistance is a major component of MetS. The presence of hyperinsulinemia and IR, insulin and insulin-like growth factors are known to induce the proliferation of keratinocytes and fibroblasts[6]. In diabetic patients with sign of IR, the frequencies of acrochordons and acanthosis nigricans were reported as 26.2% and 5%, respectively[7].

In many studies, conflicting results have been reported, as to the relationship among acrochordons, seborrheic keratosis, pseudoacanthosis nigricans, DM, IR and MetS,[8-12] and MetS components rather than the presence of MetS have been evaluated. As well as the limited number of literature including only two studies that investigated the presence of MetS in patients with acrochordons,[10, 13] we also aimed at evaluating the presence of MetS in patients with acrochordons under the criteria of NCEP-ATP III.

Materials and methods:

One hundred and two patients admitted to the department of dermatology in Konya Health Application and Research Center, University of Health Sciences between June 2013 and June 2014 with at least one complaint of acrochordons (skin tag) were enrolled into this prospective and controlled study. However, 76 age- and sex-matched individuals without acrochordons, lack of following exclusion criteria and admitted to the same clinic within the same time period constituted our control group in the study. While constituting the control group, BMI similarity between both groups was not evaluated because obesity and related diseases, such as hyperglycemia, dyslipidemia and hypertension are the main components of MetS.

Upon the approval by the Local Ethics Committee of Selcuk University, written informed consents were taken from all participants. Patients with pregnancy, malignancy of autoimmune diseases and under the age of 18 were excluded from the study. Age, gender, weight, height, waist circumference (WC), blood pressure, previous history of DM and hypertension, estimated detection time of acrochordons, and number and localization of acrochordons were measured and recorded in both groups. Height (m) and weight (kg) were measured with underwear. Waist circumference was measured as the minimum size between iliac crest and lateral costal margin. Body mass index (BMI) was calculated as weight (kg) divided by height square (m^2).

Blood pressure was measured by a mercury sphyngomanometer after resting for 10 min in both arms. After overnight fasting, blood samples were drawn at 08:00-09:00 am and centrifuged for 5 min at 3000 rpm. The sera were separated and stored at -80 °C until analysis. Glucose was measured using hexokinase method; high density lipoprotein (HDL)-cholesterol and triglycerides (TGs) were assessed with a routine enzymatic method using an auto analyzer by Abbott Architech C16000 (Abbott Laboratories, Abbott Park IL, US). Insulin levels were measured by Adviva Cetaur XP (Siemens Healthcare Diagnostics, Siemens AG, Germany) with chemiluminescence method. Insulin resistance was calculated by homeostasis model assessment-insulin resistance (HOMA-IR) [fasting plasma glucose (mmol/l) x fasting serum insulin (μIU/ml)/22.5]. Intra- and inter-assay coefficients of variations for insulin were 4.6 and 5.9, respectively. HOMA-IR levels were calculated in 78 patients with acrochordons and 67 controls whose insulin levels were measured and that were on no anti-diabetic medication.

As the determinants of MetS presence, the diagnosis of MetS was performed under the criteria of NCEP-ATP III[4] in accordance with the presence of three of the following five criteria: 1) fasting blood glucose levels ≥100 mg/dL or drug use for diabetes, 2) HDL-cholesterol <40 mg/dL in men, <50 mg/dL in women, or receiving lipid lowering treatment, 3) TG levels ≥150 mg/dL or receiving lipid lowering treatment, 4) WC ≥102 cm for men, ≥88 cm for women, and 5) blood pressure ≥130/85 mmHg or on antihypertensive drug treatment.

Statistical Analysis:

IBM SPSS statistical software was used for data analysis. Data normality was determined with the Shapiro-Wilk test. The descriptive statistics for variables with normal distribution, continuous data (mean±standard deviation), not normally distributed variables [median (minimum- maximum)], frequencies for categorical variables and percentage [n (%)] were indicated. The student's *t* and the Mann-Whitney U tests were used in the comparison of two independent samples for normally and abnormally distributed continuous data, respectively.

In the analysis of categorical data, the Pearson's chi-square test was used. As the significance, the threshold level was determined as α=0.05. Power analyses were made, and statistically significant values were indicated bold in the tables.

Results:

Socio-demographic and study characteristics of study population are given in Table 1.

Table 1: Socio-demographic and study characteristics of cases with acrochordons and controls.

		Patients (n=102)	Controls (n=76)	*p*
Age		50.93±11.32	47.99±10.07	0.074
Gender	Female n (%)	83 (81.4%)	64 (84.2%)	0.621
	Male n (%)	19 (18.6%)	12 (15.8%)	
DM history	No	73 (71.6%)	68 (89.5%)	0.004
	Yes	29 (28.4%)	8 (10.5%)	
Hypertension history	No	63 (61.8%)	63 (82.9%)	0.002
	Yes	39 (38.2%)	13 (17.1%)	
Weight (kg)		86.07±15.50	74.61±10.85	<0.001
Height (cm)		157 (144-180)	160 (145-170)	0.070
Waist circumference (cm)		107.67±12.09	95.95±10.35	<0.001
BMI (kg/m^2)		33.69 (24.74-53.96)	28.92 (19.56-41.08)	<0.001
Systolic blood pressure (mmHg)		129.31±22.96	121.34±16.86	0.019
Diastolic blood pressure (mmHg)		81.32±11.16	75.49±8.81	<0.001
Glucose (mg/dl)		117.35±51.64	103.58±29.04	0.090
HDL-Cholesterol (mg/dl)		46.94±11.00	49.43±12.06	0.177
Triglyceride (mg/dl)		201.00±157.67	137.20±80.35	<0.001
Insulin (μIU/ml)		12.61 (4.77-3.60) (n=74)	8.48 (1.47-36.31) (n=67)	<0.001
HOMA-IR		3.02 (1.10-3.52) (n=74)	1.90 (0.27-9.14) (n=67)	<0.001

Note: Values are expressed as mean ± standard deviation, median (minimum-maximum), or n (%). *DM: Diabetes Mellitus, BMI: Body-mass index, HDL-Cholesterol: High density lipoprotein-Cholesterol. HOMA-IR: Homeostasis model assessment-insulin resistance*

Nineteen (18.6%) out of 102 patients with acrochordons were male while controls consisted of 12 men (15.8%) and 64 women (84.2%), indicating no gender difference (p=0.621). The mean age rates of patients with acrochordons and of controls were 50.93±11.32 years and 47.99±10.07 years, (p=0.074), respectively. In patients with acrochordons and controls, 28 and 9 patients were treated with anti-diabetic medications, respectively. The mean duration of acrochordons was 10.94±9.86 months (min. 1, max. 46). The localizations of the acrochordons are shown in Table 2.

Table 2. Localization of acrochordons.

Localization	N (%)
Face	10 (9.8)
Neck	98 (96.1)
Axillae	31 (30.4)
Trunk	21 (20.6)
Under breast	7 (6.8)
Upper extremity	2 (1.9)
Lower extremity	0
Inguinale	5 (4.9)

As the most affected area, neck was determined (n=98) followed by axillary region (n=31), trunk (n=21) and face (n=10). The mean number of acrochordons was 15.04±15.04. Given the absence and presence of MetS components, the numbers of acrochordons were 9.88±4.82 vs 15.48±15.54 (p=0.473) according to WC criterion, respectively; 15.27±16.80 vs 14.80±13.21 (p=0.875) according to blood sugar criterion, respectively; 16.95±18.32 vs 13.81±12.49 (p=0.305) according to HDL-cholesterol criterion, respectively; 13.83±11.57 vs 16.35±18.10 (p=0.401) according to TG criterion, respectively; and, 14.64±16.99 vs 15.26±13.99 (p=0.844) according to blood pressure criterion, respectively. The mean numbers of acrochordons in nonobese (n=2), overweight (n=21) and obese (n=79) were 21.00±22.63, 11.48±12.00 and 15.84±15.64, (p=0.09), respectively.

Body weight (p<0.001), WC (p<0.001), BMI (p<0.001), levels of systolic (p<0.014) and diastolic blood pressure (p<0.001), TG (p<0.001), insulin (n=74) (p<0.001) and HOMA-IR levels (n=74) (p<0.001) were higher in patients with

acrochordons, compared to controls (Table 1). In patients group, BMI values of two patients (1.9%) were less than 25 kg/m^2, equal and/or higher than 25 kg/m^2 in 100 patients (98.1%) and equal and/or higher than 30 kg/m^2 in 79 patients (77.5%). Glucose and HDL-cholesterol levels were found similar in both groups (Table 1). Previous history of DM was higher in patients with acrochordons, compared to controls [29 (28.4%) vs 8 (%10.5) cases, p=0.004, respectively]. Similarly, the number of patients with previous history of hypertension was found to be higher among those with acrochordons, compared to controls [39 (38.2%) vs 13 (17.1%) cases, p=0.002, respectively]. The number and percentage of patients with acrochordons meeting NCEP-ATP III criteria are

HDL-Cholesterol: High density lipoprotein-Cholesterol, FBG: Fasting blood glucose, NCEP-ATP III: National Cholesterol Education Program-Adult Treatment Panel III. presented in Table 3.

Table 3: Presence of metabolic syndrome components under NCEP-ATP III criteria.

		Patients, n (%)	Controls, n (%)	*p*
Waist circumference ≥102 cm for men, ≥88 cm for women	No	8 (7.8)	21 (27.6)	<0.001
	Yes	94 (92.2)	55 (83.7)	
Triglyceride levels ≥150 mg/dL or on lipid lowering treatment	No	53 (52.0)	55 (72.4)	<0.001
	Yes	49 (48.0)	21 (27.6)	
HDL-Cholesterol <40 mg/dL in men, <50 mg/dL in women, or on lipid lowering treatment,	No	40 (39.2)	38 (50.0)	<0.001
	Yes	62 (60.8)	38 (50.0)	
Blood pressure ≥130/85 mmHg or on anti-hypertensive treatment	No	36 (35.3)	49 (64.5)	0.017
	Yes	66 (64.7)	27 (35.5)	
FBG levels ≥100 mg/dL or on anti-diabetic treatment	No	51 (50.0)	48 (63.2)	0.081
	Yes	51 (50.0)	28 (36.8)	
Presence of MetS under NCEP-ATP III	No	29 (28.4)	45 (59.2)	<0.001
	Yes	73 (71.6)	31 (40.8)	

The presence of MetS was higher in patients with acrochordons, compared to controls [73 (71.6%) vs 31 (40.8%), (p<0.001), respectively]. When also compared to controls, the number and percentage of patients with acrochordons meeting the blood pressure criterion of NCEP-ATP III were [66 (64.7%) vs 27 (35.5%), (p<0.001), respectively], as well as those meeting the TG criterion of NCEP-ATP III [49 (48.0%) vs 21 (27.6%), (p=0.006), respectively] and meeting the criterion WC of NCEP-ATP III [94 (92.2%) vs 55 (83.7%) (p<0.001), respectively]. Considering the remaining two criteria of NCEP-ATP III, including blood sugar and HDL-cholesterol, the number and percentage were found as similar.

Discussion

In the study, patients with acrochordons were determined to have higher levels of WC, body weight, BMI, systolic and diastolic blood pressure, TG, insulin and HOMA-IR. Moreover, the number of those with MS and its three components, WC, blood pressure and TG, was higher among patients.

Known as the primary and widespread causes of atherosclerosis and type 2 DM, MetS whose most common characteristics are abdominal obesity, elevated blood pressure, lipid disorders, hyperinsulinemia, IR and IGT is an increasing health challenge worldwide[3-5, 14]. Acrochordons are benign connective tissue tumors of the dermis and commonly seen in obese and insulin resistant patients. High insulin concentration has been shown to play a role in the development of acrochordons[15]. In keratinocytes and fibroblasts, insulin has a direct and/or indirect effect on growth factor receptors such as insulin-like growth factors 1 (IGF-1) and epidermal growth factor (EGF) receptors and induces their proliferation[16].

The association between acrochordons and DM was first described in 1951[17]. Since then, limited data targeting to investigate the relationship between acrochordons and the components of MetS have been published with conflicting results[8-13, 18]. In a study performed by Sudy et al.,[11] it was reported that eight or more acrochordons are related to basal and postprandial hyperinsulinemia and postprandial hyperglycemia, and that multiple acrochordons are

more sensitive, but less specific than acanthosis nigricans in the evaluation of glucose/insulin metabolism. In the study published by Tamega et al.,[12] it was also reported that acrochordons had been associated with HOMA-IR, TG, BMI, waist/hip ratio (WHR) and the presence of DM. In another study, Agarwal et al.[19] found that the frequencies of overt DM and IGT were, respectively, 30.5% and 10.1% in patients with acrochordons, and that there was no correlation between glucose intolerance and the localization, size, color, and number of acrochordons. As one of the limitations in our study, the size and color of acrochordons were not evaluated, as well as determining no correlation between the components of MetS and the number and localization of acrochordons (No data were presented). In another study performed by Akpinar et al.,[8] it was emphasized that DM is more frequently observed in patients with acrochordons, compared to controls. Although finding similar fasting plasma glucose levels in both patients and controls, Akpinar et al. determined higher postpradial glucose levels in patients, compared with controls. In addition, when they re-classified their patients as blood glucose ≥100 mg/dL and <100 mg/dL, patients with blood glucose levels ≥100 mg/dL were found to have more acrochordons, compared to those with blood glucose levels <100 mg/dL (9.87±2.93 vs 6.85±1.79, p=0.043, respectively). In the subgroup analysis, patients with DM were detected to have 22 more acrochordons mostly located under breast area. In a study performed to investigate the frequency of acrochordons by Margolis et al.[20] the frequency of acrochordons was determined as 47 in 500 outpatients. Of these 47 cases, 34 were diagnosed with DM, and it was determined that an increasing risk of developing DM is present at a higher rate in male patients with bilateral, hyperpigmented, large and multiple lesions. In a study with a smaller sample size and published by Erdogan et al.,[13] it was reported that patients with acrochordons have higher BMI and HOMA-IR levels while displaying similar fasting blood glucose levels and DM frequencies. Demir et al.[21] reported that the frequencies of overt DM and IGT were 73.3% and 5% in patients with acrochordons, respectively. In the study, Sari et al.[10] reported higher levels of glucose, insulin, HOMA-IR and HbA1c in patients with acrochordons. Bhargava et al. [18] also found the frequency of DM or IGT as 28% in patients with acrochordons and reported that multiple number of acrochordons (3 or more) and their sites are a significant risk factor for the development of DM. Although previous history of DM was more commonly seen in our patients with acrochordons, serum glucose levels and NCEP-ATP III blood sugar criterion were found to be similar in both groups. On the other hand, insulin levels, and as a consequence of higher insulin levels, HOMA-IR levels were found higher in patients with acrochordons. Although serum fasting glucose and the blood sugar criterion of NCEP-ATP III were similar, glucose metabolism in patients with acrochordons should be meticulously evaluated in terms of IR and previous history of DM.

Abdominal obesity plays a role in the development of MetS and is reported to precede other MetS components[22]. In our study, patients with acrochordons exhibited higher WC, body weight and BMI values than controls. Under NCEP ATP III criteria, the frequency of abdominal obesity in our acrochordon group was higher. Of patients with acrochordons, moreover, 98.1% and 77.5% were detected as overweight and obese, respectively. Only 1.9% of patients had normal BMI. Various studies suggest that abdominal obesity is more closely associated with IR,[3-5] and higher insulin levels could play a role in the development of acrochordons by stimulating IGF-1 and EGF receptors, as discussed earlier[16]. Acrochordons are more commonly observed in obese patients, and a positive correlation is present between acrochordons and the severity of obesity[1]. As consistent with the findings of previous studies, elevated insulin and HOMA-IR levels were determined in patients with acrochordons. In the study Akpinar et al.[8] reported that BMI values were higher in patients with acrochordons. However, they reported no WC values although the presence of MetS was evaluated. Likewise, Tanega et al.[12] reported acrochordons are associated with BMI and WHR. In their study, Sarı et al.[10] found higher levels of BMI and WC in patients with acrochordons, in line with the findings of the present study. Demir et al.[21] also found that 70.8% of patients with acrochordons were obese. Hence, it can be concluded that obesity, especially abdominal obesity, can contribute to the development of acrochordons.

Of our patients with acrochordons, 64.7% met the blood pressure criterion of NCEP ATP III and also were determined to have higher systolic and diastolic blood pressure. Likewise, Sari et al.[10] reported higher systolic and diastolic blood pressure in patients with acrochordons, along with a hypertension frequency of 30.1%. Similar results were reported by Akpinar et al.[8] In their study, Demir et al.[21] also reported that 65% of patients with acrochordons had hypertension.

Therefore, while patients with acrochordons were being evaluated, the presence of hypertension should be considered by health professionals in line with the findings of the present and previous studies.

In our study, serum TG levels were found to be higher in patients with acrochordons, compared to controls. Furthermore, the number of patients with TG ≥150 g/dL or treated with TG-lowering medicine, one of MetS criteria under NCEP ATP III, were higher among patients with acrochordons, compared with controls. On the other hand, levels of HDL-cholesterol and the number of patients meeting the HDL-cholesterol criterion of NCEP-ATP III were detected similar in both groups. In literature, various reports investigating the relationship between acrochordons and dyslipidemia are present. In different studies performed by, Tamega et al.,[12] Sari et al.[10] and Akpinar et al.,[8] it was reported that TG levels were elevated in patients with acrohordons. Other studies performed by Crook et al.,[23] Akpinar et al.[8] and Sari et al.[10] reported decreased HDL-cholesterol levels. In their studies, Gorpelioglu et al.[9] reported higher levels of total cholesterol and LDL-cholesterol while Erdogan et al.[13] reported higher total cholesterol levels in patients, compared with controls. The frequency of dyslipdemia was reported as 45.8%[21] and 59.3%[10] in patients with acrochordons. In the present study, no total and LDL-cholesterol levels were measured because of the fact that they are not included among NCEP-ATP III criteria. Therefore, only HDL-cholesterol and TG levels were measured in our study. No matter how similar HDL-cholesterol levels were found among our findings, we recommend that all patients with acrochordons be evaluated in terms of the presence of dyslipidemia, especially considering the existence of increased levels of TG .

In the present study, the frequency of MetS syndrome was higher in patients with acrochordon, compared to controls [73 patients (71.6%) vs 31 patients (40.8%), $p<0.001$, respectively]. To the best of our knowledge, only two studies evaluating the frequency of MetS in patients with acrochordons, in which Sari et al.[10] reported the frequency of MetS as 39.3% while Akpinar et al.[8] were reporting as 56.2%, are present in literature.

In conclusion, such features as WC, body weight, BMI, systolic and diastolic blood pressure, TG, insulin and HOMA-IR levels, frequency of MetS and its components, including NCEP-ATP III criteria related to WC, blood pressure and TG were determined to be increased in patients with acrochordons. Therefore, in the presence of acrochordons, we consider that patients should be evaluated as to the presence of MetS and accompanying components in order to prevent and treat MetS earlier.

Acknowledgements: This study was supported by Konya Training and Research Hospital's Research Fund, and the authors thanks Numan Duran for language editing.

Conflict of interest: Authors declare no conflict of interest.

Key message:

1. Metabolic syndrome and its componets, such as waist circumference, blood pressure, triglyceride, frequency increased in patients with acrochordons.
2. Patients with acrochordon should be evaluated in terms of the presence of metabolic syndrome and its components.

References:

1. Garcia Hidalgo L. Dermatological complications of obesity. *American journal of clinical dermatology*. 2002;**3**(7):497-506. PubMed PMID: 12180897. https://doi.org/10.2165/00128071-200203070-00006
2. Rasi A, Soltani-Arabshahi R, Shahbazi N. Skin tag as a cutaneous marker for impaired carbohydrate metabolism: a case-control study. *International journal of dermatology*. 2007 Nov;**46**(11):1155-9. PubMed PMID: 17988334. https://doi.org/10.1111/j.1365-4632.2007.03287.x
3. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. *Lancet*. 2005 Apr 16-22;**365**(9468):1415-28. PubMed PMID: 15836891. https://doi.org/10.1016/S0140-6736(05)66378-7

4. Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. *Circulation*. 2005 Oct 25;**112**(17):2735-52. PubMed PMID: 16157765. https://doi.org/10.1161/CIRCULATIONAHA.105.169404
5. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation*. 2009 Oct 20;**120**(16):1640-5. PubMed PMID: 19805654. https://doi.org/10.1161/CIRCULATIONAHA.109.192644
6. DeLapp NW, Dieckman DK. Effect of basic fibroblast growth factor (bFGF) and insulin-like growth factors type I (IGF-I) and type II (IGF-II) on adult human keratinocyte growth and fibronectin secretion. *The Journal of investigative dermatology.* 1990 Jun;**94**(6):777-80. PubMed PMID: 2192001. https://doi.org/10.1111/1523-1747.ep12874637
7. Ragunatha S, Anitha B, Inamadar AC, Palit A, Devarmani SS. Cutaneous disorders in 500 diabetic patients attending diabetic clinic. *Indian journal of dermatology*. 2011 Mar;**56**(2):160-4. PubMed PMID: 21716540. Pubmed Central PMCID: 3108514.
8. Akpinar F, Dervis E. Association between acrochordons and the components of metabolic syndrome. *European journal of dermatology : EJD*. 2012 Jan-Feb;**22**(1):106-10. PubMed PMID: 22063265.
9. Gorpelioglu C, Erdal E, Ardicoglu Y, Adam B, Sarifakioglu E. Serum leptin, atherogenic lipids and glucose levels in patients with skin tags. *Indian journal of dermatology*. 2009;**54**(1):20-2. PubMed PMID: 20049263. Pubmed Central PMCID: 2800864. https://doi.org/10.4103/0019-5154.48980
10. Sari R, Akman A, Alpsoy E, Balci MK. The metabolic profile in patients with skin tags. *Clinical and experimental medicine*. 2010 Sep;**10**(3):193-7. PubMed PMID: 20033751. https://doi.org/10.1007/s10238-009-0086-5
11. Sudy E, Urbina F, Maliqueo M, Sir T. Screening of glucose/insulin metabolic alterations in men with multiple skin tags on the neck. *Journal der Deutschen Dermatologischen Gesellschaft = Journal of the German Society of Dermatology : JDDG*. 2008 Oct;**6**(10):852-5, -6. PubMed PMID: 18397315.
12. Tamega Ade A, Aranha AM, Guiotoku MM, Miot LD, Miot HA. [Association between skin tags and insulin resistance]. *Anais brasileiros de dermatologia*. 2010 Jan-Feb;**85**(1):25-31. PubMed PMID: 20464083. Associacao entre acrocordons e resistencia a insulina. https://doi.org/10.1590/S0365-05962010000100003
13. Erdogan BS, Aktan S, Rota S, Ergin S, Evliyaoglu D. Skin tags and atherosclerotic risk factors. *The Journal of dermatology*. 2005 May;**32**(5):371-5. PubMed PMID: 16043900. https://doi.org/10.1111/j.1346-8138.2005.tb00909.x
14. Alberti KG, Zimmet P, Shaw J. Metabolic syndrome--a new world-wide definition. A Consensus Statement from the International Diabetes Federation. *Diabetic medicine : a journal of the British Diabetic Association*. 2006 May;**23**(5):469-80. PubMed PMID: 16681555.
15. Jowkar F, Fallahi A, Namazi MR. Is there any relation between serum insulin and insulin-like growth factor-I in non-diabetic patients with skin tag? *Journal of the European Academy of Dermatology and Venereology : JEADV.* 2010 Jan;**24**(1):73-4. PubMed PMID: 19453787. https://doi.org/10.1111/j.1468-3083.2009.03268.x
16. Dunaif A, Xia J, Book CB, Schenker E, Tang Z. Excessive insulin receptor serine phosphorylation in cultured fibroblasts and in skeletal muscle. A potential mechanism for insulin resistance in the polycystic ovary syndrome. *The Journal of clinical investigation.* 1995 Aug;**96**(2):801-10. PubMed PMID: 7635975. Pubmed Central PMCID: 185266. https://doi.org/10.1172/JCI118126
17. Touraine A. [A new hereditary chain; cutaneous fibromas, diabetes, obesity]. *Annales de dermatologie et de syphiligraphie.* 1951 Jul-Aug;**78**(4):409-16. PubMed PMID: 14857413. Une nouvelle chaine hereditaire: fibromes cutanes, diabete, obesite.
18. Bhargava P, Mathur SK, Mathur DK, Malpani S, Goel S, Agarwal US, et al. Acrochordon, diabetes and associations. *Indian journal of dermatology, venereology and leprology.* 1996 Jul-Aug;**62**(4):226-8. PubMed PMID: 20948060.
19. Agarwal JK, Nigam PK. Acrochordon: a cutaneous sign of carbohydrate intolerance. *The Australasian journal of dermatology.* 1987 Dec;**28**(3):132-3. PubMed PMID: 3504146. https://doi.org/10.1111/j.1440-0960.1987.tb00354.x
20. Margolis J, Margolis LS. Letter: A frequent sign of diabetes mellitus. *The New England journal of medicine.* 1976 May 20;**294**(21):1184. PubMed PMID: 1264123. https://doi.org/10.1056/NEJM197605202942121
21. Demir S, Demir Y. Acrochordon and impaired carbohydrate metabolism. *Acta diabetologica.* 2002 Jun;**39**(2):57-9. PubMed PMID: 12120914. https://doi.org/10.1007/s005920200014
22. Cameron AJ, Boyko EJ, Sicree RA, Zimmet PZ, Soderberg S, Alberti KG, et al. Central obesity as a precursor to the metabolic syndrome in the AusDiab study and Mauritius. *Obesity*. 2008 Dec;**16**(12):2707-16. PubMed PMID: 18820650. https://doi.org/10.1038/oby.2008.412
23. Crook MA. Skin tags and the atherogenic lipid profile. *Journal of clinical pathology.* 2000 Nov;**53**(11):873-4. PubMed PMID: 11127274. Pubmed Central PMCID: 1731117. https://doi.org/10.1136/jcp.53.11.873