



Paper Accepted\*

ISSN Online 2406-0895

Original Article / Оригинални рад

Funda Sari<sup>1,†</sup>, Ayca Inci<sup>2</sup>, Suleyman Dolu<sup>3</sup>, Ramazan Sari<sup>4</sup>

**Skin tags associated with obesity and diabetes mellitus in patients with chronic kidney disease**

Кожни полипи удружени са гојазношћу и шећерном болести код болесника са хроничном бубрежном болести

<sup>1</sup> Division of Nephrology, Department of Internal Medicine, Akdeniz University, Antalya, Turkey;

<sup>2</sup> Division of Nephrology, Department of Internal Medicine, Antalya Training and Research Hospital, Antalya, Turkey;

<sup>3</sup> Department of Internal Medicine, Antalya Training and Research Hospital, Antalya, Turkey;

<sup>4</sup> Division of Endocrinology, Department of Internal Medicine, Akdeniz University, Antalya, Turkey

Received: July 21, 2016

Accepted: August 1, 2017

Online First: August 8, 2017

DOI: <https://doi.org/10.2298/SARH160721158S>

\* **Accepted papers** are articles in press that have gone through due peer review process and have been accepted for publication by the Editorial Board of the *Serbian Archives of Medicine*. They have not yet been copy edited and/or formatted in the publication house style, and the text may be changed before the final publication.

Although accepted papers do not yet have all the accompanying bibliographic details available, they can already be cited using the year of online publication and the DOI, as follows: the author's last name and initial of the first name, article title, journal title, online first publication month and year, and the DOI; e.g.: Petrović P, Jovanović J. The title of the article. *Srp Arh Celok Lek*. Online First, February 2017.

When the final article is assigned to volumes/issues of the journal, the Article in Press version will be removed and the final version will appear in the associated published volumes/issues of the journal. The date the article was made available online first will be carried over.

† **Correspondence to:**

Funda Sari M.D.

Akdeniz University, School of Medicine, Division of Nephrology, Antalya, Turkey

E-mail: [fundasari@ymail.com](mailto:fundasari@ymail.com)

## Skin tags associated with obesity and diabetes mellitus in patients with chronic kidney disease

Кожни полипи удружени са гојазношћу и шећерном болести код болесника са хроничном бубрежном болести

### SUMMARY

**Introduction/Objective** Both chronic kidney disease and skin tags are associated with similar cardiovascular risk factors such as obesity, diabetes mellitus, dyslipidemia, hypertension etc.

**Objective** The aim of this study was to determine the prevalence of skin tags in patients with chronic kidney disease, and to assess the relationship between skin tags and cardiovascular risk factors such as diabetes, hypertension, dyslipidemia, obesity and metabolic syndrome.

**Methods** We evaluated 358 patients [149 (41.6%) female and 209 (58.1%) male; on predialytic 197 (55%) and dialytic 161 (45%)] with chronic kidney disease. All patients were examined for skin tags by the same clinician, and evaluated for body mass index, diabetes mellitus, hypertension, and dyslipidemia.

**Results** Skin tags were detected in 199 (55%) patients. Prevalence of skin tags was higher in male than female ( $p=0.041$ ), in diabetic patients than nondiabetic patients ( $p=0.013$ ). body mass index was higher in patients with skin tags when compared in patients without skin tags ( $p=0.047$ ). Skin tags prevalence were detected 48.3% in normal, 58% in overweight, 66% in obese patients ( $p=0.029$ ).

**Conclusion** We conclude that presence of skin tag is merely related to male gender, obesity and diabetes mellitus in patients with chronic kidney disease likely normal population.

**Keywords:** skin tags; obesity; diabetes mellitus; chronic kidney disease

### САЖЕТАК

**Увод/Циљ** Хронична болест бубрега и кожни полипи су повезани са кардиоваскуларним факторима ризика као што су гојазност, дијабетес мелитус, дислипидемија, хипертензија итд. Циљ рада је био да се утврди учесталост кожних полипа код болесника са хроничним бубрежним обољењем и да се процени однос кожних полипа и кардиоваскуларних фактора ризика као што су дијабетес, хипертензија, дислипидемија, гојазност и метаболички синдром.

**Метод** Испитано је 358 болесника: 149 (41,6%) жена и 209 (58,1%) мушкараца, и то предијализних 197 (55%) и на дијализи 161 (45%). Сви су испитивани од истог клиничара, а испитани су и индекс телесне масе, дијабетес мелитус, хипертензија и дислипидемија.

**Резултати** Кожни полипи су нађени код 199 (55%) болесника, чешће код мушкараца него жена ( $p=0.041$ ), код болесника са дијабетесом ( $p=0.013$ ). Индекс телесне масе био је већи код пацијената са кожним пилипима када се упореде код пацијената без ознака коже ( $p=0.047$ ). Учесталост кожних полипа је откривена код 48,3% болесника са нормалном, код 58% са прекомјерном тежином, а у 66% код гојазних ( $p=0,029$ ).

**Закључак** Присуство кожних полипа повезано је за мушки род, гојазност и дијабетес мелитус код болесника са хроничним бубрежним обољењем у односу на нормалну популацију.

**Кључне речи:** кожни полипи; гојазност; шећерна болест; хронично бубрежно обољење

### INTRODUCTION

Chronic kidney disease (CKD) is a growing health problem worldwide that leads to end-stage kidney failure and cardiovascular complications [1]. CKD is defined as kidney damage and/or decreased kidney function expressed as glomerular filtration rate (GFR) for at least 3 months, regardless of the cause. CKD is classified into five stages based on the severity of the disease [2, 3]. The overall prevalence of CKD is 15.7% in Turkey. In addition, the prevalence rates of dyslipidemia is 83.4%, hypertension is 56.3%, metabolic syndrome is 46%, obesity is 29.2% and diabetes mellitus is 26.6% in subjects with CKD in our country [4].

Skin tags are stalked or sessile papules which are the size of a pinhead or larger, with a colour ranging from native skin to dark brown. They have been reported with an incidence of 46% in the general population [5]. Although the aetiology is unknown; skin aging, obesity, diabetes mellitus, pregnancy, acromegaly and genetic predisposition are thought to be associated with skin tags [5-12].

There are some studies showing associations between skin tags and diabetes mellitus, impaired glucose tolerance, insulin resistance, and disorders of lipid metabolism [8,10-13]. In addition, skin tags is a one of the independent predictors of the occurrence of cardiac disease [14].

As mentioned above, both CKD and skin tags are associated with similar cardiovascular disease (CVD) risk factors such as obesity, diabetes mellitus, dyslipidemia, hypertension etc. Although there have been a few reports that the presence of skin tags is associated with diabetes mellitus, hypertension, obesity and atherogenic lipid profile [5,8,10-13,15], no data in the literature show that the presence of skin tags in patients with CKD.

The aim of this study was to determine the prevalence of skin tags in patients with CKD, and to assess the relationship between skin tags and the other cardiovascular risk factors such as diabetes, hypertension, dyslipidemia, obesity and metabolic syndrome.

## METHODS

We evaluated 358 patients [149 (41.6%) female and 209 (58.1%) male; on predialytic 197 (55%) and dialytic 161 (45%)] with CKD. All patients were examined by the same physician. Information on smoking habits were recorded.

All patients were evaluated for blood pressure, body mass index, creatinine, lipids, glucose, HbA<sub>1c</sub>. Samples for plasma glucose, creatinine, HbA<sub>1c</sub> and lipids level determinations were taken at morning after at least 8-hour fast. Fasting glucose levels were measured by enzymatic colorimetric assay method (GLU, Roche Diagnostics GmbH, Mannheim, Germany). Fasting cholesterol and triglyceride levels were measured by enzymatic colorimetric assay method (Roche Diagnostics GmbH, Mannheim, Germany). Glycated hemoglobin (HbA<sub>1c</sub>) was measured by "Turbidimetric inhibition immunoassay (TINIA) method (HBAIC II, Roche Diagnostics GmbH, Mannheim, Germany).

CKD was defined as kidney damage with or without a decrease in GFR, which was calculated using a simplified version of the Modification of Diet in renal Disease (MDRD) formula [ $186 \times (S_{cr})^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if women})$ ] [16].

Height and weight were measured by the same person with the subjects wearing light clothing but not shoes. Body mass index (BMI) was calculated as weight in kilograms divided by the square of the height in meters. Overweight was defined as a BMI 25–30 kg/m<sup>2</sup>, and obesity was defined as a BMI of 30 kg/m<sup>2</sup>.

All blood pressure measurements were made with calibrated mercury manometers (Riester, Germany) in the right arm with the patient in a sitting position after a rest of 5 minutes. Hypertension was defined as a systolic/diastolic blood pressure of 140/90 mmHg or higher, and/or a current antihypertensive treatment.

Dyslipidemia was defined in presence of at least one of the following conditions; raised serum triglycerides (>200 mg/dl), total cholesterol (>200 mg/dl), LDL-cholesterol (>100 mg/dl), low HDL-cholesterol (<35 mg/dl for men and <45 mg/dl for women), and/or a current antilipidemic treatment.

Diabetes mellitus was defined in presence of at least one of the following conditions; raised fasting plasma glucose level ( $\geq 126$  mg/dl), plasma glucose level after 2 hours of oral glucose tolerance test ( $\geq 200$  mg/dl), HbA1c ( $\geq 6.5\%$ ), and/or a current hypoglycemic treatment.

### Statistical Analysis

Statistical analysis was done by SPSS statistical software (SPSS 10.0 for Windows, standard version). The results were presented as mean  $\pm$  SD. Continuous variables were tested for normality according to the Kolmogorov-Smirnov test. Univariate analysis of variance and Mann-Whitney U tests were performed to compare the groups. For comparing categorical data, Chi-square ( $\chi^2$ ) test was performed. The correlation analysis was done using Spearman's test. A p value of  $<0.05$  was considered statistically significant.

### RESULTS

Age was  $61.7 \pm 32.4$  years, GFR was  $38.6 \pm 20.0$ , CKD duration was  $5.0 \pm 1.57$  years, BMI was  $27.7 \pm 6.9$  kg/m<sup>2</sup>. Total 31.1% of patients were normal, 34.2% of patients were overweight, 34.7% of patient were obese.

**Table 1. Prevalence of skin tags in patients.**

		Skin tags		p value
		Present (%)	Absent (%)	
<b>Gender</b>	Male	60	40	0.041
	Female	49	51	
<b>Body mass index</b>	Normal	48.3	51.7	0.029
	Overweight	58	42	
	Obese	66	34	
<b>Diabetes mellitus</b>	Present	66	34	0.013
	Absent	52.5	47.5	
<b>Hypertension</b>	Present	58.3	41.7	0.18
	Absent	51	49	
<b>Dyslipidemia</b>	Present	62	38	0.099
	Absent	54	46	
<b>Dialysis treatment</b>	Present	59.4	40.6	0.061
	Absent	50.1	49.9	
<b>Proteinuria</b>	Present	58.9	41.1	0.49
	Absent	60	40	
<b>Cardiovascular disease</b>	Present	57.4	42.6	0.51
	Absent	56.8	43.2	

Skin tags were detected in 199 (55%) patients. Total 143 (40%) patients were diabetic, 268 (75%) were hypertensive, 143 (40%) were dyslipidemic. Prevalence of skin tags was higher in male than female ( $p=0.041$ ), in diabetic patients than nondiabetic patients ( $p=0.013$ ) (Table 1). BMI was higher in patients with skin tags when compared in patients without skin tags ( $p=0.047$ ). Skin tags prevalence were detected 48.3% in normal, 58% in overweight, 66% in obese

**Table 2. Comparison of parameters in patients with and without skin tags.**

	Skin tags		p value
	Present	Absent	
Age (years)	62,2 $\pm$ 13,0	61,3 $\pm$ 16,4	0.79
Body mass index (kg/m <sup>2</sup> )	28,3 $\pm$ 5,58	26,8 $\pm$ 8,3	0.047
Glomerular filtration rate (mL/min/1.73 m <sup>2</sup> )	37,1 $\pm$ 19,1	41,1 $\pm$ 21,2	0.17
Duration of chronic kidney disease (years)	5,0 $\pm$ 1,5	5,0 $\pm$ 1,6	0.82

patients ( $p=0.029$ ) (Table 2).

## DISCUSSION

Skin tags, which appear to be associated with some endocrine diseases, are skin growths histologically characterized by a papillomatous acanthotic pattern in the epidermis [17]. Recent studies suggest an association between skin tags and type 2 diabetes mellitus, glucose intolerance, obesity, insulin resistance atherogenic lipid profile and cardiovascular disease [5,7-13]. On the other hand, CKD is a growing health problem worldwide that leads to end-stage kidney failure and cardiovascular complications and/or risk factors [1].

As mentioned above, both CKD and skin tags are associated with similar CVD risk factors such as obesity, diabetes mellitus, dyslipidemia, hypertension etc. Although there have been a few reports that the presence of skin tags is associated with diabetes mellitus, hypertension, obesity and atherogenic lipid profile [5,8,10-13,15], no data in the literature show that the presence of skin tags in patients with CKD. The main purpose of this study was to determine the prevalence of skin tags in patients with CKD, and to assess the relationship between skin tags and the other cardiovascular risk factors such as diabetes, hypertension, dyslipidemia, obesity and metabolic syndrome.

Skin tags have been reported with an incidence of 46% in the general population [5]. Skin tags were detected in 55% in our patients. Duration of CKD and GFR were not different in patients with and without skin tags. In this connection, our result suggest that the prevalence of skin tags was not increased in patients with CKD.

Recent studies suggest an association between skin tags and obesity. It has been reported that patients who have insulin resistance may develop acanthosis nigricans and skin tags with increasing incidence as BMI rises [7, 8, 12]. In addition to frequent skin irritation that occurs in obese patients, hormonal factors (oestrogen levels and position peripheral aromatization androgens to the oestrogens), and aging of the skin is also thought to be contributing to the development of skin tags [6, 18-20]. The prevalence of obesity is 29.2% in patients with CKD [4]. Obesity prevalence was found 34.7% in our study population. We found higher BMI in patients with skin tags when compared without skin tags. In addition, skin tags prevalence was gradual increment in overweight and obese patients. Our findings suggest that the relationship between obesity and skin tags in CKD patients, similarly normal population.

There have been a few reports that the presence of skin tags is associated with diabetes mellitus and insulin resistance [5,8,10-13]. The prevalence rates of diabetes mellitus is 26.6% in subjects with CKD in our country [4]. Total 40% of patients were diabetic in our study. We also detected high prevalence of skin tags in CKD patients with diabetes mellitus likely normal population.

The prevalence rates of hypertension is 56.3% in subjects with CKD in our country [4]. Total 75% of patients were hypertensive in our study. On the other hand, we detected numerical but not statistical increased prevalence of skin tags in patients with hypertension. The reason for this result may be associated with development hypertension depend on CKD but not etiologic cause of CKD.

There are reports describing an association between skin tags and an atherogenic lipid profile [11, 12, 21]. This lipid profile is thought to be strongly associated with atherosclerosis, cardiovascular disease and macroangiopathic diabetic complications. Crook looked at the association between cardiovascular disease and skin tags in a small cohort study of 4 patients with the atherogenic lipid profile [11]. The prevalence rates of dyslipidemia is 83.4% in subjects with CKD in our country [4]. Total 40% of patients were dyslipidemic in our study. We detected numerical but not statistical increased prevalence of skin tags in patients with dyslipidemia. Prevalence of skin tags were similar in patients with and without cardiovascular disease. We speculate that increased of cardiovascular disease risk is not associated with skin tags in patients with CKD.

## CONCLUSION

We conclude that presence of skin tag is merely related to male gender, obesity and diabetes mellitus in patients with CKD likely normal population. Further studies with large patient population are required to elucidate the association between the presence of skin tag and cardiovascular disease in patients with CKD.

## REFERENCES

1. Sarnak MJ, Levey AS, Schoolwerth AC, Coresh J, Culleton B, Hamm LL, et al; American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. Kidney disease as a risk factor for development of cardiovascular disease: a statement from the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. *Hypertension*. 2003; 42(5): 1050–65.
2. Levey AS, Eckardt KU, Tsukamoto Y, Levin A, Coresh J, Rossert J, et al. Definition and classification of chronic kidney disease: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). *Kidney Int*. 2005; 67(6): 2089–100.
3. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis*. 2002; 39(2 Suppl 1): S1–266.
4. Süleymanlar G, Utaş C, Arınoy T, Ateş K, Altun B, Altıparmak MR, Eçder T, Yılmaz ME, Çamsarı T, Başçı A, Odabas AR, Serdengeçti K. A population-based survey of Chronic RENal Disease In Turkey--the CREDIT study. *Nephrol Dial Transplant*. 2011; 26(6): 1862–71.
5. Banik R, Lubach D. Skin tags: localization and frequencies according to sex and age. *Dermatologica* 1987; 174(4): 180–3.
6. 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? *J Eur Acad Dermatol Venereol*. 2010; 24(1): 73–4.
7. Garcia Hidalgo L. Dermatological complications of obesity. *Am J Clin Dermatol*. 2002; 3(7): 497–506.
8. Mathur SK, Bhargava P. Insulin resistance and skin tags. *Dermatology*. 1997; 195(2): 184.
9. Agarwal JK, Nigam PK. Acrochordon: a cutaneous sign of carbohydrate intolerance. *Australas J Dermatol*. 1987; 28(3): 132–3.
10. Kahana M, Grossman E, Feinstein A, Ronnen M, Cohen M, Millet MS. Skin tags: a cutaneous marker for diabetes mellitus. *Acta Derm Venereol*. 1987; 67(2): 175–7.
11. Crook MA. Skin tags and the atherogenic lipid profile. *J Clin Pathol* 2000; 53: 873–4.
12. Sari R, Akman A, Alpsoy E, Balci MK. The metabolic profile in patients with skin tags. *Clin Exp Med*. 2010; 10: 193–7.
13. Rasi A, Soltani-Arabshahi R, Shahbazi N. Skin tag as a cutaneous marker for impaired carbohydrate metabolism: A case-control study. *Int J Dermatol*. 2007; 46(11): 1155–9.
14. El Safoury OS, Ezzat M, Abdelhamid MF, Shoukry N, Badawy E. The Evaluation of the Impact of Age, Skin Tags, Metabolic Syndrome, Body Mass Index, and Smoking on Homocysteine, Endothelin-1, High-sensitive C-reactive Protein, and on the Heart. *Indian J Dermatol*. 2013; 58(4): 326.

15. Deedwania PC. Diabetes is a vascular disease: the role of endothelial dysfunction in pathophysiology of cardiovascular disease in diabetes. *Cardiol Clin*. 2004; 22(4): 505–9.
16. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med*. 1999; 130(6): 461–70.
17. Habif TP. Benign skin tumours. In: *Clinical Dermatology* (5th ed). Toronto: Mosby; 2010: 784.
18. Sudy E, Urbina F, Maliqueo M, Sir T. Screening of glucose/insulin metabolic alterations in men with multiple skin tags on the neck. *J Dtsch Dermatol Ges* 2008; 6(10): 852–5.
19. Hermanns-Lê T, Scheen A, Piérard GE. Acanthosis nigricans associated with insulin resistance: pathophysiology and management. *Am J Clin Dermatol*. 2004; 5(3): 199–203.
20. El Safoury O, Rashid L, Ibrahim M. A study of androgen and estrogen receptors alpha, beta in skin tags. *Indian J Dermatol*. 2010; 55(1): 20–4.
21. Twomey P. Skin tags and the atherogenic lipid profile. *J Clin Pathol*. 2002; 55(8): 639.

Paper accepted