TJFM&PC Turkish Journal of Family Medicine and Primary Care

Original Research / Özgün Araştırma

A New Comorbidity Accompanying Obesity: Renal Angiomyolipoma

Obeziteye Eşlik Eden Yeni Bir Komorbidite: Renal Anjiyomiyolipom

Aysima Bulca Acar[*1]*, Remziye Nur Eke*[1]

ABSTRACT

Objective: Obesity is an important health concern all around the world and considered in relation to a number of comorbidities. In this study, we aimed to evaluate the incidence of renal angiomyolipoma (AML) in obese patients. **Method:** This retrospective study included 288 obese patients, who were followed up at the Obesity Center of the University of Health Sciences, Antalya Training and Research Hospital between 01/11/2018 and 01/02/2020. The laboratory parameters and the reports of the abdominal ultrasound scans (USG) taken when the patients first presented to our unit were all reviewed. The patients were divided into two groups: those with and without renal AML based on the abdominal USG reports, and were compared in terms of serum hemoglobin (HGB), hematocrit (HCT), mean corpuscular volume (MCV), erythrocyte count (RBC), blood urea nitrogen (BUN), creatinine and uric acid levels. **Results:** Of the patients, 93.05% were female and 6.94% were male. The mean age was 51.91±9.31 (21-73) years, the average body mass index (BMI) was 36.4 (30-65.19) kg/m^2. Ten patients (3.47%) had renal AML found on the abdominal USG imaging reports. While the incidence of renal AML in the general population is reported to be 0.13%-0.44%, it was found 3.47% in our study with obese patients. **Conclusion:**The incidence of renal AML is increasing in obese patients. Associated with many comorbidities, obesity may also constitute a risk factor for renal AML. In order to determine the relationship between obesity and AML, more studies are needed with multi-centered and broader scopes.

Key words: Angiomyolipoma, obesity, prevalence

ÖZET

Amaç: Obezite bütün dünya için önemli bir sağlık sorunudur ve birçok komorbidite ile ilişkili olarak değerlendirilmektedir. Bu çalışmada; obez hastalarda renal anjiomyolipom (AML) görülme sıklığının değerlendirilmesi amaçlanmıştır. **Yöntem:** Retrospektif çalışmaya 01/11/2018 ile 01/02/2020 tarihleri arasında Sağlık Bilimleri Üniversitesi Antalya Hastanesi Obezite Merkezinde takipli 288 obez hasta dahil edildi. Hastaların birimimize ilk başvuruları esnasında istenmiş olan abdomen ultrasonografi (USG) raporları ile laboratuvar parametreleri tarandı. Hastalar abdomen USG raporlarında renal AML olan ve olmayan şeklinde iki gruba ayrılarak serum hemoglobin (HGB), hematokrit (HCT), ortalama eritrosit hacmi (MCV), eritrosit sayısı (RBC), kan üre azotu (BUN), kreatinin ve ürik asit düzeyleri açısından karşılaştırıldı. **Bulgular:** Hastaların %93,05'i kadın, %6,94'ü erkekti. Ortalama yaş 51,91±9,31 (21-73) yıl, ortalama vücut kitle indeksi (VKİ) 36,4 (30-65,19) kg/m^2 idi. On hastanın (%3,47) abdomen USG raporunda renal AML vardı. Genel popülasyonda %0,13-% 0,44 olarak bildirilen renal AML insidansı, obez hastalarla yaptığımız bu çalışmada %3,47 olarak bulundu. **Sonuç:** Obez hastalarda renal AML görülme sıklığı artmaktadır. Birçok komorbidite ile ilişkili olan obezite durumu, renal AML için de bir risk faktörü olabilir. Obezite ile AML arasındaki ilişkiyi saptamaya yönelik çok merkezli, daha geniş kapsamlı çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Anjiomyolipom, obezite, prevelans

Received / Geliş tarihi: 28.09.2020, **Accepted / Kabul tarihi:** 18.12.2020

[1] University Of Health Sciences Antalya Training and Research Hospital, The Clinic Of Family Medicine Antalya-TURKEY.
***Address for Correspondence / Yazışma Adresi:** Aysima Bulca Acar, University Of Health Sciences Antalya Training and Research Hospital, The Clinic Of Family Medicine Antalya-TURKEY.
E-mail: aysimabulca@gmail.com

Bulca Acar A, Eke RN. A New Comorbidity Accompanying Obesity: Renal Angiomyolipoma. TJFMPC, 2021;15(1): 136-141.

DOI: 10.21763/tjfmpc.800756

INTRODUCTION

Accepted as a complex and multifactorial disease, adversely affecting the well-being of people, obesity is the most preventable cause of mortality worldwide.[1] The two continents with the highest worldwide prevalence of excess weight and obesity were America and Europe, while the two countries were the United States and Turkey, respectively, for the year 2015.[2]

The prevalence of obesity in the adult population in Turkey has already exceeded the critically high rate of 30%. Although the incidence of obesity is higher in women, there has also been a rapid increase in men in recent years.[3]

Obesity is associated with many medical conditions such as type 2 diabetes, dyslipidemia, hypertension, heart attack, stroke, non-alcoholic fatty liver, obstructive sleep-apnea syndrome, hypoventilation syndrome, osteoarthritis, polycystic ovary syndrome, gout disease, gastroesophageal reflux, and cholelithiasis.[4]

There are also a number of studies showing that severe obesity (BMI≥35 kg/m2) increases the need for intensive care in patients with COVID-19, which is a current issue.[5]

Obesity has also been identified as an independent risk factor for many types of cancers. There are studies showing that approximately 40% of all cancers are associated with overweight and obesity.[6] Obesity is known to be associated with breast, endometrium and colon cancer.[7] In 2018, the World Cancer Research Fund/the American Institute for Cancer Research (WCRF/AICR) reported that obesity is also associated with esophagus, liver, pancreas, gallbladder, ovarian, thyroid, kidney cancers and multiple myeloma.[8]

Considered as a benign tumor of mesenchymal origin, AML consists of different amounts of adipose tissues, abnormal blood vessels, as well as smooth muscle tissues. It is generally observed in people in the fourth decade of life, in women at 0.2% and in men at 0.1%. Of all the cases, 80% are sporadic and solitary. AML is mostly seen in kidneys. Renal AML can be seen as isolated or may be associated with tuberous sclerosis[9]. Yet, 80% of all the cases are isolated. While isolated cases are usually single, large and asymptomatic, the type that is associated with tuberous sclerosis is multiple, bilateral, small and frequently bleeding.[10] AML may show a clinical course ranging from a randomly detected small size kidney mass to life-threatening retroperitoneal bleeding. Most patients are the cases that are incidentally detected. Although the majority of AMLs have benign character, a small number of them have a very aggressive behavior pattern, causing local invasion. Symptoms develop in approximately 80% of masses larger than 4 cm, hemorrhage occurs in approximately 60%, and hypovolemic shock develops in 1 of every 3 patients with hemorrhage.[11]

This study aimed to investigate the ratio of the prevalence of renal AML in obese patients compared to the general population.

MATERIALS AND METHODS

Study Groups

The cohort of this retrospective study was 288 obese patients aged 21-73, who were treated between 01/11/2018 and 01/02/2020 at the Obesity Center of the University of Health Sciences, Antalya Training and Research Hospital.

The patients' weight, height, waist, waist circumference (WC), hip circumference (HC), and blood pressure (BP) were measured and recorded on data collection forms together with their demographic characteristics. Tanita MC 580 device was used for weight measurement. The BMI was calculated by the formula of BMI=weight (kg)/height (m^2). The levels of HGB (mg/dL), HCT (%), MCV (fL), RBC (10^6/uL), BUN (mg/dL), creatinine (mg/dL), and uric acid (mg/dL) were checked in blood samples taken after twelve hours of fasting. All anthropometric measurements were made with the same measurement tools and analyses were performed in the same laboratory. Hemogram parameters were analyzed using the Beckman Coulter LH780 hematology autoanalyzer. Serum BUN, creatinine and uric acid levels were measured with the spectrophotometric method in Beckham Coulter AU 5800 autoanalyzer in addition to Beckham Coulter (Beckman Coulter Diagnostics, Brea, CA) commercial kits. We examined the reports of the abdominal USG tests ordered at the initial admission of patients to the obesity center and recorded the patients who were evaluated as having renal AML. According to the abdominal USG reports, the patients in the study were divided into two groups, those with and without renal AML, and compared with one another in terms of study parameters.

Prior to the start, the study was approved by the Clinical Research Ethics Committee of the University of Health Sciences, Antalya with the Decision No 3/11, dated February 13, 2020. The study was conducted in accordance with the Helsinki Declaration.

Statistical Evaluation of Data

The data obtained in the study were analyzed with IBM SPSS 23.0 package program (IBM Corp., Armonk, NY). Descriptive statistics were presented as n (%) and mean ± standard deviation and median (min-max) values. Fisher's Exact test was used to analyze the relationships between categorical variables. Normality was analyzed with the Shapiro Wilks test. The difference between the measurement values of the two groups was analyzed with the Mann-Whitney U test when it did not fit the normal distribution and with the Student's t test when it did. The p values less than 0.05 were considered statistically significant.

RESULTS

The study involved 288 obese patients with a mean age of 51.91±9.31 (21-73) years. Of all the patients 93.05% (n=268) were female, while 6.94% (n=20) were male. The average BMI value was 36.4 kg/m2 (30-65.19). Table 1 presents the demographic, clinical and laboratory features of the patients.

Table 1. Comparison of demographic characteristics and anthropometric measurements of patients with and without renal AML.

	Total (n: 288)	**Patients without renal AML (n: 278)**	**Patients with renal AML (n: 10)**	**p value**
Age	51.91 ± 9.31 (21-73)	52.5 (21-73)	48.5 (40-67)	0.104[1]
Gender (Male)	20 (6.9)	20 (7.2)	0 (0)	0.999[2]
Smoking				
No	218 (75.7)	208 (74.8)	10 (100)	0.325[2]
Yes	32 (11,1)	32 (11,5)	0 (0)	
Quit	38 (13.2)	38 (13.7)	0 (0)	
Weight (kg)	92.7 (68.5-152.6)	92.6 (68.5-152.6)	96.25 (80.3-142)	0.395[1]
Height (cm)	163.6 ± 82.4 (138-153)	158.69 ± 6.83 (138-179)	160 ± 4.88 (154-169)	0.549[3]
BMI (kg/m2)	36.4 (30-65.19)	36.4 (30-65.19)	38.35 (30.3-49.5)	0.483[1]
Waist Circumference (cm)	109 (84-189)	109 (84-189)	107.5 (92-135)	0.882[1]
Hip Circumference (cm)	117 (97-182)	117 (97-182)	123 (110-155)	0.093[1]
SBP (mmHg)	120 (80-180)	120 (80-180)	120 (100-140)	0.867[1]
DBP (mmHg)	80 (60-130)	80 (60-130)	80 (70-90)	0.872[1]

The results are presented with n (%), mean±SS (min-max) or median (min-max) values. [1]Mann-Whitney U test, [2]Fisher's Exact test, and [3]Student's t test. (SBP: Systolic blood pressure DBP: Diastolic blood pressure)

The patients were divided into two groups based on the presence and absence of renal AML. When the two groups were compared in terms of the levels of HGB, HCT, MCV, RBC, BUN, creatinine and uric acid, the levels of HGB and HCT were statistically significantly lower in the group with renal AML with the values of p=0.020 and p=0.035, respectively, while the levels of MCV, RBC, creatinine and uric acid showed no significant relationship. Similar values were observed in both groups when the BMI average of the patients were compared. The mean BP value of the patients was 120/80 mmHg, indicating similar results in both groups. Ten patients with renal AML were non-smokers. Table 2 shows detailed information on the comparison of patients with and without renal AML in terms of the study parameters.

Table 2. The comparison of laboratory findings of patients with and without renal AML.				
	Total (n:288)	**Patients without renal AML (n: 278)**	**Patients with renal AML (n: 10)**	**p value**
Uric Acid (mg/dL)	5.5 (2.8-10.3)	5.5 (2.8-10.3)	5.45 (4.3-6.7)	0.821[1]
BUN (mg/dL)	12 (5-29)	12 (5-29)	11.5 (7-17)	0.695[1]
Creatinine (mg/dL)	0.83 (0.53-2.26)	0.83 (0.53-2.26)	0.76 (0.67-1.28)	0.358[1]
HGB (mg/dL)	13.31±1.16 (9.5-17.2)	13.34±1.15 (9.5-17.2)	12.48±1.23 (10.7-14.8)	**0.020[2]**
HCT (%)	39.86±3.15 (30.8-51.2)	39.94±3.12 (30.8-51.2)	37.8±3.26 (33.2-44)	**0.035[2]**
MCV (fL)	84.5 (41.3-99)	84.55 (41.3-99)	82.6 (60.2-86.9)	0.136[1]
RBC (10^6/uL)	4.71 (3.4-6.4)	4.74 (3.4-6.4)	4.55 (4.4-5.7)	0.945[1]

The results are presented with mean ± SD (min-max), median (min-max) values. [1]Mann-Whitney U test and [2]Student's t test.

None of the patients with renal AML in our study group were symptomatic and did not report any abdominal pain, flank pain or hematuria. However, when the urine tests of the patients were evaluated simultaneously, hematuria was found in 2 (20%) of 10 patients with renal AML. Table 3 presents the comorbidities in both groups.

Table 3. The comparison of patients with and without renal AML compared to accompanying chronic diseases.				
Chronic diseases	**Total (n: 288)**	**Patients without renal AML (n: 278)**	**Patients with renal AML (n: 10)**	***p value**
HT	118 (41)	113 (40.6)	5 (50)	0.745
DM	80 (27.8)	77 (27.7)	3 (30)	0.999
HL	30 (10.4)	28 (10.1)	2 (20)	0.280
CAD	11 (3.8)	11 (4)	0 (0)	0.999
Hypothyroidism	69 (24)	65 (23.4)	4 (40)	0.258
Asthma	20 (6.9)	19 (6.8)	1 (10)	0.519

The results are presented with n (%) values. *Fisher's Exact test. (HT: Hypertension, DM: Diabetes mellitus, HL: Hyperlipidemia, CAD: Coronary artery disease)

The Spearman correlation test was used to examine the correlation between the AML size and weight, BMI, WC and HC in the group with renal AML, in which no relationship was found between the AML size and the parameters (Table 4).

Table 4. The correlation between AML size and body weight, BMI, waist circumference and hip circumference.		
	AML size	
	r	***p value**
Weight	0.073	0.841
BMI	0.049	0.894
Waist circumference	0.195	0.590
Hip circumference	0.091	0.802

*Spearman's correlation test.

DISCUSSION

In this study, the incidence of renal AML in obese patients was found to be very high with a rate of 3.47% compared to the general population. In addition, the levels of HGB and HCT in obese patients with renal AML were significantly lower than in those without renal AML.

Several studies in the literature have demonstrated the incidence of renal AML in the general population, indicating that its prevalence in the community is between 0.2% and 0.6%.[12] Although there are studies showing that obesity increases the risk of the formation of renal neoplasms, the relationship between obesity and renal AML is still unknown.[13] In this study, we examined the prevalence of renal AML in obese patients and found that it is approximately 10-30 times higher than that of the general population, which was one of the strengths of our research. Another strength was the fact that we did not find any study investigating the relationship between obesity and renal AML in the literature.

In a prevalence study, abdominal USG reports of 61.389 patients were reviewed and 270 patients (0.44%) were found with sporadic AML. The study concluded that the rate corresponded to a higher general prevalence than previously reported.[14] Conducted with only obese patients, our study found this rate to be 3.47%.

In a study by Kun-Han Lee et al., 587 cases with renal AML were examined and 44.3% of them were reported on the right, 44.3% on the left and 11.4% bilaterally. In the same study, the mean HGB value of the patients was 12.6 gr/dL (4.7-16.6 gr/dL), and the mean creatinine value was 0.8 mg/dL (0.1-11.4 mg/dL). Also, hematuria was detected in 6% of sporadic cases.[13] Similarly, in our study, renal AML was detected on the right in 50% of patients, 40% on the left, and 10% bilaterally, with the average HGB value of 12.48 gr/dL (10.70-14.80 gr/dL) and the mean creatinine value of 0.76 mg/dL (0.67-1.28 mg/dL). Unlike the study of Lee et al., the rate of hematuria in patients with renal AML was higher in our study with the rate of 20%. In our study, the significantly lower HGB values in patients with renal AML compared to those without can be explained by a possible relationship between renal AML and hematuria and/or the relationship between renal AML and the production of erythropoietin.

A study by Yılmaz et al. evaluated 41 patients with renal AML, who were diagnosed through abdominal imaging, with follow-up imaging, and suggested that renal AML be monitored radiologically, as there was an increase in size in 12% of the cases.[15] Our study reviewed the reports of abdominal USG examinations, ordered only at the initial admission of patients to our obesity unit. Patients with renal AML were referred to the nephrology outpatient clinic and suggested that they should have follow-up abdominal imaging within one year.

Considered as an important health concern for the whole world, obesity is known to be likely to cause an increase in the incidence of hypertension, kidney cancer and proteinuria in relation to the renal system.[16] In their study, Kambham et al. stated that obesity is associated with focal segmental glomerulosclerosis.[17] Obesity is also known to be a risk factor for the development of renal cell carcinoma (RCC).[18] In another study by Yasuhisa Fujii et al., the patients diagnosed with RCC based on preoperative imaging methods were operated, and 5.7% of them were reported as AML when the masses resected were examined histopathologically after the operation.[19]

In our study, abdominal USG reports of 288 obese patients were examined and renal AML was detected in 10 patients, all of whom were female, supporting the fact that the incidence of renal AML was higher in women than in men. Renal AML is generally known to be unilateral. Only one of 10 patients with renal AML in our study group had an abdominal USG report observed as bilateral renal AML, which was not related to tuberous sclerosis.
The study by Oesterling et al. concluded that the AML size was larger than four cm in the majority of symptomatic AML cases.[20] When the sizes of renal AML were examined in our study, the largest was found to be 30 mm in diameter, while the smallest was five mm. None of the patients in our study group were symptomatic and did not describe any abdominal pain, flank pain or hematuria. However, full urine analysis revealed hematuria in two (20%) of 10 patients with renal AML.

The limitation of our study is that it was performed only with obese patients and there was no control group with a normal BMI. Another limitation is that the incidence of renal AML in male obese patients could not be evaluated because obesity is more common in women and the patients who apply to our center are mostly female.

CONCLUSION

As a result, renal AML was detected incidentally in 3.47% of the obese patients that we followed, suggesting that obesity may increase the incidence of renal AML. More studies are needed with multi-centered and broader scopes to determine the relationship between obesity and AML.

The studies in the literature have indicated that the sizes of renal AML may grow during the follow-up and that the growth may cause complications. Patient complaints should, therefore, be carefully listened to in patients with renal AML, and particular attention should be paid to the sizes of renal AML. Masses larger than 4 cm should be followed closely. It should also be noted that renal AML may be confused with RCC in imaging methods.

REFERENCES

1. Kıyan E. Obezite ve akciğer. Türkiye Klinikleri Göğüs Hastalıkları-Özel Konular 2020; 13 (1), 94-98.
2. Chooi YC, Ding C, Magkos F. The epidemiology of obesity. Metabolism Clinical and Experimental 2019; 92: 6-10.
3. Türkiye Endokrinoloji ve Metabolizma Derneği Obezite tanı ve tedavi kılavuzu 2019. Available online at http://temd.org.tr/admin/uploads/tbl_kilavuz/20190506163904-2019tbl_kilavuz5ccdcb9e5d.pdf. Accessed June 8, 2020.
4. Dixon JB. The effect of obesity on health outcomes. Molecular and cellular endocrinology, 2010; 316 (2), 104-108.
5. Kalligeros M, Shehadeh F, Mylona EK, Benitez G, Beckwith CG, Chan PA, et al. Association of Obesity with Disease Severity Among Patients with Coronavirus Disease 2019. Obesity, 2020; 28 (7), 1200-1204.
6. Keum N, Greenwood DC, Lee DH, Kim R, Aune D, Ju W, et al. Adult weight gain and adiposity-related cancers: a dose-response meta-analysis of prospective observational studies. Journal of the National Cancer Institute, 2015; 107 (2), 1-14.
7. Arnold M, Pandeya N, Byrnes G, Renehan AG, Stevens GA, Ezzati M, et al. Global burden of cancer attributable to high body-mass index in 2012: a population-based study. The Lancet Oncology, 2015; 16 (1), 36-46.
8. World Cancer Research Fund. Continuous Update Project Expert Report 2018. Available online at http://dietandcancerreport.org. Accessed July 8, 2020.
9. Vuruşkan B, Akyol S, Vuruşkan H. Renal anjiomyolipomaların klinik ve histopatolojik özellikleri: 21 olguluk seri. Uludağ Üniversitesi Tıp Fakültesi Dergisi, 2018; 44 (1), 41-44.
10. dos Santos MM, Proença SM, Reis MI, Viana RM, Martins LM, Colaço JM, et al. Spontaneous rupture of renal angiomyolipoma during pregnancy. Revista Brasileira de Ginecologia e Obstetrícia, 2014; 36 (8): 377-80.
11. Korğalı E, Ayan S. Renal anjiomiyolipomlara güncel yaklaşım. Üroonkoloji Bülteni, 2010; 9 (3), 43-46.
12. Vos N, Oyen R. Renal angiomyolipoma: the good, the bad, and the ugly. Journal of the Belgian Society of Radiology, 2018; 102 (1).
13. Lee KH, Tsai HY, Kao YT, Lin HC, Chou YC, Su SH, et al. Clinical behavior and management of three types of renal angiomyolipomas. Journal of the Formosan Medical Association, 2019; 118 (1), 162-169.
14. Fittschen A, Wendlik I, Oeztuerk S, Kratzer W, Akinli AS, Haenle MM, et al. Prevalence of sporadic renal angiomyolipoma: a retrospective analysis of 61,389 in-and out-patients. Abdominal imaging, 2014; 39 (5), 1009-1013.
15. Yılmaz E. Renal anjiomyolipom olgularının 5 yıla kadar takip görüntüleme bulguları. Kocatepe Tıp Dergisi, 2019; 20 (3), 115-120.
16. Adelman RD. Obesity and renal disease. Current opinion in nephrology and hypertension; 2002; 11 (3), 331-335.
17. Kambham N, Markowitz GS, Valeri AM, Lin J, D'Agati VD. Obesity-related glomerulopathy: an emerging epidemic. Kidney international, 2001; 59 (4), 1498-1509.
18. Aurilio G, Piva F, Santoni M, Cimadamore A, Sorgentoni G, Beltran AL, et al. The role of obesity in renal cell carcinoma patients: clinical-pathological implications. International journal of molecular sciences, 2019; 20 (22), 5683.
19. Fujii Y, Komai Y, Saito K, Iimura Y, Yonese J, Kawakami S, et al. Incidence of benign pathologic lesions at partial nephrectomy for presumed RCC renal masses: Japanese dual-center experience with 176 consecutive patients. Urology, 2008; 72 (3), 598-602.
20. Oesterling, JE, Fishman, EK, Goldman SM, Marshall FF. The management of renal angiomyolipoma. The Journal of urology, 1986; 135 (6): 1121-1124.