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RESEARCH

İnsan immun yetmezlik virüsü ile yaşayan kişilerde adrenal bezin morfometrik analizi

Morphometric analysis of adrenal gland in people living with human immunodeficiency virus

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Abstract

Purpose: We aimed to evaluate the effect of Human Immunodeficiency Virus (HIV) infection on adrenal gland morphometry according to age, gender, body weight, survival status and CD4/CD8 parameters.

Materials and Methods: In this study, the CT archives (130 men and 30 women) of 160 people living with HIV infection who had imaging for any reason between 2008 and 2020 were scanned. Ages, years of follow-up, body weights, heights, CD4 and CD8 values of people with human immunodeficiency virus were obtained simultaneously with the CT examinations of the people. Anatomical measurements, adrenal gland shapes, length, corpus thickness, medial thickness, lateral thickness, distance to next anatomical structures (esophagus, vertebral column, vena cava inferior, aorta abdominalis and diaphragm) were evaluated.

Results: In our study, the average age was 40.29±13.19 (male: 39.78±12.50, female: 42.53±15.88), body weight and height were respectively 67.04±18.10 kg 157.92±6.21 cm in women and 77.06±12.93 kg, 171.67±8.97 cm in men, living with HIV infection were included. As anatomical measurements, the length, corpus thickness, medial crus thickness, lateral crus thickness, distance to the esophagus, columna vertebralis, vena cava inferior, aorta abdominalis and diaphragm of the adrenal gland were found respectively on the right; 4.77±1.70 cm, 3.59±1.23 mm, 2.76±0.83 mm, 2.79±0.87 mm, 3.21±1.21 cm, 1.45±0.85 cm, 0.92±0.57 cm, 2.41±0.65 cm, 1.57±0.84 cm and on the left; 5.78±2.8 cm, 3.77±1.43 mm, 3.38±1.17 mm, 2.92±1.06 mm, 3.10±1.26 cm, 2.11±0.7 cm, 4.10±0.83 cm, 0.90±0.45 cm, 1.21±0.73 cm. The most common adrenal gland type was recorded as Y. Additionally, the mean values of CD4 and CD8 were

Öz

Amaç: İnsan immün yetmezlik virüsü (HIV) enfeksiyonunun adrenal bez morfometrisi üzerine etkisini yaş, cinsiyet, vücut ağırlığı, hayatta kalma durumu ve CD4/CD8 parametrelerine göre değerlendirmeyi amaçladık.

Gereç ve Yöntem: Bu çalışmada, 2008 ve 2020 yılları arasında herhangi bir nedenle görüntülemesi olan 160 HIV enfeksiyonu ile yaşayan kişinin BT (130 erkek ve 30 kadın) arşivi tarandı. BT görüntüleri üzerinde planlanan anatomik ölçümler yapıldı. İnsan immün yetmezlik virüsü taşıyan kişilerin yaşları, takip süreleri, vücut ağırlıkları, boyları, CD4 ve CD8 değerleri, kişilerin BT incelemeleri ile eş zamanlı olarak elde edildi. Anatomik ölçüm olarak adrenal bez şekilleri, uzunluğu, corpus kalınlığı, medial kalınlığı, lateral kalınlığı, komşu anatomik yapılara (özefagus, columna vertebralis, vena cava inferior, aorta abdominalis ve diyafragma) uzaklığı değerlendirildi.

Bulgular: Çalışmamıza, yaş ortalaması 40,29±13,19 (erkek: 39,78±12,50, kadın: 42,53±15,88) olan, vücut ağırlığı ve boy uzunluğu sırasıyla kadınlarda, 67,04±18,10 kg ve 157,92±6,21 cm, erkeklerde ise 77.06±12.93 kg ve 171.67±8.97 cm olan HIV enfeksiyonu ile yaşayan kişiler dahil edildi. Anatomik ölçüm olarak adrenal bezin uzunluğu, corpus kalınlığı, medial crus kalınlığı, lateral crus kalınlığı, ösefagus'a, columna vertebralis'e, vena cava inferior'a, aorta abdominalis'e ve diyafragma'ya uzaklığı sırasıyla sağda; 4.77±1.70 cm, 3.59±1.23 mm, 2.76±0.83 mm, 2.79±0.87 mm, 3.21±1.21 cm, 1.45±0.85 cm, 0.92±0.57 cm, 2.41±0.65 cm, 1.57±0.84 cm ve solda; 5.78±2.8 cm, 3.77±1.43 mm, 3.38±1.17 mm, 2.92±1.06 mm, 3.10±1.26 cm, 2.11±0.7 cm, 4.10±0.83 cm, 0.90±0.45 cm, 1.21±0.73 cm olarak bulundu. En yaygın görülen adrenal bez tipi ise Y olarak kaydedildi. Ayrıca

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found to be 322.66±309.35 and 1024.48±930.15, respectively.
Conclusion: Some anatomical measurements of the adrenal gland of people living with HIV can be affected by age, gender, body weight, survival status and CD4/CD8 parameters.
Keywords:. Adrenal gland; adrenal insufficiency; anatomy; human immunodeficiency virus.

CD4 ve CD8 ortalama değerlerini sırasıyla 322,66±309,35 ve 1024,48 ±930,15 olarak bulundu.
Sonuç: HIV'le yaşayan kişilerin adrenal bezine ait bazı anatomik ölçümlerin yaş, cinsiyet, vücut ağırlığı, hayatta kalım durumu ve CD4/CD8 parametrelerinden etkilenebildiğini bulduk.
Anahtar kelimeler: Adrenal bez; adrenal yetmezlik; anatomi; insan immün yetmezlik virüsü.

INTRODUCTION

The dimensions of the adrenal glands (AG) in adults in vivo have been defined by Vincent and colleagues (1994) using computed tomography. The right AG lies posterior to the vena cava inferior, from which it is only separated by a thin layer of fascia and connective tissue. It lies posterior to the right lobe of the liver and anterior to the right crus of the diaphragm and superior pole of the right kidney. On the other hand, the left AG lies closely applied to the left crus of the diaphragm and is separated from it only by a thin layer of fascia and connective tissue[1].

The bilateral symmetrical AG, located above the cranial poles of the kidneys within the retroperitoneal space, are the source of two major types of hormones: steroids and catechol amines [2]. Adrenal steroid hormones serve to modulate a wide range of processes that are central to physiologic responses to stress, including energy metabolism, immune response, electrolyte homeostasis, and fluid balance [3]. In addition, AG change is an independent prognostic factor for mortality in people living with human immunodeficiency virus (HIV) infection in some cases [4]. Functional adrenal insufficiency, subnormal corticosteroid production during acute illness, results in high morbidity and mortality in critically ill patients. Functional adrenal insufficiency is common among people living with HIV, with incidence rates up to 75% [5]. However, studies examining effect of the HIV infection to the adrenal gland morphometry are limited in the literature. In this study, we aimed to evaluate the effect of HIV infection on adrenal gland morphometry. In addition, the anatomical parameters in our study may be guide surgeons in people living with HIV who will undergo surgical operation in AG due to adrenal insufficiency. For example, during laparoscopic surgery, vena cava inferior is easily identified behind the peritoneum, exposing the AG in the angle between the vena cava inferior and liver. The peritoneal reflection along the lateral aspect of the inferior vena cava is divided and the AG is than mobilized laterally exposing the suprarenal vein, which often emerges from the posterior aspect of the vena cava inferior. Therefore, the evaluation of the distance of the AG to the near anatomical structures is important for the surgical approach [2-5]. So, we evaluated in our study distances between AG and esophagus, columnar vertebral is, vena cava inferior, aorta abdominal is, diaphragm on the right and left sides. In particular, the reason why we prefer the population living with HIV is that they are predisposed to increase in adipose tissue for some reasons [6]. Because in obese patients' identification of a relatively normal sized AG can be extremely difficult and time consuming. Therefore, we hypothesize that human immunodeficiency virus (HIV) infection affects adrenal gland morphometry. For this reason, we aimed to evaluate the effect of HIV infection on adrenal gland morphometry according to age, gender, right and left sides, body mass index, mortality status, patient follow-up year and distance to next anatomical structures in CT images in people living with HIV. We believe that the findings of our study will contribute to the literature in understanding the adrenal gland of people living with HIV in the field of anatomy, radiology, and infectious diseases. The study was carried out with specialists from the Infection and Clinical Microbiology, Radiology and Anatomy departments of Cukurova University Faculty of Medicine.

MATERIALS AND METHODS

Sample

This study was conducted over 12 years from 2008 to 2020 retrospectively from the archive of Infection and Clinical Microbiology and Radiology departments of Cukurova University Faculty of Medicine. Measurement parameters and interpretation were made by anatomists 160 CT scans (130 males and 30 females) that had imaging for any reason retrospectively for this study were scanned. The informed consent was waived due to the retrospective nature of the study and the assessment utilized anonymous research findings. Measurements

were performed by the same radiology specialist and measurements were used kg and cm/mm as units of measurement. The relevant guidelines and regulations were strictly followed when conducting the study. Necessary permissions for the study were obtained from Cukurova University Medical Faculty, Non-invasive clinical research Ethic Board with conclusion number 115/17 (date: October 1, 2021). In addition, necessary permissions were obtained from the collaboration with us in the Department of Infectious Diseases and Clinical Microbiology The experimental procedures were conducted in accordance with the Declaration of Helsinki.

Inclusion criteria were living with HIV over the age of 18, living with HIV without adrenal insufficiency, having CT images and followed by the Cukurova University Department of Infection and Clinical Microbiology

Study design

First of all, a list of patients who were diagnosed with HIV and followed up in 2008-2020 from the Department of Infection and Clinical Microbiology was obtained. This list included 921 people living with HIV without adrenal insufficiency. Secondly, the existence of CT images of people living with HIV on this list was checked in the Radiology Department. It was determined that 160 (130 males, 30 females) of 921 people living with HIV had CT images. Planned anatomical measurements were performed on CT images. Our parameters were measured twice by the same person, and there was no significant difference between the two measurements. Ages, years of follow-up, body weights, heights, and CD4 and CD8 values of people with HIV were obtained simultaneously with the CT examinations of the people.

Assessment of anatomical parameters

Adrenal Gland (AG) Shape: There are four shapes as Y-type, linear type, triangular type, and V- type according to the literature [7].

AG Height: Axial and coronal plain measurement circles were determined as containing AG and lipoid tissue around the AG height measurements on the right and left sides.

AG Corpus Thickness (AGCT), AG Medial Thickness (AGMT), and AG Lateral Thickness (AGLT): After the detection of AG images, corpus, medial, and lateral branch thickness measurements were performed on the axial. Also, corpus measurements were done in the transverse plane on the right and left sides.

Distance to Next Anatomical Structures of AG: After the detection of AG on axial reformat images, we assessed the distances between AG and esophagus (AGDO), columna vertebralis (AGDCV), vena cava inferior (AGDVC), aorta abdominalis (AGDA), diaphragm (AGDD) on the right and left sides (Figure 1).

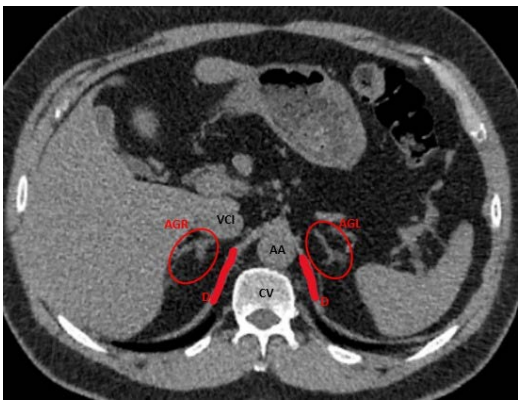

Figure 1. Land markers of anatomical parameters on the axial formatted image

(AGL: Adrenal Gland Left, AGR: Adrenal Gland Right, VCI: Vena Cava Inferior, AA: Aorta Abdominalis, D: Trace of Diaphragma, CV: Columna Vertebralis).

Computed tomography protocol

The patient was evaluated with thorax and abdomen CT. The contrast agent was carried out to be for the examination. The images were obtained with 160 detector CT devices (Aquilion; Toshiba Medical Systems, Tokyo, Japan). The images were captured from the thyroid gland to the hips. Scan parameters KV: 100-120, MAS:50-100, slice thickness: 0.5 mm, Pitch: 1.4, rotation speed: 0.5 s. After the images were obtained, multiplane reconstructions were analyzed at the workstation (Vitrea; Vital Images Inc., Minn., USA).

Clinical biomarkers

CD4 AND CD8: CD4, CD8 cell counts, and traditional biomarkers for HIV disease are inadequate. HIV advanced disease is defined as a CD4 cell count <200 cells/mm3 [3].

CD4/CD8: The relative risk of disease progression in individuals is determined as low (<0.3) and high (>0.45) [8].

Statistical analysis

Participant age, gender, weight, height, CD4, CD8 values, mortality status, and patient follow-up year were evaluated with the SPSS v.22 package program. Statistical findings were shown as mean±standard deviation. The distribution of data was analyzed through the Kolmogorov Smirnov test. The relationship of AGH, AGCT, AGMT, AGLT, AGDO, AGDCV, AGDVC, AGDA, and AGDD to gender and between the two sides was evaluated using the Student-t test (normally distributed), Mann Whitney U test (not normally distributed), and the Analysis of Variance (ANOVA) test (normally distributed). The relationship between the bilateral AGH, AGCT, AGMT, AGLT, AGDO, AGDCV, AGDVC, AGDA, and AGDD versus age, weight, height, BMI, CD4, CD8 values, mortality status, and patient follow-up year was calculated through the Pearson's correlation coefficient test (95% confidence interval). Statistically significant was considered as p=0.05. Post-hoc testing (Dunn Bonferroni test) was performed to determine in which age decade there was a statistically significant difference. Also, categorical variables (AG shape) were assessed as frequency and percent rates.

RESULTS

Our study included 160 (130 males and 30 females) individuals between the ages of 18-74, with a mean age of 40.29±13.19 (male: 39.78±12.50, female: 42.53±15.88). In the individuals in our study, body weight and height were found respectively in women; 67.04±18.10 kg and 157.92±6.21 cm, in males; 77.06±12.93 kg and 171.67±8.97 cm. A total of 160 people living with HIV in our study are being followed up 1-12 years (male: 5.79±2.94 years and female: 6.7±3.72 years) in the Department of Infection and Clinical Microbiology. In addition, we found the mean values of CD4 and CD8, which are biomarkers in HIV infection, to be 322.66±309.35 and 1024.48±930.15, respectively.

A significant difference was obtained between the genders from the anatomical measurements of the right AG, except for AGDCV, AGDVC, AGDA parameters. In other words, anatomical measurements of the right AG were significantly higher in male than in female. Similarly, in the left AG, a significant difference was found between genders, except for the AGDD parameter. Anatomical measurements of the left adrenal gland were found to be significantly higher in male than in female (Table 1). When the AG shape types were examined, type Y was seen at a rate of 95.77% in males and 88.33% in females. While type was most common in both the right AG (47.69%) and the left AG (48.08%) in males, type V (0.77%) was the least common. Similarly, in females, the most common AG type on both the right (45%) and left (43.33%) side were type Y, while type linear (1.67%) was the least common (Table 2).

Also, there was a significant difference in AGCT (R) (p=0.016), AGLT (R) (p=0.022), AGDCV (R) (p=0.035), AGH (L) (p=0.049), AGDCV (L) (p=0.005) and AGDVC (L) (p=0.017) between decades of age and anatomical parameters. Also, a significant positive correlation was found between AGDCV (R), AGDCV (L) and AGDVC (L) parameters and age decades (Table 4). According to the post-hoc test (Dunn Bonferroni test) we conducted to determine in which age decade there is a statistically significant difference, we found that there were differences AGDD (R), AGDO (L) parameters in the 18-25 age decade, AGDO (R), AGCT (L) parameters in the 26-35 age decade, AGH (R), AGMT (R), AGLT (R), AGDCV (R), AGH (L), AGMT (L), AGLT (L), AGDD (L) parameters in the 36-45 age decade, AGCT (R), AGDVC (R), AGDA (L) parameters in the 46-55 age decade and AGDCV (L) parameter in the 56 and above age decade (Table 4). Moreover, there was a significant difference (p=0.044) only in AGDO (L) parameter between anatomical parameters and mortality (survivors or non survivors) status (Table 5). In addition, there was a significant difference between anatomical parameters and CD4/CD8 ratio in AGH (R) (p=0.005) and AGMT (L) (p=0.041) parameters, along with a significant relationship between AGH (R) (negative correlation) and AGDVC (R) (positive correlation) parameters and CD4/CD8 ratio (Table 6).

Finally, a significant difference was found between CD4 values and anatomical parameters in AGH(R) (p=0.003) and AGDVC (R) (p=0.021) parameters (Table 7).

Table 1. Assessment of anatomical parameters according to the gender and right/left sides

Parameter	Total Right side Mean±SD (Min-Max)	Total Left side Mean±SD (Min-Max)	Male (R) Mean±SD (Min-Max)	Male (L) Mean±SD (Min-Max)	Female (R) Mean±SD (Min-Max)	Female (L) Mean±SD (Min-Max)	P
AGH (cm)	4.77±1.70 (1.5-9.5)	5.78±2.8 (1.50-20)	5.24±1.47 (2-9.5)	6.51±2.56 (1.5-20)	2.68±0.86 (1.5-5.3)	2.57±0.81 (1.5-5.5)	0.00 (R) 0.00(L)
AGCT (mm)	3.59±1.23 (0.5-7.38)	3.77±1.43 (1.69-8.87)	3.82-1.22 (0.5-7.38)	4.06±1.41 (1.70-8.87)	2.59±0.61 (1.52-4.15)	2.51±0.55 (1.69-3.91)	0.00 (R) 0.00(L)
AGMT (mm)	2.76±0.83 (1.3-5.94)	3.38±1.17 (1.53-7.6)	2.87±0.87 (1.30-5.94)	3.57±1.20 (1.53-7.60)	2.28±0.35 (1.49-2.96)	2.55±0.47 (1.57-3.85)	0.00 (R) 0.00(L)
AGLT (mm)	2.79±0.87 (1.31-6.9)	2.92±1.06 (1.04-7.24)	2.91±0.90 (1.5-6.90)	3.11±1.09 (1.52-7.24)	2.23±0.41 (1.31-2.95)	2.15±0.42 (1.04-2.95)	0.00 (R) 0.00(L)
AGDO (cm)	3.21±1.21 (0.75-5.6)	3.10±1.26 (0.82-5.6)	3.46-1.06 (1.5-5.6)	3.34±1.22 (1-5.6)	2.13±1.21 (0.75-5.4)	2.03±0.83 (0.82-4.30)	0.00 (R) 0.00(L)
AGDCV (cm)	1.45±0.85 (0.58-5.13)	2.11±0.7 (0.81-4.37)	1.49-0.89 (0.58-5.13)	2.21±0.71 (0.87-4.37)	1.25±0.64 (0.6-3.04)	1.67±0.44 (0.81-2.63)	0.162(R) 0.00(L)
AGDVC (cm)	0.92±0.57 (0.1±2.76)	4.10±0.83 (1.84-6,81)	0.95±0.59 (0.1-2.76)	4.25±0.82 (1.84-6.81)	0.82±0.47 (0.1-1.71)	3.46±0.49 (2.63-4.7)	0.380 (R) 0.00(L)
AGDA (cm)	2.41±0.65 (0.76-4.15)	0.90±0.45 (0.18-2.5)	2.51±0.61 (0.76-4.15)	0.96±0.46 (0.23-250)	1.97±0.62 (1.03-3.3)	0.63±0.25 (0.19-1.25)	0.061 (R) 0.00(L)
AGDD (cm)	1.57±0.84 (0.35-3.42)	1.21±0.73 (0.31-3.12)	1.52±0.87 (0.35-3.42)	1.18±0.77 (0.31-3.12)	1.81±0.68 (0.50-3.18)	1.35±0.46 (0.45-2.34)	0.00 (R) 0.035 (L)

P: Mann-Whitney U test value, R: Right, L: Left, Min: Minimum, Max: Maximum, SD: standard deviation, AGH: Adrenal Gland Height, AGCT: Adrenal Gland Corpus Thickness, AGMT: Adrenal Gland Medial Thickness, AGLT: Adrenal Gland Lateral Thickness, AGDO: Adrenal Gland Distance Oesophagus, AGDCV: Adrenal Gland Distance Columna Vertebralis, AGDVC: Adrenal Gland Distance Vena Cava Inferior, AGDA: Adrenal Gland Distance Aorta Abdominalis, AGDD: Adrenal Gland Distance Diaphragma.

Table 2. Distribution of adrenal gland shape types by gender

Gender	N	Type Y n (%)	Type Linear n (%)	Type Triangular n (%)	Type V n (%)
Male (R)	130	124 (47.69)	3 (1.15)	1 (0.39)	2 (0.77)
Male (L)	130	125 (48.08)	2 (0.77)	3 (1.15)	0 (0)
Total	260	249 (95.77)	5 (1.92)	4 (1.54)	2 (0.77)
Female (R)	30	27 (45)	1 (1.67)	0 (0)	2 (3.33)
Female (L)	30	26 (43.33)	0 (0)	3 (5)	1 (1.67)
Total	60	53 (88.33)	1 (1.67)	3 (5)	3 (5)

n: number of people, R: Right, L: Left

Table 3. Assessment of anatomical parameters according to the body mass index status

Parameter	Underweight Mean±SD	Normal Mean±SD	Overweight Mean±SD	p*	p**	r
AGH (cm) (R)	4.00±2.18	4.61±1.63	4.84±2.1	0.718	0.442	0.094
AGCT (mm) (R)	2.8±1.04	3.56±1.25	3.66±1.05	0.441	0.326	0.118
AGMT (mm) (R)	1.84±0.39	2.75±0.88	2.75±0.86	0.169	0.282	0.128
AGLT (mm) (R)	1.99±0.44	2.56±0.51	2.83±0.86	0.115	0.043	0.253
AGDO (cm) (R)	3.0±1.8	3.32±1.26	3.12±1.18	0.782	0.704	-0.046
AGDCV (cm) (R)	1.96±0.97	1.61±1.26	1.55±0.89	0.802	0.589	-0.065
AGDVC (cm) (R)	0.57±0.82	0.83±0.45	0.91±0.51	0.467	0.251	0.137
AGDA (cm) (R)	2.94±0.5	2.39±0.78	2.3±0.57	0.251	0.178	-0.161
AGDD (R) (R)	1.07±0.54	1.47±0.69	1.55±0.89	0.613	0.411	0.098
AGH (cm) (L)	4.50±2.65	6.45±2.93	5.66±2.99	0.430	0.736	-0.042
AGCT (mm) (L)	3.06±0.74	3.80±1.45	3.72±1.31	0.672	0.759	0.037
AGMT (mm) (L)	2.30±0.85	3.77±1.12	3.22±0.99	0.026	0.527	-0.076
AGLT (mm) (L)	2.48±1.17	2.71±0.82	2.83±0.89	0.723	0.428	0.096
AGDO (cm) (L)	1.90±0.96	3.01±1.39	3.01±1.27	0.361	0.407	0.101
AGDCV (cm) (L)	2.10±0.96	2.11±0.71	2.15±0.60	0.980	0.847	0.023
AGDVC (cm) (L)	4.11±1.29	3.89±0.81	4.08±0.72	0.613	0.506	0.080
AGDA (cm) (L)	1.36±0.28	0.78±0.28	0.90±0.43	0.047	0.803	-0.030
AGDD cm (L)	1.67±1.21	1.61±0.80	1.17±0.76	0.075	0.029	-0.259

p*: Analysis of Variance (ANOVA) test, p** and r: Pearson's correlation coefficient test, R: Right, L: Left, SD: standard deviation, Underweight: BMI<18.5, Normal: 18.5<BMI<24.9, Overweight: 25<BMI. AGH: Adrenal Gland Height, AGCT: Adrenal Gland Corpus Thickness, AGMT: Adrenal Gland Medial Thickness, AGLT: Adrenal Gland Lateral Thickness, AGDO: Adrenal Gland Distance Oesophagus, AGDCV: Adrenal Gland Distance Columna Vertebralis, AGDVC: Adrenal Gland Distance Vena Cava Inferior, AGDA: Adrenal Gland Distance Aorta Abdominalis, AGDD: Adrenal Gland Distance Diaphragma.

Table 4. Assessment of anatomical parameters according to decades of age

Parameter	18-25 years n=24 Mean±SD	26-35 years n=47 Mean±SD	36-45 years n=34 Mean±SD	46-55 years n=36 Mean±SD	56< years n=19 Mean±SD	p*	p**	r
AGH (cm) (R)	4.30±1.86	4.87±1.60	5.11±1.93[B]	4.88±1.36	4.30±1.82	0.311	0.865	0.014
AGCT (mm) (R)	3.13±1.18	3.82±1.33	3.68±1.26	3.85±1.14[B]	2.95±0.77	0.016	0.851	-0.015
AGMT (mm) (R)	2.32±0.62	2.80±0.86	2.91±0.85[B]	2.81±0.71	2.87±1.05	0.083	0.057	0.153
AGLT (mm) (R)	2.30±0.45	2.81±0.97	3.08±0.92[B]	2.92±0.87	2.68±0.77	0.022	0.116	0.133
AGDO (cm) (R)	3.24±1.24	3.33±1.11[B]	3.20±1.13	3.28±1.25	2.74±1.48	0.530	0.281	-0.087
AGDCV (cm) (R)	1.16±0.69	1.25±0.66	1.74±1.14[B]	1.57±0.77	1.56±0.86	0.035	0.018	0.188
AGDVC (cm) (R)	0.98±0.45	0.82±0.52	0.84±0.55	1.08±0.64[B]	0.90±0.67	0.257	0.442	0.061
AGDA (cm) (R)	2.47±0.54	2.47±0.66	2.44±0.59	2.34±0.59	2.24±0.92	0.680	0.161	-0.112
AGDD (cm) (R)	1.71±0.75[B]	1.62±0.83	1.42±0.79	1.65±0.94	1.41±0.87	0.566	0.358	-0.073
AGH (cm) (L)	4.76±2.01	6.01±2.59	6.67±3.71[B]	5.92±2.56	4.72±2.17	0.049	0.906	0.010
AGCT (mm) (L)	3.51±1.25	4.05±1.68[B]	3.97±1.18	3.69±1.37	3.17±1.34	0.153	0.245	-0.093
AGMT (mm) (L)	3.32±1.32	3.26±1.11	3.70±1.23[B]	3.51±1.18	3.00±0.90	0.250	0.947	-0.005
AGLT (mm) (L)	2.66±1.02	2.78±0.94	3.22±1.05[B]	2.99±1.09	2.95±1.31	0.281	0.186	0.106
AGDO (cm) (L)	3.18±1.23[B]	3.09±1.27	3.10±0.98	3.15±1.44	2.87±1.42	0.951	0.640	-0.038
AGDCV (cm) (L)	1.73±0.73	1.98±0.57	2.24±0.72	2.26±0.55	2.37±0.89[B]	0.005	0.000	0.287
AGDVC (cm) (L)	3.89±0.76	3.95±0.60	4.00±1.03	4.49±0.72[B]	4.23±1.03	0.017	0.006	0.217
AGDA (cm) (L)	0.93±0.54	0.83±0.40	0.93±0.43	0.94±0.42[B]	0.89±0.56	0.790	0.682	0.033
AGDD (cm) (L)	1.09±0.53	1.29±0.90	1.42±0.79[B]	1.04±0.71	1.11±0.58	0.181	0.536	-0.049

n: number of people, SD: standard deviation, p*: Analysis of Variance (ANOVA) test, p** and r: Pearson's correlation coefficient test, [B]: Benferroni (post hoc test), R: Right, L: Left, n: number of people, AGH: Adrenal Gland Height, AGCT: Adrenal Gland Corpus Thickness, AGMT: Adrenal Gland Medial Thickness, AGLT: Adrenal Gland Lateral Thickness, AGDO: Adrenal Gland Distance Oesophagus, AGDCV: Adrenal Gland Distance Columna Vertebralis, AGDVC: Adrenal Gland Distance Vena Cava Inferior, AGDA: Adrenal Gland Distance Aorta Abdominalis, AGDD: Adrenal Gland Distance Diaphragma.

Table 5. Assessment of anatomical parameters according to the mortality

Parameter	Survival n=137 Mean±SD (Min-Max)	Non-Survival n=23 Mean±SD (Min-Max)	P
AGH (cm) (R)	4.80±1.69 (1.50-9.50)	4.57±1.78 (2.00-7.50)	0.586
AGCT (mm) (R)	3.55±1.21 (0.50-7.38)	3.85±1.38 (2.21-6.40)	0.455
AGMT (mm) (R)	2.73±0.82 (1.30-5.94)	2.92±0.90 (1.65-4.25)	0.356
AGLT (mm) (R)	2.73±0.77 (1.31-5.40)	3.15±1.25 (1.66-6.90)	0.166
AGDO (cm) (R)	3.23±1.16 (0.80-5.60)	3.08±1.48 (0.75-5.20)	0.812
AGDCV (cm) (R)	1.48±0.87 (0.58-5.13)	1.26±0.70 (0.60-3.48)	0.220
AGDVC (cm) (R)	0.90±0.55 (0.10-2.00)	1.00±0.71 (0.10-2.76)	0.713
AGDA (cm) (R)	2.42±0.63 (7.60-39.81)	2.34±0.74 (10.35-41.54)	0.435
AGDD (R) (R)	1.52±0.81 (0.35-3.40)	1.86±0.97 (0.38-3.42)	0.162
AGH (cm) (L)	5.65±2.46 (1.50-15.00)	6.54±4.34 (2.10-20.00)	0.492
AGCT (mm) (L)	3.76±1.42 (1.70-8.87)	3.82±1.52 (1.69-6.82)	0.943
AGMT (mm) (L)	3.37±1.16 (1.53-7.60)	3.47±1.26 (1.57-6.82)	0.701
AGLT (mm) (L)	2.88±1.06 (1.04-7.24)	3.18±1.09 (1.65-5.94)	0.146
AGDO (cm) (L)	3.18±1.23 (0.85-5.60)	2.59±1.32 (0.82-5.00)	0.044
AGDCV (cm) (L)	2.13±0.72 (0.81-4.37)	1.96±0.51 (0.93-3.13)	0.336
AGDVC (cm) (L)	4.10±0.85 (18.43-68.11)	4.15±0.76 (26.32-57.15)	0.518
AGDA (cm) (L)	0.92±0.46 (1.87-24.96)	0.80±0.40 (3.80-17.10)	0.207
AGDD (cm) (L)	1.23±0.75 (0.31-3.12)	1.13±0.54 (0.33-2.00)	0.816

p: Mann Whitney U test, R: Right, L: Left, n: number of people, SD: standard deviation, Min: Minimum, Max: Maximum, AGH: Adrenal Gland Height, AGCT: Adrenal Gland Corpus Thickness, AGMT: Adrenal Gland Medial Thickness, AGLT: Adrenal Gland Lateral Thickness, AGDO: Adrenal Gland Distance Oesophagus, AGDCV: Adrenal Gland Distance Columna Vertebralis, AGDVC: Adrenal Gland Distance Vena Cava Inferior, AGDA: Adrenal Gland Distance Aorta Abdominalis, AGDD: Adrenal Gland Distance Diaphragma.

Table 6. Assessment of anatomical parameters according to CD4/CD8

Parameter	CD4/CD8< 0.3 n=98 Mean±SD	0.3<CD4/CD8<0.45 n=22 Mean±SD	0.45<CD4/CD8 n=40 Mean±SD	p*	p**	r
AGH (cm) (R)	5.12±1.66	4.67±1.55	4.10±1.64	0.005	0.004	-0.234
AGCT (mm) (R)	3.55±1.20	4.00±0.96	3.53±1.39	0.291	0.710	0.030
AGMT (mm) (R)	2.82±0.84	2.62±0.66	2.73±0.90	0.740	0.564	-0.047
AGLT (mm) (R)	2.82±0.90	2.86±0.91	2.70±0.82	0.843	0.605	-0.044
AGDO (cm) (R)	3.18±1.24	3.53±1.29	3.19±1.06	0.175	0.610	0.042
AGDCV (cm) (R)	1.42±0.84	1.40±0.75	1.54±0.95	0.889	0.503	0.054
AGDVC (cm) (R)	0.82±0.56	1.08±0.46	1.05±0.63	0.088	0.020	0.184
AGDA (cm) (R)	2.38±0.64	2.59±0.57	2.41±0.68	0.336	0.516	0.052
AGDD (R) (R)	1.61±0.84	1.51±0.95	1.47±0.77	0.811	0.338	-0.077
AGH (cm) (L)	5.89±2.29	6.68±3.92	5.15±2.94	0.102	0.402	-0.069
AGCT (mm) (L)	3.83±1.49	3.75±1.19	3.72±1.40	0.754	0.783	-0.022
AGMT (mm) (L)	3.58±1.26	3.05±0.93	3.18±0.94	0.041	0.074	-0.143
AGLT (mm) (L)	2.97±1.12	2.70±0.85	2.95±1.06	0.699	0.841	-0.016
AGDO (cm) (L)	2.98±1.31	3.59±1.32	3.09±1.07	0.176	0.371	0.073
AGDCV (cm) (L)	2.13±0.68	2.04±0.70	2.11±0.74	0.597	0.961	-0.004
AGDVC (cm) (L)	4.13±0.87	4.29±0.67	3.96±0.81	0.144	0.596	-0.043
AGDA (cm) (L)	0.85±0.40	1.01±0.53	0.97±0.51	0.288	0.096	0.133
AGDD (cm) (L)	1.17±0.71	1.37±0.95	1.21±0.63	0.718	0.674	0.034

p*: Analysis of Variance (ANOVA) test, p** and r: Pearson's correlation coefficient test, R: Right, L: Left, n: number of people, SD: standard deviation, AGH: Adrenal Gland Height, AGCT: Adrenal Gland Corpus Thickness, AGMT: Adrenal Gland Medial Thickness, AGLT: Adrenal Gland Lateral Thickness, AGDO: Adrenal Gland Distance Oesophagus, AGDCV: Adrenal Gland Distance Columna Vertebralis, AGDVC: Adrenal Gland Distance Vena Cava Inferior, AGDA: Adrenal Gland Distance Aorta Abdominalis, AGDD: Adrenal Gland Distance Diaphragma.

Table 7. Assessment of anatomical parameters according to values of CD4.

Parameter	CD4<200 n=73 Mean±SD	200<CD4 n=87 Mean±SD	P
AGH (cm) (R)	5.25±1.73	4.43±1.57	0.003
AGCT (mm) (R)	3.70±1.19	3.53±1.25	0.420
AGMT (mm) (R)	2.81±0.87	2.74±0.80	0.624
AGLT (mm) (R)	2.81±0.87	2.79±0.88	0.881
AGDO (cm) (R)	3.20±1.18	3.26±1.23	0.791
AGDCV (cm) (R)	1.44±0.85	1.45±0.86	0.906
AGDVC (cm) (R)	0.80±0.55	0.80±0.55	0.021
AGDA (cm) (R)	2.36±0.70	2.36±0.70	0.297
AGDD (R) (R)	1.67±0.86	1.67±0.86	0.139
AGH (cm) (L)	6.10±2.42	5.60±3.04	0.275
AGCT (mm) (L)	3.67±1.31	3.89±1.51	0.318
AGMT (mm) (L)	3.52±1.21	3.31±1.12	0.258
AGLT (mm) (L)	2.96±1.07	2.90±1.07	0.730
AGDO (cm) (L)	3.07±1.32	3.13±1.22	0.762
AGDCV (cm) (L)	2.18±0.67	2.06±0.72	0.308
AGDVC (cm) (L)	4.16±0.92	4.07±0.75	0.476
AGDA (cm) (L)	0.85±0.42	0.94±048	0.224
AGDD (cm) (L)	1.17±0.74	1.24±0.73	0.538

p: The Independent Samples t Test, R: Right, L: Left, n: number of people, SD: standard deviation, AGH: Adrenal Gland Height, AGCT: Adrenal Gland Corpus Thickness, AGMT: Adrenal Gland Medial Thickness, AGLT: Adrenal Gland Lateral Thickness, AGDO: Adrenal Gland Distance Oesophagus, AGDCV: Adrenal Gland Distance Columna Vertebralis, AGDVC: Adrenal Gland Distance Vena Cava Inferior, AGDA: Adrenal Gland Distance Aorta Abdominalis, AGDD: Adrenal Gland Distance Diaphragma

DISCUSSION

Adrenal insufficiency is one of the oldest and most important side effects seen in people living with HIV. For example, in a study in the literature, adrenal insufficiency was found in 17% of 74 patients [9].

Adrenal dysfunction is a condition that can increase morbidity and mortality among people living with HIV and can be treated with cortisol replacement [10]. But the literature examining the effect of HIV on adrenal morphological changes is quite limited. Therefore, in our study, we included measurements of the length, thickness, and distance of the AG to the next anatomical structures in people living with HIV. We also analyzed the relationship with age, sex, body mass index, mortality status and their relationship with CD4, and CD8 values. In our study, 130 people were males in the 160 people, which supports the literature on the prevalence of HIV in males [11].

In the literature, four types of AG shapes ("Y", "linear", "triangular", and "V") have been classified. In a CT study conducted by Akın et al. with 420 non-HIV adults with a mean age of 63 years, the most common AG shape in males and females was reported as "Y" and the second most common was the "triangular" shape. In another study by Gurun et al. with 115 non-HIV adults in the CT images, both AG (right) and AG (left) reported "Y" shape was the most common form shape of AG in both males and females. Similarly, "linear" was the second most common shape in AG (right), while the second most common shape in AG (left) was found to be "triangle" [7,12]. In our study, both AG (right) (and AG (left) were reported in accordance with the literature "Y" shape (94.33%) was the most common form of AG in females (88.33%) and males (95.77%). Similarly, "linear" and "V" types were the second most common shape in AG (right), while the second most common shape in AG (left) was found to be "triangle. Types of AG shape distributions were found as follows; In males, Y-type (47.69%), linear-type (1.15%), triangular-type (0.39%), and V-type (0.77%) on the right side, and Y-type (48.08%), linear-type (0.77%), triangular-type (1.15%), and V-type (0%) on the left side, in females Y-type (45%), linear-type (1.67%), triangular-type (0%), and V-type (3.33%) on the right side and Y-type (43.33%), linear type (0%), triangular type (5%), and V type (1.67%) on the left side.

It is stated in the literature that AG thickness parameters may be the most useful in the initial evaluation of proven adrenal pathology. Therefore, in our study, we examined the AG thickness measurements in people living with HIV. There are many studies in the literature examining AG morphometric values in the normal population. The length, width, thickness of right adrenal body, the thickness of medial limb and lateral limb were, respectively, 34.02±2.12 mm, 10.91±0.89 mm, 5.82±0.26 mm, 2.78±0.08 mm, 2.62±0.06 mm, whereas the measurements of left AG were 28.31±2.46 mm, 18.40±1.06 mm, 6.84±0.24 mm, 3.02±0.08 mm, 2.86±0.07 mm, respectively (aged from 15 to 55 years) in the Chinese population [13]. The mean maximum thickness of the adrenal corpus, medial, and lateral limbs respectively were 7.2±1.8, 4.1±1.1, and 4.3±1.1 mm on the right side and 8.8±1.9, 4.7±1.1, and 4.9±1.3 mm on the left. The thickness of the corpus and the limbs were 15.6±3.7 mm and 18.4±3.8 mm on the right and left sides, respectively (range: 18-85 years) in the Indian population [14].

In another study included that the mean age of the participants (700 males and 300 females) was 54±7.5 years. The thickness of the right AG corpus, AG medial limb, and AG lateral limb respectively were 7.16±1.67mm, 4.23±1.45mm, and 4.45±1.19 mm [15]. In our study, the values of the AG height, medial, and lateral thickness parameters were found to be lower than the values measured in the normal population in the literature. AG volume also gives clues about gland structure, but volume measurement is time-consuming and not suitable for normal clinical settings. In addition, misleading results can be obtained due to the irregular inspiration effect. Therefore, we did not evaluate the AG volume in our study. Therefore, the fact that the adrenal limb values of the people living with HIV in our study were lower than the normal population may reveal that HIV may cause AG hypoplasia. Already adrenal insufficiency is one of the most common endocrine diseases in people living with HIV [3]. Therefore, the size and morphology of the adrenal glands may be affected by HIV.

The CD4/CD8 ratio is one of the most recent markers of HIV exposure and response to treatment in people living with HIV [16,17]. Therefore, we evaluated the relationship between anatomical parameters and CD4/CD8 in our study. While there was a negative significant correlation between the AGH (R) ($p=0.004$, $r=-0.234$) parameter and

CD4/CD8, a positive significant correlation was found between the AGDVC (R) (p=0.020, r=0.184) parameter and CD4/CD8. This result supports that the size and morphology of the adrenal glands may be affected by HIV. In addition, we think that anatomical parameters such as CD4/CD8 ratio can be used as a marker of immunological response in individuals treated with a diagnosis of HIV.

The determination adrenal localization of associated with the next anatomical structure is very important to predict other organ involvement. Therefore, we examined the distances of the AG to the esophagus (AGDO), columna vertebralis (AGDCV), vena cava inferior (AGDVC), aorta abdominalis (AGDA) and diaphragm (AGDD) on both sides (right and left). Studies on these distance measurements in both non-HIV populations and people living with HIV are very limited. In the study of Akin et al. with 420 non-HIV adults aged 50-84 years, AGDO (cm), AGDCV (cm), AGDVC (cm), AGDA (cm), and AGDD (cm) parameters were found on the right, respectively; 5.15±1.09, 2.21±0.84, 0.21±0.18, 2.47±0.73 and 0.84±0.39, on the left, respectively; 3.45±1.23, 2.67±0.80, 4.68±0.85, 1.46±0.53 and 1.09±048 [12]. In our study, the values of these parameters were found to be lower than the values measured in the normal population in the literature (except GDVC (R), AGDD (R) and AGDD (L) parameters). Our study consisted of individuals with HIV between the ages of 18-74. We think that the differences between studies are due to the age range.

Study limitations; We think that the fact that the number of men in the study population is significantly higher than women will affect the statistical reliability in the evaluation of the gender factor. We also recommend conducting similar studies that include evaluation of the data with a normal population and more image analysis.

In conclusion, we found that some anatomical measurements of the adrenal gland of people living with HIV can be affected by age, gender, body weight, survival status and CD4/CD8 parameters. True and quick diagnosis and treatment of adrenal insufficiency, which is an important complication of HIV infection, is important. Although adrenal insufficiency poses a risk for people living with HIV, little is known about the incidence, clinical features, and outcomes of the complication in these patients. In addition, there is no study examining the effect of AG morphometry on adrenal insufficiency. We think that our study will contribute to the literature on a correct diagnosis of adrenal insufficiency as an auxiliary method. Besides, surgical intervention is an indispensable treatment method for people living with HIV due to symptoms related to the disease at some point in their lives. We think that the anatomical measurements of the suprarenal gland revealed in our study will guide the surgical treatment to be applied in this region.

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