

# Journal of Global Pharma Technology

Available Online at www.jgpt.co.in

**RESEARCH ARTICLE** 

# Role of Testosterone on Waist to Hip Ratio in Women with Hirsutism

Abdulsamie H. Alta'ee, Khawla A. Shemran, Shahlaa Kh Chabuk

College of Medicine, University of Babylon, P. Code 51002, Hilla PO Box 473, Iraq.

#### Abstract

Hirsutism is a series problem faced women in the present days. It is usually associated with elevated levels of androgen hormones. This study aims to investigate the role of testosterone in the waist-to-hip ratio (WHR), and body mass index (BMI) of 54 women with hirsutism and 54 healthy women match in age, in a case control study. Free testosterone and thyroid stimulated hormone (TSH) were determined using ELISA technique. WTR, BMI and hirsutism score were examined in the study groups. Free testosterone, TSH, WTR, BMI and hirsutism score found to be significantly increased when compared with control group. The result of the present study may hypothesize that testosterone has a central role in the path physiological changes occur in hirsutism, such as fat storage pattern and as consequence the HWR and the stimulation effect to induce TSH and its effect on hair growth.

Keywords: Hirsutism, WTR, Testosterone, TSH, BMI.

# Introduction

Hirsutism is a disease affect women which characterized by an excessive presence of terminal hair in a manner similar to that of the male pattern [1]. It affects about 5-10 % of women worldwide. In most cases, it is associated with increase androgen levels [2].

The regulation of hair growth is subject to local and systemic factors such as sex steroids particularly androgens, cytokines and growth factors, as well as, growth and thyroid hormones which are reported to change the patterns of hair-growth [3]. Accumulated evidence are grown concerning the essential function of androgens in the kind of hair formation and distributed over the body.

These reports are shown direct proportion between androgen levels and development of terminal hair during puberty [4]. The main cause of hirsutism is the interaction between the amount of androgen and the hair follicle sensitivity to androgens [5]. Many factors determine if vellus hair turns into terminal hair such as the period of their exposure to high androgens concentration, the adequate activity of enzyme 5- $\alpha$ -reductase and the intrinsic sensitivity to androgen action by the follicle of hair [6]. The previous study found positive correlation between а

hirsutism and waist-to-hip ratio (WHR), and when this study adjusts both of body mass index (BMI) and age; it was found a significant positive correlation between WHR and blood pressure. This study attributed their results to the effect of local metabolism of the androgenic steroids [7]. The most commonly used criteria in anthropometric measurement by physicians are BMI and WHR as indexes of metabolic abnormalities and risk of cardiovascular diseases in both gender, in favor to WHR increment in many pathogenic conditions hypertension ranging from and cardiovascular disease to cancer, diabetes mellitus and infertility [8].

On the other hand, sex hormones such as estradiol and testosterone play an important role in the regulation of WHR. Previous studied found high estradiol levels are responsible for low WHR due to its role in the regulation of fat accumulation in the hip, buttocks, bosom, and thighs [9, 10]. In contrast, testosterone plays a contrary role to estradiol, particularly in psychological and metabolic processes involving WHR. High testosterone is correlated with an increment WHRsin women with preof and perimenopausal, morbid obesity and polycystic syndrome [11, 12].Generally,

females have a fold of body fat more than males but the distribution of this fat is distinctly different. Through adulthood, men deposit adipose tissues in the upper part of the body, while women deposit adipose tissues in the lower part of the body particularly in the buttocks and thighs [13]. Sex hormones especially estrogens and testosterone play the central role in the distribution of body fat in human, where at puberty estrogens regulate the women body shape (gynoid), while testosterone regulates men body shape (android) [14]. Administration of hormones sex was reported to affect the body fat distribution in both genders, where it was found that males treated with estrogens were developed the gynoid fat pattern, while females that treated with testosterone were developed the pattern of android fat [15]. The previous study carried out on normal men was reported that aging process is accompanied by low concentrations of testosterone that leads to increase abdominal fat deposition and decrease lean body mass [16]. The current study aims to investigate the role of testosterone in the WHR and BMI of women with hirsutism and healthy women.

#### **Patients and Methods**

Fifty-four females with hirsutism attended to the private dermatology clinic for laser hair removal during a period extended from September 2016 to March 2017, as well as fifty-four non-hirsute females match in age as a control group in case control study in Hilla city, Babylon Province, Iraq. The severity of hirsutism was evaluated by a physician using modified Ferriman- Gallway This scoring system [17].studvwas approved by the local ethical committee, and all persons participated in this study were

signed an informed consent. The onset and duration of disease, family history, and the rate of progression, marital status, and menstrual history, the method of hair epilation and its frequency and therapy history were recorded. Physical examination such as participant's height, weight, hip and waist circumference was measured. WHR≥ 0.85 was indicated android obesity and BMI  $\geq 25-29$  kg/m2 indicate over weight and BMI of 30 kg/m2 indicate obesity. The exclusion included criteria were patients administrated hormonal any or ant androgenic therapy three months before the present study.Serum free testosterone and thyroid stimulating hormone (TSH) was determined by use ELISA Monobind Inc. (USA) kits and obeyed the manufacturer manual.

### Results

The mean age of patients was  $29.24 \pm 7.43$ years, whereas the mean age of control group was  $30.65 \pm 5.52$  years. The mean of disease duration of patients was  $8.85 \pm 5.34$  years and the onset of disease was  $18.78 \pm 5.34$ . The hirsutism score of patients was  $13.79 \pm$ 4.05. Family history of hirsutism (with first or second degree relatives in more than two members of family) was recorded in 38 (84.44%) hirsute females. Twenty (44.04%) patients were married, five (11.11%) of them were not yet have children. Twenty two (48.88%) suffer from irregular menstrual cycles.

The mean of body weight and BMI of hirsute females found to be significantly increased when compared with control group. Whereas, there was no statistically deference in mean length in the same groups, as shown in Table 1.

Table 1: Mean weight, length a	and body mass index of hirsute fem	ales and control group
	D. C. L	$\alpha \rightarrow 1$

Denometers	Patients	Control	P value	
Farameters	$Mean \pm SD$	$Mean \pm SD$		
Weight (kg)	$70 \pm 18.34$	$60 \pm 5.67$	0.02	
Length (M)	$1.59 \pm 0.05$	$1.55 \pm 0.03$	0.31	
BMI	$27.63 \pm 4.87$	$24.14 \pm 2.25$	0.04	

Thirty one (68.88%) of hirsute females found to be over weight (BMI  $\geq$ 25), twenty two of them had android obesity, and the remaining nine had non-android obesity. Waist, hip and WHR of hirsute females found to be significantly increased when compared with control group, as shown in Table 2

Table 2: Waist, hip and waist/hip ratio of hirsute females and control group

Demonsterne	Patients Control		D 1	
Parameters	$Mean \pm SD$	$Mean \pm SD$	P value	
Waist (cm)	$81 \pm 14.03$	$69.5 \pm 13.52$	0.012	
Hip (cm)	$97 \pm 14.64$	$91.5 \pm 11.3$	0.027	
W/H Ratio	$0.83 \pm 0.15$	$0.75\pm0.13$	0.019	

Free testosterone and TSH of hirsute females found to be significantly increased

when compared with control group, as shown in Table 3.

$T_{-}$ [1] $= 9$ , $T_{-}$ $= 4$ = 4 = 4 = -4 = -4 = -4 = 1 + 1		· 1	
Table 3: Free testosterone and th	vroid stimulating	2 normone of nirsute	iemales and control group
	/		

Denometer	Patient Control		Dualua	
rarameter	$Mean \pm SD$	$Mean \pm SD$	r value	
Free Testosterone pg/ml	$3.2 \pm 1.71$	$1.6 \pm 0.58$	0.001	
TSH µIU/ml	$1.87 \pm 1.11$	$1.18 \pm 0.78$	0.04	

The correlation among study parameters were investigated to conclude the benefits of

this study and shown positive significant correlations, as shown in Table 4.

Table 4: The	correlation	among stu	udy param	leters of hirsu	te females

Study Parameters		Hirsutism	BMI	WHR	Free	TSH
		Score			Testosterone	
Hirsutisn	n Score Person Correlation	1.00	0.3872	0.6866	0.7351	0.7954
	P value		0.0012	0.004	0.001	0.0001
BMI	Person Correlation	0.3872	1.00	0.6414	0.3598	0.3313
P value		0.0012		0.0001	0.038	0.0421
WHR	Person Correlation	0.6866	0.6414	1.00	0.6061	0.6166
P value		0.004	0.0001		0.0004	0.0031
Free testo	osterone Person Correlation	0.7351	0.3598	0.6061	1.00	0.4740
	P value	0.001	0.038	0.0004		0.0023
TSH	Person Correlation	0.7954	0.3313	0.6166	0.4740	1.00
	P value	0.0001	0.0421	0.0031	0.0023	

# Discussion

Hirsutism represents a serious problem due to its psychological impact on hirsute females making them distress [18]. In the present study, patients with hirsutism found to be with a high degree of distress as a consequence of its interaction with women femininity, marital and social life, and this is agreed with previous studies [18,19]. The onset age and disease progression of hirsute females in this study are approximately similar to other studies [18-20].

The family history is reported in the present study to be 84.44% of hirsute females and this result is in agreement with other previous studies [18],[21], [22] [19], whereas, family history were found in other Iraqi studies less than the result of present study [23, 24].

The family history of hirsute females may point to the genetic base of hyperandrogenism disorders like congenital adrenal hyperplasia and polycystic ovary syndrome [21, 25]. The results of the present study found appreciated percentage of patients with irregular menstrual cycles and decreased rate of infertility and this is agreed with previous studies [18- 21]. The weight and BMI of hirsute females in the present study were significantly elevated in comparison with the control group and this is in agreement with other studies carried out in Iraq [18, 19, 26]. All of this studies

mentioned that obesity is a common feature in females with hirsutism and another hyperandrogenism disease such as polycystic ovary syndrome [18, 19, 26].There are about half (48.88%) of hirsute females participated in the present study with android obesity and with significant increase in WHR when compared with control group, and this is in agreement with other studies done in Iraq and Iran, which attributed their finding to the anomaly androgen behavior that in turn may cause increase WHR, decrease fertility rate and irregular menstrual cycles. [18, 19, 27].

The levels of free testosterone in the current study were significantly increased in compassion with control, and this result is agreed with the previous study [18,19] [21] and disagreed with another study [24]. The elevated free testosterone levels thought to play the central role in hyperandrogenism manifestation of hirsute females and the hirsutism severity is associated with high free testosterone levels (the high free testosterone level the more hirsutism score) [28-29]. The level of TSH in the present study increased significantly when compared with control and this is agreed with previous studies, [30, 31] which attributed their finding to hypophyseal hypothyroidism that can act as a cofactor in hirsutism resulting in elevated TSH. The study parameters were examined and found positive correlation among hirsutism score, BMI, WHR, free testosterone and TSH with each other. The significant correlation among hirsutism score with each of BMI and WHR are agreed with previous studies [18, 27].

There was also a significant correlation between hirsutism score and free testosterone levels in the present study, and this finding is agreed with the result of previous studies [18, 25] and disagrees with other [32]. This study also found a significant positive correlation between testosterone and TSH concentrations, and this could be explained by the finding of the earlier study carried out on rats [33, 34]. These animal studies were indicated that testosterone possesses a primary stimulatory role in the controlling and secretion of TSH in circulation, in that testosterone result in raise levels of both of baseline TSH and thyrotropin releasing hormone [33, 34]. The TSH elevation may affect the hair growth because the human hair follicle responds to TSH the stimulation by [35],and hypothyroidism is a clinical feature of hirsutism [31]. An epidemiological study that done on healthy men, reports that free

testosterone has a negative relation with intra-abdominal fat mass, risk of coronary artery disease and type 2 diabetes mellitus. This study was also found that the treatment of middle-aged men with testosterone is associated with a decrease in blood glucose concentrations and visceral fat in addition to insulin sensitivity improvement [36]. Other studies indicate that when testosterone depleted with a progress of age, the adiposity of visceral is being high in men [37,38].

Whereas the situation is different in hyperandrogenism women such as PSOS and hirsutism, the testosterone concentration behaves in a manner similar in the men. It is usually, but not consistently is accompanied with high abdominal adiposity [39, 40], and this is agreed with the result of the current study. In conclusion, the result of this study may hypothesize that testosterone has a central role in the path physiological changes occur in hirsutism, ranging from the change in fat storage pattern and as consequence the HWR, to the stimulation effect of testosterone to induce TSH and its effect on hair growth. Figure 1 illustrates the role of testosterone on HWR in hirsute women.



Figure 1: Role of the testosterone on HWR in hirsute women

# Acknowledgment

Author of this study would like to thank Dr. Zena S. Alfadily for her wonderful help in samples collection and diagnosis of patients.

#### References

- 1. David Bode, Dean A Seehusen, Drew Baird (2012) Hirsutism in Women Am Fam Physician. 85(4):373-380.
- Martin KA, Chang RJ, Ehrmann DA, et al (2008) Evaluation and treatment of hirsutism in premenopausal women: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 93(4):1105-1120.
- John Mihailidis, Racha Dermesropian, Pamela Taxel, Pooja Luthra, Jane M, Grant-Kels (2015) Endocrine evaluation of hirsutism, International Journal of Women's Dermatology 1 90–94.
- 4. Akiyama M, Smith LT, Holbrook KA (1996) Growth factor and growth factor receptor localization in the hair follicle bulge and associated tissue in human fetus, J Invest Dermatol, 106:391–396.
- 5. Rosenfield RL (2005) Hirsutism N Engl J Med 353:24.
- 6. Hawryluk EB (2009) English III JC. Female adolescent hair disorders. J Pediatr Adolesc Gynecol 22(4):271–81.
- Muti P, Trevisan M, Panico S, Micheli A, Celentano E, Freudenheim JL, Berrino F(1996) Body fat distribution, peripheral indicators of androgenic activity, and blood pressure in women, Ann Epidemiol. 6(3):181-187.
- Ricardo Mondragón-Ceballos, Mónica Dafne, García Granados, Ana Lilia, Cerda-Molina, Roberto Chavira-Ramírez, Leonor Estela, Hernández-López (2015) Waist-to-Hip Ratio, but Not Body Mass Index, Is Associated with Testosterone and Estradiol Concentrations in Young Women, International Journal of Endocrinology, 654046, 6.
- 9. P Björntorp (1991) Adipose tissue distribution and function," International Journal of Obesity, 15, 67–68.
- SB Pedersen, K Kristensen, PA Hermann, JA Katzenellenbogen, B Richelsen (2004) "Estrogen controls lipolysis by up-regulating α2A-adrenergic receptors directly in human adipose tissue through the estrogen receptor α. Implications for the female fat distribution," J Clin Endocrin and Metab, 89, (4): 1869–1878.
- 11. SM van Anders, E Hampson (2005) "Waistto-hip ratio is positively associated with bio available testosterone but negatively

associated with sexual desire in healthy premenopausal women," Psychosomatic Medicine, 67, 2, 246–250.

- 12. N Santoro, J Torrens, S Crawford et al (2005) "Correlates of circulating androgens in mid-life women: the study of women's health across the nation," The Journal of Clinical Endocrinology and Metabolism, 90, 8, 4836-4845.
- 13. B Finky, N Neavez, JT Manning (2003) Second to fourth digit ratio, body mass index, waist-to-hip ratio, and waist-to-chest ratio: their relationships in heterosexual men and women, Annals of Human Biology, 30(6) 728–738.
- Bjorntrop P (1997) Body fat distribution, insulin resistance, and metabolic diseases. Nutrition, 13, 795–803.
- Vague J, Meignen JM, Negrin JF (1984) Effects of testosterone and estrogens on deltoid and trochanter adipocytes in two cases of trans sexualism. Hormone Metabolic Research, 16, 380–381.
- Vermeulen A, Goemaere S, Kaufman JM (1999) Testosterone, body composition and aging. Journal of Endocrinological Investigation, 22, 110–116.
- Bulent O Yildiz (2008) Assessment, diagnosis and treatment of a patient with hirsutism, Nature Clinical Practice Endocrinology & Metabolism 4, 294-300.
- Zena Saeed, Al-Fadhily (2012) Hirsutism: A Clinical and Biochemical Study among Iraqi Women in Hilla City, Med J Babylon, 2012, 9,1, 120-131.
- Khawla Abed, Al-Hemza Shemran (2012) Total, free testosterone and insulin hormone levels in patients with hirsutism, Med J Babylon, 9, 2, 307-312.
- Qazi Masood Ahmad, Iffat Hassan Shah, Farah Sameem, Qurat-ul-ain Kamili, Javeed Sultan (2009) Hirsutism in Kashmir: an etiological study. Indian J Dermatol. 54(1): 80-82.
- Burns T, Breathnach S, Cox N, Griffiths C, Christopher A (2004) Disorders of hair. In: Rook's Textbook of Dermatology, 7th edition, 4, (63): Blackwell publishing company, oxford 63.98-63.107.
- 22. Melissa H, Peter J (2003) Evaluation and Treatment of Women with Hirsutism. American Family Physician 67(12):2565-2572.
- 23. Sharquie KE, Al-Khafaji KA (1992) The prevalence of hirsutism in Iraqi females. Ann Saudi Med. 12(5): 453-455.

- 24. Mohammad Y, Dana S (2010) Clinical and hormonal evaluation of women presenting with hirsutism at child bearing age in Slemani city. The Iraqi postgraduate medical journal 9(4): 393-398.
- 25. Al-Robaee A, Al-Zolibani A, Al-Shobaili A, Aslam M (2008) Update on hirsutism. Acta Dermatoven APA 17(3): 103-119.
- 26. Alsantali A, Shapiro J (2009) Management of hirsutism. Skin Therapy Letter 14(7): 1-3.
- 27. Sotoudeh G, Mirdamadi S, Siassi F, Khosravi S, et al (2003) Relationships of overweight and obesity with hormonal and metabolic parameters in hirsute women. Act Medical Iranica 41(1):37-44.
- 28. Habif TP (2010) Clinical dermatology: A color guide to diagnosis and therapy, 5th edition, chapter 24, Mosby Elsevier inc., china 926-931.
- 29. Ralf P, Elise A, Andrew G (2008) Hair Growth Disorders. In: Fitzpatrick's Dermatology in General Medicine, 7th edition, 1, (86), McGraw-Hill 775-776.
- 30. Sachdeva S (2010) Hirsutism: Evaluation and treatment. Indian J Dermatol 55:3-7
- 31. Alterihy F, Shemran KA, Alta'ee AH, Jabuk S Kh (2012) The association between thyroid hormones and lipid profile in patients with primary hyperthyroidism. Medical Journal of Babylon, 9(4), 721-727.
- 32. Qazi Masood Ahmad, Iffat Hassan Shah, Farah Sameem, Qurat-ul-ain Kamili, Javeed Sultan (2009) Hirsutism in Kashmir: an etiological study. Indian J Dermatol. 54(1): 80-82.
- 33. Farbota L, Hofmann C, Oslapas R, Paloyan E (1987) Sex hormone modulation of serum TSH levels, Surgery. 102(6):1081-1087.

- 34. Borges PP, Curty FH, Pazos-Moura CC, Moura EG (1998) Effect of testosterone propionate treatment on thyrotropin secretion of young and old rats in vitro, Life Sci. 62(22):2035-2043.
- 35. Gáspár E, Hardenbicker C, Bodó E, Wenzel B, Ramot Y, Funk W, Paus R (2010) Thyrotropin releasing hormone (TRH): a new player in human hair-growth control. The FASEB Journal, 24(2), 393-403.
- 36. Bhasin S (2003) Effects of testosterone administration on fat distribution, insulin sensitivity, and atherosclerosis progression, Clin Infect Dis. 37 Suppl 2:S142-9.
- 37. Allan CA, Strauss BJ, Burger HG, Forbes EA (2008) Mc Lachlan RI: Testosterone therapy prevents gain in visceral adipose tissue and loss of skeletal muscle in nonobese aging men. J Clin Endocrinol Metab 93:139–146.
- 38. Stevens J, Katz EG, Huxley RR (2010) Associations between gender, age and waist circumference. Eur J Clin Nutr 64:6–15.
- 39. Carmina E, Bucchieri S, Esposito A, Del Puente A, Mansueto P, Orio F, Di Fede G, Rini G (2007) Abdominal fat quantity and distribution in women with polycystic ovary syndrome and extent of its relation to insulin resistance. J Clin Endocrinol Metab 92:2500-2505.
- 40. Barber TM, Golding SJ, Alvey C, Wass JA, Karpe F, Franks S (2008) Mc Carthy MI: Global adiposity rather than abnormal regional fat distribution characterizes women with polycystic ovary syndrome. J Clin Endocrinol Metab 2008, 93:999–1004.