Hirsutism in patients with lichen planopilaris (LPP)

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Background
Lichen planopilaris (LPP) is a form of autoimmune scarring alopecia with unknown etiology. Androgenic hormones may have a role in progression of LPP especially in menopausal women which could be associated with hirsutism. Therefore, we investigated the frequency of hirsutism as one of the clinical manifestations of androgen excess in women with LPP.

Patients and methods
This cross-sectional study was done during 5 years on 60 female LPP patients. Patients' data were age, age-onset of LPP, menstrual status, body mass index (BMI), presence or absence of hirsutism, age-onset and location of hirsutism and history of nonfollicular lichen planus.

Results
Patients' mean age was 46.53±10.03 years. Mean of age-onset of LPP in women was 41.35±10.48 years. Hirsutism was detected in 28.3% of cases. The mean of age-onset of LPP was 30.47±9.11 in women with hirsutism. Less than half of LPP patients (48.3%) were nonmenopausal women, of whom 41.4% had irregular menstrual periods. Overweight and obesity was detected in 43 (43.71%) of LPP cases. Age-onset of LPP in menopausal women was significantly higher than nonmenopausal women ($P < 0.001$). Frequency of obesity in the menopausal and nonmenopausal groups was not significantly different.

Conclusion
More than a quarter of LPP patients had hirsutism. Due to high frequency of hirsutism in Iranian women, our findings do not show higher frequency of hirsutism in LPP cases compared with other women.

Keywords:
androgen, hirsutism, lichen planopilaris, menstruation

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Introduction

Lichen planopilaris (LPP) is a follicular form of lichen planus (LP) that is more frequent in middle-aged female patients [1,2]. It has been described as an uncommon autoimmune scarring alopecia in which stem cells of hair follicles have been damaged by T lymphocytes infiltration [3,4]. Some inflammatory cytokines may result in activation of fibroblasts and scarring alopecia. Main target antigen for LPP is unknown. Recent studies show that increased levels of androgenic hormones may have a role in progression of LPP especially in menopausal women. Also LP has been associated with metabolic syndrome, obesity, and polycystic ovary syndrome in which androgenic hormones could be elevated [1,2,5–8]. Naturally, in menopausal women levels of testosterone and dehydroepiandrosterone sulfate (DHEAS) usually decrease, but in menopausal women with LPP, levels of androgenic hormones increase [8]. Androgens may increase peri-follicular inflammation in LPP patients [9,10].

Hirsutism has been defined as terminal hair growth in a male pattern distribution. It mainly occurs in androgen sensitive area such as chin, upper lip, cheek, chest, medial thighs, peri-areolar and peri-umbelical areas. It has been estimated that about 5–15% of women are affected by hirsutism world-wide, but in some countries including Iran it has a higher prevalence [11–13]. The exact prevalence of hirsutism in Iran is unknown but hirsutism in Iranian women in reproductive ages is more frequent compared with European countries. It has been estimated as 15% up to 36% in prior reports [14–16].

We proposed that if there is any pathogenic role for androgenic hormones in LPP, frequency of hirsutism as a variably expressed presentation of androgen excess may be increased in LPP patients. Considering of this concept, the frequency of hirsutism in female patients with LPP has been investigated in this study but

evaluation of androgenic hormone levels was not the aim of this study.

Patients and methods

In this cross-sectional study, 60 women with LPP diagnosis during 5 years were evaluated for clinical presentation of hirsutism on androgen dependent areas such as chin, upper lip, cheek, neck, peri-areolar, peri-umbelical and medial thighs. LPP was confirmed by dermoscopy and histopathologic evaluation for a more accurate diagnosis [17]. Patients' data included age, menstrual status, body mass index, history of hirsutism, location of hirsutism, age-onset of hirsutism, age-onset of LPP and history of nonfollicular involvement of cutaneous lichen planus. Regular Menstruation has been defined as cycle repeated about once every 28–32 days with duration 5–7 days and other than this definition was considered as irregular menstruation [18]. Data about age-onset of hirsutism and age-onset of LPP was collected based on the patients' history so it had a recall bias.

Cases of frontal fibrosing alopecia (FFA) and drug-induced hirsutism were not included in this study. Due to extensive use of hair removal modalities, exact evaluation of hirsutism score was not considered in our study. Also patients with a history of hirsutism who had removed permanently unwanted hairs with laser modalities were excluded.

Data were analyzed using SPSS Software 18 (SPSS Inc., Chicago, Illinois, USA). Quantitative variables were described using mean±standard deviation and median (minimum–maximum) and qualitative data were described using number and percent. Comparison of age-onset of LPP, body mass index (BMI) and menstruation status in hirsute and non-hirsute patients was performed using Mann–Whitney and χ^2Chi-Square tests. Significance level was set as P less than 0.05

Results

Sixty LPP female patients with mean age of 46.53 ±10.03 (17–70 years) were enrolled. Mean of age-onset of LPP was 41.35±10.48 (13–61 years old).

We found two patients of early-onset LPP in our study; a 17-year-old female patient who had LPP from 4 years ego (13 years old), and a 36-year-old obese woman (BMI=31) who had LPP since 16 years old and early-onset hirsutism since 9 years old with a family history of LPP in her mother and grandmother. Forty three (71.67%) of LPP patients were obese or overweight. Most of LPP patients, 41 (68.3%) cases, had no other involvement but scalp area. (Table 1)

Hirsutism was detected in 17 (28.3%) of female patients with LPP. Mean age of hirsutism onset in LPP patients with hirsutism was 30.47±9.11 (9–43 years old). The mean age of hirsutism onset in menopausal LPP patients was 36.14±6.49 and the mean age of hirsutism onset in nonmenopausal women was 26.6±8.77 years old. Hirsutism in all postmenopusal women had been developed gradually during many years before menopause. The mean duration of hirsutism in menopausal LPP patients was 16±7.6 years and in nonmenopausal LPP patients was 14.1±7.38 years.

Median age-onset of LPP was 49 years old in menopausal women and 36 years old in nonmenopausal women which shows a significant difference ($P<0.001$). Chin area was involved in 16 (94.1%) of LPP patients with hirsutism. Other locations of involvement in hirsute cases were medial thigh [8 (47.1%) cases); upper lip [7 (41.2%) cases]; peri-areolar (7 (4.2%) cases]; peri-umbelical [4 (23.5%) cases], and cheek [1 (5.9%) case].

There was no significant difference in frequency of obesity between LPP patients with and without

Table 1 Characteristics of Lichen planopilaris patients (*N*=60)

Variable			No. (%)
Body mass index (BMI) (Kg/m^2)	18.5–24.9	17 (28.3)	
	25.0–29.9	22 (36.7)	
	≥30	21 (35.9)	
Menstruation status	Nonmenopause	Regular menstruation	17 (58.6)
		Irregular menstruation	12 (41.4)
	Menopause	31 (51.7)	
Lichen planus lesions in other areas (other than scalp) in LPP patients	No lesion	41 (68.3)	
	Only skin lesions	12 (20.0)	
	Only mucosal lesions	1 (1.7)	
	Skin and mucosa	5 (8.3)	
	Nail involvement	1 (1.7)	

hirsutism (P=0.218). Also, there was no significant difference in frequency of obesity between menopausal or nonmenopausal patients (P=0.244).

Age-onset of LPP, body mass index and menstruation status in LPP patients with and without hirsutism were compared in Table 2 which shows no significant difference between two groups.

Discussion

In our study, age-onset of LPP was 13-61 years old and we found two cases of juvenile LPP. In one case there was a family history of LPP. Cutaneous LP may have a familial pattern but we could not find familial classic LPP in previous reports. However familial FFA and graham little syndrome have been reported [19–21].

Age-onset of LPP has been reported as 16–76 years by Lyakhovitsky and 25–70 years by Brankov *et al.* [5,20]. However, 30–60 years old was the most common age range for the first presentation of LPP. Early-onset LPP in juvenile patients is a rare finding which is usually not associated with extra-scalp involvement. It has been reported in children aged 10–16 years old. Childhood LPP is more frequent in boys compared with adulthood LPP which is more frequent in women [19]. We found that 51.7% of our patients were menopause and age-onset of LPP in menopausal women was significantly higher than nonmenopausal cases. In previous reports, 69 and 65.8% of LPP cases were menopausal women [6,22]. This difference could be explained in two ways; more incidence of LPP cases in younger women or late-onset menopause in our cases.

We observed that more than two thirds of LPP patients had no extra-scalp involvement and about one-third of cases had mucosal and cutaneous lesions. Extra-scalp lesions were observed in 17–28% of LPP patients in previous reports [1,2].

We observed that 28.3% of LPP cases had hirsutism. Frequency of hirsutism in Iranian women has been estimated as 15, 22, and 36% in previous reports [14–16]. Therefore, it seems that hirsutism is not a more frequent finding in women with LPP compared with other Iranian women. However, we did not have an age-matched control group in our research. Also, the population enrolled in this study was a combination of nonmenopausal and postmenopausal women and we had no estimation about the prevalence of hirsutism in postmenopausal women in our country, so different prevalence of hirsutism in postmenopausal women makes a bias for the final results of this study.

More than one-third of LPP patients (35.9% of cases) had obesity similar to Branko study which found 32.6% of LPP cases were obese without significant difference with control group [5]. Tabrizi and colleagues reported that 32.2% of Iranian women were obese. Also, Bahrami and colleagues observed that 68.6% of Iranian women were overweight or obese similar to our study which showed overweight or obesity in about 70% of cases [23,24].

Hirsutism could be associated with obesity. We observed that BMI of LPP patients with hirsutism was higher that nonhirsute LPP cases but this difference was not significant and most of our patients in both groups were overweight. This lack of difference could be explained by small size of this study and high prevalence of obesity in Iran. Although cutaneous LP is associated with metabolic syndrome and obesity, association of LPP with obesity is questionable [8]. Ranasinghe and colleagues reported that 31% of LPP cases were hirsute, 27.6% had ovarian dysfunction, 14.9% had irregular mensturation, 36.9% of LPP cases had BMI higher than 30 and 21.4% were overweight [2]. However, Brankov, et al. in a research of Cleveland Clinic Foundation reported that 1.3% of control women and 11.4% of LPP cases had hirsutism with a significant difference. It seems that frequency of hirsutism in their population was significantly lower than our country. Brankov and colleagues observed no significant difference in frequency of obesity in LPP and control group [5]. BMI usually increases in

Table 2 Comparison of age-onset of Lichen planopilaris, body mass index and mePP patients with and without hirsutism

Variables	LPP with hirsutism (N=17)	LPP without hirsutism (N=43)	P value
Age-onset of LPP (y)			
Mean±SD	40.29±10.29	41.77±10.64	0.554*
Median (Min-max)	42 (16–56)	45 (13–61)	
Body Mass Index (Kg/m^2)			
Mean±SD	29.28±3.61	27.51±4.29	0.104*
Median (Min-max)	29.90 (23.07–36.16)	26.77 (19.14–40.0)	
Menstruation status			
Menopause	7 (41.2%)	24 (55.8%)	0.307**
Nonmenopause	10 (58.8%)	19 (44.2%)	

*Mann-Whitney Test.

postmenopausal women; however we did not find significant difference in BMI of LPP cases in pre and postmenopausal women.

Ranasinghe explained that hyperandrogenism and polycystic ovary syndrome have been associated with LPP but hypoandrogenism has been associated with FFA [2]. Androgenic hormones have a role in progression of LPP and increased incidence of LPP in post-menopausal women could occur due to this hyperandrogenic status [2,25]. Levels of Testosterone and DHEAS hormones usually decrease with menopause but in LPP cases the levels of these hormones are similar to non-menopausal status. It has been recommended that levels of androgenic hormones should be evaluated in LPP cases with hirsutism and obesity, because these patients may have benefits from anti-androgen treatments for LPP as antiandrogens could suppress inflammatory process in these women [6]. However, some researchers believe that androgenic hormones are not the main cause for LPP as there is non-androgen dependent involvement of hair follicles in occipital, parietal area of scalp and eyebrow or eyelashes in LPP cases [8]. Also, we found that all cases of LPP associated with hirsutism had a long history of hirsutism before LPP onset, so it may fade the role of androgenic hormones. However, we had only one patient with early-onset LPP and hirsutism with severe obesity.

We found hirsutism in menopausal LPP women was presented about 10 years after nonmenopausal women. Delayed-onset hirsutism in menopausal women may show a late-onset hormonal disturbance in this group. New-onset hirsutism in an old woman should be checked for androgen secreting tumors [25] but we had no case of new-onset hirsutism in menopausal women. Production of ovarian estrogen hormone decreases with aging which results in decreased level of sex hormone binding globulin but ovarian androgen production does not change. Therefore free testosterone level increases which could result in late-onset hirsutism [25].

Androgen levels in LPP cases were not evaluated in this research and frequency of hirsutism in LPP cases was evaluated as one of the clinical manifestations of androgen excess. However hirsutism could be a manifestation of peripheral pilosebaceous sensitivity to normal levels of androgens [25].

FFA patients were not enrolled in this study because it has a different clinical presentation compared with classic LPP with fronto-temporal and eyebrow involvement. Nasiri and colleagues observed that DHEAS and androstenedione levels were significantly lower in FFA but total testosterone and free testosterone level were not significantly different compared with control group. They showed that 26.7% of FFA patients had hirsutism and obesity. DHEAS could prevent scar formation because it has an anti-inflammatory and inhibitory effect on dermal fibroblasts. Therefore, DHEAS deficiency may increase the chance of scarring alopecia [26].

We did not find higher frequency of hirsutism in LPP cases compared with estimated prevalence of hirsutism in Iranian women as the prevalence of hirsutism in our country is higher than USA or European countries. There were some limitations in this study; small sample-sized study, not considering an age-matched control group, no measurement of androgenic hormones, no evaluation of other cutaneous presentations of androgenic hormones other than hirsutism such as acne, seborrhea and female pattern androgenetic alopecia.

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Ethics declarations

Ethical approval: This research project was approved by the ethics committee of Guilan University of Medical Sciences (code: IR.GUMS.REC.1400.074) and supported by the Vice Chancellor of Research and Technology, Guilan University of Medical Sciences. This study was conducted in accordance with the principles for human experimentation as defined in the Declaration of Helsinki.

Consent to participate: Informed consent was obtained from all individual participants included in the study.

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Conflicts of interest

The authors declare no competing interests.

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