

Evaluation of the Demographic Characteristics and the Factors Related to Eyebrow Involvement in Frontal Fibrosing Alopecia: A Retrospective, Cross-sectional, Single Center Study

Frontal Fibrozan Alopesili Hastalarda Demografik Bulguların ve Kaş Tutulumunu Etkileyen Faktörlerin Değerlendirilmesi: Geri Dönük, Kesitsel, Tek Merkezli Çalışma

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ABSTRACT Objective: Frontal fibrosing alopecia (FFA) is a rare subtype of primary cicatricial alopecia leading to the gradual recession of the frontotemporal hairline. Eyebrow and facial hair alopecia commonly accompany the scalp hair loss. The usual FFA patient is a postmenopausal female. The most common comorbid diseases in FFA patients are thyroid diseases. In this retrospective, cross sectional study, we aimed to determine the demographic characteristics of the patients with FFA, prevalence of eyebrow involvement and the factors that are associated with eyebrow involvement at the time of evaluation. **Material and Methods:** A total of 16 patients who were diagnosed with FFA at our department from January 2010 to January 2020 were enrolled in this study. Demographic features and histopathological data were collected from medical records in our Hair Disorders Polyclinic. The statistical analysis was performed with the SPSS-21. **Results:** A total of 16 patients were included in this study. All of the patients were females. Eyebrow loss was observed in 12 (75%) of our patients. The age of the patients had no statistically significant relationship to the eyebrow involvement ($p=0.666$). Likewise, there is no statistically significant relationship of disease duration to eyebrow involvement ($p=0.668$). Eyebrow involvement was also more common (75%) in patients who have comorbidity. **Conclusion:** Similar to the literature, FFA was found to be more common in postmenopausal female patients in our study. There was no statistically significant relationship between eyebrow loss and the duration of the disease or the age of the patient, but it was striking that the frequency of eyebrow involvement was more common in patients with comorbidities. These data obtained from our study have not been reported in the literature before, and larger patient series are needed to explain the relationship more clearly.

Keywords: Frontal fibrosing alopecia; eyebrows; comorbidity; cicatricial alopecia; age

ÖZET Amaç: Frontal fibrozan alopesi (FFA), nadir görülen, frontotemporal saç çizgisinde progresif geriye doğru saç kaybı ile karakterize bir primer skatrisyel alopesi alt tipidir. Hastalarda, saçlı derideki kayıpların yanı sıra sıklıkla kaş tutulumu ve yüz kıllarında da kayıp izlenmektedir. En sık postmenopozal kadın hastalarda görülür ve en sık eşlik eden hastalık tiroid bezi hastalıkları olarak bildirilmiştir. Bu retrospektif, kesitsel çalışmada, kliniğimize başvuran klinik ve histopatolojik bulguları ile FFA tanısı alan hastaların demografik bulgularının, kaş tutulumu sıklığının ve kaş tutulumunu etkileyebilecek faktörlerin değerlendirilmesi amaçlanmıştır. **Gereç ve Yöntemler:** Bu çalışmaya, Ocak 2010 ve Ocak 2020 tarihleri arasında hastanemizde FFA tanısı alan 16 hasta dâhil edilmiştir. Hastalara ait demografik özellikler ve histopatolojik veriler kliniğimiz saç hastalıkları polikliniği takip dosyalarından retrospektif olarak taranmıştır. İstatistiksel analiz SPSS-21 ile yapılmıştır. **Bulgular:** Bu çalışmaya katılan 16 hastanın, hepsi kadın idi. Kaş tutulumu, hastaların 12'sinde (%75) mevcuttu. Hastaların yaşı ile kaş tutulumu arasında istatistiksel olarak anlamlı fark bulunmadı ($p=0,666$). Benzer şekilde, hastalık süresi ile kaş tutulumu arasında da anlamlı fark izlenmedi ($p=0,668$). Kaş tutulumu sıklığının komorbiditesi olan hastalarda daha sık olduğu izlendi (%75). **Sonuç:** Çalışmamızda, literatürle benzer şekilde FFA'nın postmenopozal kadın hastalarda daha sık olduğu görüldü. Kaş dökülmesi ile hastalık süresi veya hastanın yaşı arasında istatistiksel olarak önemli bir ilişki bulunamamıştır ancak kaş tutulumu sıklığının komorbiditesi olan hastalarda daha sık görülmesi dikkat çekiciydi. Çalışmamızdan elde ettiğimiz bu veriler, literatürde daha önce bildirilmemiş olup, aradaki ilişkinin daha net açıklanabilmesi için daha geniş hasta serilerine ihtiyaç duymaktadır.

Anahtar Kelimeler: Frontal fibrozan alopesi; kaşlar; komorbidite; skatrisyel alopesi; yaş

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Frontal fibrosing alopecia (FFA) is a primary form of lymphocytic cicatricial alopecia, leading to the gradual recession of the frontotemporal hairline. Eyebrow and facial hair alopecia commonly accompany scalp hair loss.^{1,2} It was first described by Kossard et al. in 1994 as cicatricial alopecia primarily affecting the postmenopausal women; however, after this report, many case reports about FFA affecting premenopausal females, males and even pediatric patients have been reported as well.³ The most common comorbid diseases in FFA patients are thyroid diseases. Increased levels of serum androgens may be observed as well; the associations need more evidence though.³ The treatment modalities that may be used in FFA are oral 5-alpha reductase inhibitors, oral hydroxychloroquine, topical calcineurin inhibitors, and excimer laser.⁴

FFA is a relatively rare disease and in this study, we aimed to evaluate the demographics, comorbid diseases, and treatment modalities used in FFA. We also wanted to determine whether there is any relationship between disease duration, patients' age and having comorbidity, and the eyebrow involvement at the time of evaluation.

MATERIAL AND METHODS

STUDY DESIGN AND PARTICIPANTS

The patients who were presented to the İstanbul University-Cerrahpaşa, Cerrahpaşa Medical Faculty, Dermatology Department, Hair Diseases Outpatient Clinic from September 2010 until September 2020 were included in the study. The patients without the histopathologic confirmation of FFA were excluded from the study. The age, gender, disease duration, eyebrow involvement, comorbid diseases, and

treatment modalities used for each patient were noted.

ETHICS

The approval of İstanbul University-Cerrahpaşa, Cerrahpaşa Medical Faculty Ethics Committee was obtained (approval date and number: 12.10.2020-134019). The patient has provided written consent to have her photo published. Informed consent was taken from each patient.

STATISTICAL ANALYSIS

The statistical analysis was performed with the SPSS-21. The normality control was examined by using the Kolmogorov-Smirnov test for the duration of the disease and age separately for the duration of the disease and for the above-mentioned normality control, and also because the number of our data is very low, non-parametric tests were used.

Continuous variables were expressed as mean±standard deviation (SD), whereas the categorical variables were expressed as (%). The relationships of disease duration and patients' age to the eyebrow involvement were analyzed with the Mann-Whitney U test and Fisher's exact test. A p value of 0.05 was accepted as the threshold for statistical significance.

RESULTS

DESCRIPTIVES

A total of 16 patients were included in this study. All of the patients were females. [Figure 1](#) shows a typical patient from the right and left-hand sides respectively. The youngest patient was 39 years old and the oldest patient was 70 years old; the mean age of the patients was 51.9 years with a standard deviation of



FIGURE 1: Cicatricial hair loss in the frontal region also affecting eyebrows.

TABLE 1: Classification of the patients according to the disease duration and age.

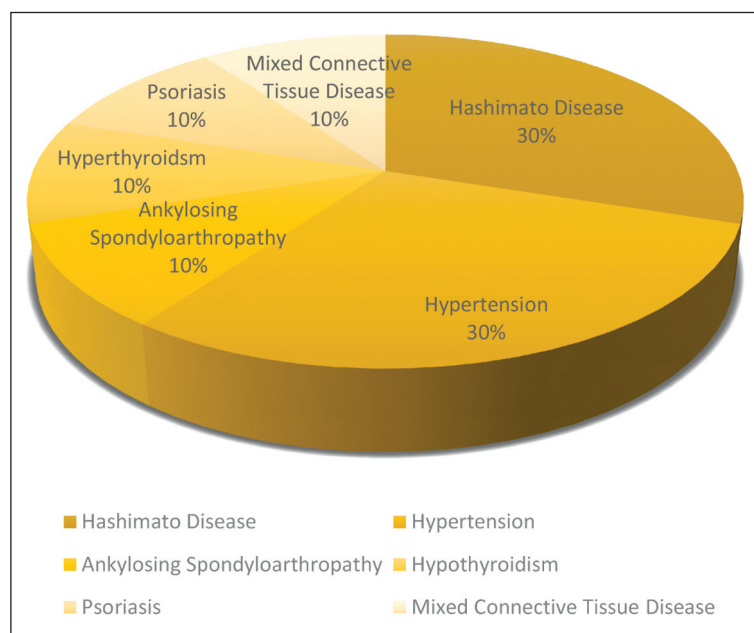
	Group 1		Group 2	
	Disease duration 60 mo> (n=10)	Age (y)	Disease duration 60 mo< (n=6)	Age (y)
Mean	28.40	51.10	104.00	53.33
Median	24.00	51.00	72.00	51.00
Standard deviation	15.108	8.478	70.245	6.890
Minumum	2	39	60	48
Maximum	48	70	120	67

7.8 years. Disease duration was classified into two groups as having disease more than 60 months and less than 60 months. Ten patients had FFA for more than 60 months and 6 patients had FFA for less than 60 months. The shortest disease duration was 2 months and the longest disease duration was 120 months (Table 1).

FREQUENCIES

Of the 16 patients, 12 (75%) had eyebrow involvement and 4 (25%) did not have eyebrow involvement. As for the comorbid diseases, 3 (30%) had Hashimoto disease, 3 (30%) had hypertension, 1 (10%) had ankylosing spondyloarthritis, 1 (10%) had hyperthyroidism, 1 (10%) had psoriasis and 1 (10%) had mixed connective tissue disease. The dis-

tribution of comorbid diseases is shown in Figure 2. The most frequent treatment modalities used were topical corticosteroids and topical minoxidil in 5 (28%) patients. Intralesional steroids were used in 4 (22%) of the patients. Systemic steroids and systemic hydroxychloroquine were used in 2 (11%) of the patients. The treatment modalities that were used are summarized in Figure 3. The relationship of the disease duration and eyebrow involvement was compared in two groups including patients who have FFA for at least five years and more than five years. There was no statistically significant difference in eyebrow involvement of the patients between the two groups (p value=0.511) (Table 2). All of the patients in our study were diagnosed in the first two years of the hair loss symptoms. In 7 (58.3%) patients the eyebrow in-

**FIGURE 2:** Comorbid diseases observed in frontal fibrosing alopecia patients.

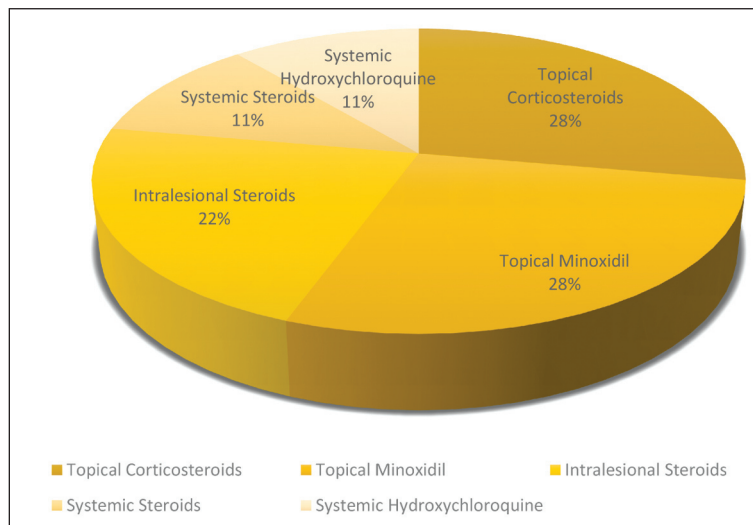


FIGURE 3: Treatment modalities used in frontal fibrosing alopecia patients.

TABLE 2: Comparison of eyebrow involvement according to disease duration.

		Eyebrow involvement		
		Negative	Positive	Total
60> months	Count	3	7	10
	% within duration	30.0%	70.0%	100.0%
	% of Total	18.8%	43.8%	62.5%
60< months	Count	1	5	6
	% within duration	16.7%	83.3	100.0%
	% of Total	6.3%	31.3%	37.5%
Total	Count	4	12	16
	% within duration	25.0%	75.0%	100.0%
	% of Total	25.0%	75.0%	100.0%

Fisher's Exact test; p value >0.05 (p= 0.511).

involvement occurred before the diagnosis of FFA and this duration was changing from 6 months-2 years. In 5 (41.7%) patients, the eyebrow involvement started concomitantly with scalp alopecia. The frequency of comorbidities was also found to be increased in patients who have eyebrow involvement. Eight of 12 (75%) patients with eyebrow involvement have existing comorbid disease. Also in 4 patients who do not have eyebrow involvement, only 1 (25%) patient has existing comorbidity. There was no statistically significant relationship between the age of the patient and the eyebrow involvement (Z=0.431, p=0.666) (Mann-Whitney U test). Likewise, there is no statistically significant relationship of disease duration to eyebrow involvement (p=0.668).

DISCUSSION

FFA is a rare subtype of primary cicatricial alopecia, characterized by a lymphohistiocytic infiltration histologically. Clinically a band-like frontal and temporoparietal recession is the characterized involvement of the disease that was named after this unique presentation. FFA is more common in women especially in the postmenopausal period, rarely in men. Our patient population was composed of exclusive females. Similar to ours, a previous study by Secchin et al. also reported an exclusively female patient population.⁵ Zhang et al. reported a population composed of 97% females, Kanti et al. of 95% females, and Maldonado Cid et al. of 97% females.^{3,6,7} Recently, a case series of 7 male FFA patients has also been published; however, male patients are still a minority.⁸ The result of this study in terms of gender distribution is in alliance with the previous literature: FFA is a disease that predominantly affects females.^{3,5-7} The increased prevalence of FFA in women especially in the postmenopausal period suggests the hormonal factors in disease pathogenesis. The role of sex hormones is not proven yet, while some studies found no correlation between sex hormones and FFA disease activity, in some studies, abnormal testosterone and estrogen values were found to be associated with lesser disease activity, and in a recent paper demonstrating that the serum levels of dehydroepiandrosterone sulfate (DHEAS) and an-

drostenedione were significantly lower in FFA patients compared to healthy controls. The authors claim that the strong antifibrotic effect of DHEAS on fibroblasts may be associated with this mechanism.⁹ These hypotheses were not proven and still needs to be investigated in a larger population.

The mean age of our patient population was 51.9 years; the youngest patient was 39 years old and the oldest patient was 70 years old. FFA predominantly affects the post-menopausal age group; only 21% of the patients being premenopausal.¹⁰ The average age of menopause is 51 years; usually ranging between 49-52 years. This age depends on environmental factors though. Thus, similar to the previous literature, our patient population is also mainly composed of postmenopausal female patients.¹¹ A previous study by Starace et al. has reported the average age of FFA patients as 62.5 years.¹⁰ Kanti et al. reported an average age of 60 years with 84% of the female patients being postmenopausal.³ Maldonado Cid et al. reported an average age of 61 years with 93% of the patients being post-menopausal.⁷ Secchin et al. reported an average age of 62 years with 94% being post-menopausal.⁵ Our results support the previous literature in that FFA is predominantly seen in the postmenopausal age group. This study could be further improved by noting the menopausal status of each patient.

In our study, eyebrow involvement was noted in 75% of the patients with FFA. Starace et al. have reported 86%, Maldonado Cid et al. 93%, and Secchin et al. 81%.^{5,7,10} Our result is lower than the previously reported in literature. Still, the majority of the patients in this study have shown the loss of eyebrows, which

supports the previous literature.^{5,7,10} Eyebrows frequently respond to therapy which intrigues clinicians to the idea that eyebrow alopecia is reversible. Yet, histologic evidence shows that fibrous tracts are present alongside active inflammatory cells implying that eyebrow alopecia, like scalp alopecia, is cicatricial in FFA.¹² Katoulis et al. have previously reported a relationship between the total loss of eyebrows in FFA to the irreversibility of scalp alopecia.¹³ Although many researchers studied the loss of eyebrows in FFA, there are no previous studies in the literature studying the relationship of disease duration, existing comorbidity, and patients' age to eyebrow involvement. We did not find a statistically significant relationship between eyebrow alopecia and the disease duration or the patient's age. Yet, our study is the first study to examine such a relationship.

The mean disease duration was 56.75 months; the shortest disease duration being 2 months and the longest disease duration being 120 months. Maldonado Cid et al. reported a mean disease duration of 48 months, Starace et al. reported 52 months, Kanti et al. reported 24 months, and Valesky et al. reported 68 months.^{3,7,10,14} Furthermore, Starace et al. showed that there is no relationship between the disease duration and disease severity.¹⁰ To our knowledge, there are no previous studies regarding the relationship between disease severity and eyebrow involvement.

The comparison of our results to previous literature is seen in [Table 3](#).

In the literature, several autoimmune diseases have been reported to be associated with FFA, suggesting that there is an autoimmune etiology in the

TABLE 3: Comparison of our results to literature.

	Female patients (%)	Average age of patients (years)	Eyebrow involvement (%)	Average disease duration (mo)
Uzuncakmak et al	100	51.9	75	56
Secchin et al. ⁵	100	62	81	-
Zhang et al. ⁶	97	-	-	-
Cid et al. ⁷	95	61	93	48
Kanti et al. ³	97	60	-	24
Starace et al. ¹⁰	-	62.5	86	52
Valesky et al. ¹⁴	-	-	-	68
Samrao et al. ¹⁸	97	60	75	-

pathogenesis of FFA.¹⁵⁻²⁰ Especially the frequency of hypothyroidism is significantly increased in these patients.¹⁹ Similarly, the most common comorbid diseases observed in our FFA patients were Hashimoto disease (hypothyroidism) and hypertension; both seen in 30% of the patients. Similar to our result, Zhang et al. also reported that the most commonly observed comorbidity was thyroid diseases seen in 45% of the patients: 35% had hypothyroidism and 10% had hyperthyroidism.⁶ Likewise, we also found that 10% of the patients had hyperthyroidism. Starace et al. have reported that 27% of the patients had hyperthyroidism.¹¹ Valesky et al. reported that 58.3% of the FFA patients had concomitant hypothyroidism and 50% had hypertension. Thus, similar to our study, Valesky et al. reported that the most commonly reported comorbid diseases were hypothyroidism and hypertension.^{14,15} It was suggested to routinely workup of the thyroid hormone levels in patients who have FFA due to this common frequency.

Ankylosing spondyloarthropathy (10%), psoriasis (10%), and mixed connective tissue diseases (10%) were the other autoimmune diseases that we have observed in our patient population. Psoriasis was observed in 7% and connective tissue diseases were observed in 6% of the FFA patient population of Zhang et al.⁶ Again, in terms of comorbid diseases, our study is in alliance with the previous literature.

Although there is no current proven therapy for FFA several treatments have been reported to be effective in FFA. Topical and systemic corticosteroids, hydroxychloroquine, oral finasteride or dutasteride, and oral antimalarials are the most commonly used agents.¹⁸⁻²⁰ Systemic tetracycline 500 mg twice daily, doxycycline 100 mg twice daily and topical tacrolimus 0.1% ointment were also offered as an initial treatment.²⁰ We observed that the most frequent treatment modalities used in our patient population were topical corticosteroids and topical minoxidil in 28% patients; intralesional steroids in 22% of the patients; systemic steroids and systemic hydroxychloroquine in 11% of the patients. It is important to note that many of the patients received more than one treatment modality during their disease. Ho et al. re-

ported that the most commonly used treatment modalities for FFA were intralesional steroids and oral 5-alpha reductase inhibitors.¹⁷ Starace et al. reported that systemic and intralesional steroids, systemic 5-alpha reductase inhibitors and systemic hydroxychloroquine were frequently used in the treatment of FFA. On the contrary, topical therapies were seldomly used.¹⁰ Similar to our results, Secchin et al. also reported that topical steroids and topical minoxidil (5%) were common treatment modalities for FFA.⁵ Thus, there is no consensus in terms of the treatment of FFA.

CONCLUSION

Our study supported the literature in that FFA is a disease that is predominantly seen in postmenopausal female patients. Eyebrow loss was observed in 75% of our patients; again in an alliance of the previous literature. We have found no significant association between eyebrow loss and disease duration or the patient's age. This makes our study unique since this relationship was not studied before. Similar to the previous literature, hypothyroidism and connective tissue diseases frequently accompanied FFA in our patient population. Topical treatment modalities were used commonly in our patient population. This result supports some of the results in the previous literature, a consensus about the treatment modalities has not been yet established though.

Limitations

The limited sample number and the retrospective nature of this study are the main restriction of this research.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Tuğba Kevser Uzunçakmak, Defne Özkoca; **Design:** Tuğba Kevser Uzunçakmak, Defne Özkoca; **Control/Supervision:** Özge Aşkın, Server Serdaroğlu; **Data Collection and/or Processing:** Tuğba Kevser Uzunçakmak, Defne Özkoca, Özge Aşkın; **Analysis and/or Interpretation:** Tuğba Kevser Uzunçakmak, Defne

Özkoca, Özge Aşkın; **Literature Review:** Tuğba Kevser Uzunçakmak, Defne Özkoca, Özge Aşkın; **Writing the Article:** Tuğba Kevser Uzunçakmak, Defne Özkoca; **Critical Review:** Özge Aşkın, Server Serdaroğlu; **References and Findings:** Tuğba Kevser Uzunçakmak, Defne Özkoca, Server Serdaroğlu; **Materials:** Tuğba Kevser Uzunçakmak, Özge Aşkın, Server Serdaroğlu.

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