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Research Article

The significance of yellow dots in diffuse non-scarring alopecia: A case-control study

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Abstract

Diffuse non-cicatricial alopecias are commonly caused by pattern baldness and telogen effluvium. Differentiating between the two may be challenging as patients may have features of both telogen efflubium and pattern baldness. The number of yellow dots that are seen on trichoscopy may help in making differentiation between these conditions, which is of significance from the treatment and prognosis aspects of view. In this case-control study, yellow dots were significantly seen in pattern baldness and in combined telogen effluvium and pattern baldness in all five scalp areas examined. In the frontal area, they had a sensitivity of 62% and 76.6% and a specificity of 96.2% and 96.2% for diagnosing pattern baldness and combined telogen effluvium and pattern baldness respectively. The smallest cutoff value for yellow dots in the frontal area in both conditions was four yellow dots while in the occipital area, it was one yellow dot.

Keywords: Pattern baldness, telogen effluvium, trichoscopy.

Introduction

Diffuse hair loss of variable intensity is a common problem faced in the practice of dermatologists. Pattern baldness and telogen effluvium (TE) are the two most common forms of diffuse non-cicatricial alopecia (Lin et al., 2019). Sometimes diagnosis can be difficult with traditional tests. Trichoscopic evaluation can provide helpful insights about the diagnosis of these conditions (Romero & Grimalt, 2015).

Yellow dots represent follicular infundibula that are filled with sebum and/or keratotic material. They differ in shape and size. They either have a single color throughout or have a distinctive inner pattern. The yellow dots are empty follicles devoid of hair shafts although sometimes they may harbor a vellus, cadaverized, or dystrophic hair. Terminal hair likely helps to push out sebaceous material from follicles; this explains the existence of yellow dots on bald sites (Suryakant et al., 2021; Waśkiel et al., 2018). In pattern baldness, sebum is secreted directly to the skin surface via a miniaturized hair follicle, and accumulates on the follicular opening, producing a yellow dot that is composed mainly of sebum and keratotic material (Rudnicka et al., 2012). Furthermore, yellow dots are commonly seen in alopecia areata, and may also be present in other conditions such as alopecia areata incognita, trichotillomania, and chemotherapy-induced alopecia (Tosti, 2016).

Children having alopecia areata show yellow dots less frequently than adults due to underdeveloped sebaceous glands, they are seen in 50% of children and 60%-94% of adults (Waśkiel-Burnat et al., 2019; Alessandrini et al., 2019). Yellow dots' number increases with chronicity of the disease, making them a marker of severity (Kibar et al., 2015). Generally, yellow dots are observed easily on lighter skin and are hardly seen on darker skin (Gómez-Quispe et al., 2022).

Yellow dots have been extensively studied in patchy alopecia, especially alopecia areata, however in diffuse alopecia, most studies were on female pattern hair loss (FPHL), our study focuses on yellow dots in the different types of diffuse non-scarring alopecia. To the best of our knowledge, this is the first research that addresses the validity of yellow dots in five scalp areas in different types of diffuse non-scarring alopecia.

Martial and methods

A case-control study enrolled 291 patients with diffuse hair fall and 184 healthy subjects without hair fall as controls. Patients and controls were chosen from attendees of the Erbil Dermatology Teaching Center who met the inclusion criteria.

Inclusion criteria: Male and female patients with diffuse hair fall of the non-scarring type, all age groups were included.

Exclusion criteria: Patients with evidence of inflammatory scalp diseases, scarring alopecia, pregnant ladies, patients on therapy for hair fall, hair shaft disorders, cancer patients, and cases when there was uncertainty about the diagnosis.

After explaining the aims and objectives of the study, proper consent was obtained from all subjects, and for those below eighteen years of age guardian assent was obtained.

History was taken, and data were recorded including age, duration of hair loss, and the type of hair loss; whether suddenly increased shedding or gradual diffuse thinning, a recent childbirth, menstrual irregularities, excessive body hair, psychological and physical stress, and family history of hair loss.

A general examination was performed and physical findings of hyperandrogenism like acne, striae, acanthosis nigricans, and hirsutism were looked for. A hair pull test was done, and a positive test was defined as pulling out 2 to 3 hairs from multiple areas of the scalp (McDonald et al., 2017). The diagnosis was made based on history, findings on physical examination, and trichoscopy. Four types of alopecia were determined:

1. Acute TE: When the duration of hair fall is less than six months and occurs two to three months after a triggering event with a positive hair pull test.
2. Chronic TE: When hair loss persists for at least six months or more, other causes have been ruled out, there are no signs of pattern hair loss, and the hair pull test is positive.
3. Pattern baldness: Typical distribution of hair thinning and a negative hair pull test. Male and female patients with diffuse thinning of the crown area and a preserved frontal hairline were classified according to Ludwig's type to grades 1,2, and 3. For females with breached frontal midline and widened central part of the scalp without diffuse hair loss, the Christmas tree pattern of hair loss was classified according to the Olsen scale. The Hamilton- Norwood classification was used in males and females when thinning was associated with bitemporal recession (Chan & Cook, 2018).
4. Combined TE and pattern baldness: When the patient has significant hair loss with evident thinning and a positive hair pull test

Trichoscopy was performed using Fotofinder Medicam 1000 video-dermoscope, manufactured by FotoFinder Systems GmbH, Bad Birnbach, Germany. Polarized mode was applied at a magnification of 40X. The device is supplied with software by which measurements can be done. Images were captured, photos were analyzed and findings were recorded. Trichoscopy was performed in hair separation lines in five scalp areas: frontal, right and left temporal, vertex, and occipital (Jayasree et al., 2021). In each area two photos were taken at 40X magnification, making a total of ten photos for each patient and control subjects. The trichoscopic examination focused on identifying the presence of specific features, namely, yellow dots number, hair shaft

diameter diversity, empty follicles, percentage of pilosebaceous units with one, vellus hairs percentage, peripilar sign, and upright regrowing hair.

Trichoscopic diagnosis of TE was given when the following were identified: Upright regrowing hairs, a predominance of follicular units with only one hair, empty hair follicles, and, lack of trichoscopic features typical of other hair loss conditions. (Saqib et al., 2021; Alessandrini et al., 2021)

For the diagnosis of male pattern baldness, the following were required: Hair shaft diameter diversity, short vellus hairs (<0.03 mm), peripilar sign, yellow dots, and, an increase in the percentage of single hair follicular units in the frontal area as compared to the occipital area.

For FPHL, the criteria came about by Rakowska et al. were applied (Rakowska et al., 2009). FPHL can be diagnosed with the fulfillment of two major criteria or one major and two minor criteria.

When trichoscopic features of pattern baldness and multiple upright regrowing hairs were identified, the diagnosis of combined pattern baldness and TE was given.

Any patient who did not fit the above clinical and trichoscopic features or when there was a doubt in the diagnosis, was excluded from the study. Controls were healthy individuals who did not have hair loss or any other scalp disorder. The study was approved by the ethics committee of the College of Medicine- Hawler Medical University.

The IBM SPSS software package, version 26.0, was used for data analysis. Quantitative data were expressed in minimum, maximum, and mean±SD. The parametric data were analyzed by independent samples t-test. Categorical data were analyzed using the Chi-square test. The level of significance was set at 0.05. ROC curve was applied, the smallest cutoff value was set and the validity of yellow dots was assessed through sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

Results

No significant difference was found between cases and controls regarding sex and age groups. A significant association of age with the diagnosis was found p-value < 0.001. Both acute TE and chronic TE were found mainly in the age group 10-39 years, and least were found in the extremes of age less than 10 years and above 50 years old, pattern baldness and cases of combined pattern baldness and TE were seen among the age groups 20-49 years. The majority of our patients were females (Table 1).

Table 1. Sex distribution in cases and controls

Sex	Acute TE No. (%)	Chronic TE No. (%)	Pattern baldness No. (%)	Combined TE& pattern baldness No. (%)	Control No. (%)	Total No. (%)	p-value
Female	36(90.0)	103(96.3)	43(86)	82(87.2)	153(83.2)	417(78.79)	
Male	4(10)	4(3.7)	7(14)	12(12.8)	31(16.8)	58(12.21)	< 0.001
Total	40(100)	107(100)	50(100)	94(100)	184(100)	475(100)	

During trichoscopic evaluation, no difference was found between the right and left temporal regions; thus, only one side results was considered. The mean yellow dot number in two fields of vision (FOV) in acute TE was not statistically significantly different from the control in all the five areas examined. In chronic TE the mean number of yellow dots was significantly more than in controls in the frontal, parietal, and vertex areas. In pattern baldness and combined pattern baldness (Figure 1) and TE, the mean number of yellow dots was significantly higher than controls in all scalp areas examined. Table (2) shows the precise value of yellow dots for each diagnosis and scalp area. The highest number of yellow dots were observed in the frontal area in combined pattern and TE and pattern baldness (5.4043±2.95238) and (4.8824±3.59248) respectively. Accordingly, the numbers in the occipital area were (0.48 ±0.877) and (0.73 ±1.801) respectively. The mean number was also higher in the combined pattern and TE than pattern baldness for the vertex area (2.14±1.788) and (1.78 ±2.129) respectively. In acute TE the highest value of yellow dots was in the frontal and temporal areas, 1.350 (±1.791) and 1.10 (±1.411) respectively, while in chronic TE they were highest in frontal and vertex areas, 1.7009(±1.4355), and 1.24(±1.607) respectively. The normal values for each area are shown in the above tables. It has been observed that the zero number of yellow dots in the control group is significantly higher than in the case groups across all areas and all four diagnoses.

Table 2. Yellow dots number in the hair loss conditions

Yellow dots in two FOV (range)		Acute TE		Chronic TE		Pattern baldness		Combined TE & Pattern baldness		Control
		No. (%)	p-value	No. (%)	p-value	No. (%)	p-value	No. (%)	p-value	No. (%)
Frontal area	0	12 (30.0)	0.267*	19 (17.8)	0.005*	5 (10.0)	<0.001*	3 (3.2)	<0.001	62 (33.7)
	1-4	27 (67.5)		85 (79.4)		21 (42.0)		32 (34.0)		120 (65.2)
	5-8	0 (0.0)		3 (2.8)		17 (34.0)		46 (48.9)		2 (1.1)
	>8	1 (2.5)		0 (0.0)		7 (14.0)		13 (13.8)		0 (0.0)
Temporal area	0	19 (47.5)	0.605*	45 (42.1)	0..065*	12 (24.0)	<0.001*	20 (21.3)	<0.001*	99 (53.8)
	1-4	20 (50.0)		58 (54.2)		29 (58.0)		63 (67.0)		82 (44.6)
	5-8	1 (2.5)		4 (3.7)		8 (16.0)		9 (9.6)		3 (1.6)
	>8	0		0		1 (2.0)		2 (2.1)		0 (0.0)
Vertex area	0	20 (50.0)	0.284	48 (44.9)	0.001*	20 (40.0)	0.002*	18 (19.1)	<0.001*	109 (59.2)
	1-4	20 (50.0)		53 (49.5)		27 (45.0)		70 (74.5)		75 (40.8)
	5-8	0		6 (5.6)		2 (4.0)		5 (5.3)		0
	>8	0		0		1 (2.0)		1 (1.1)		0
Occipital area	0	32 (80.0)	0.156*	84 (78.5)	0.201	31 (62.0)	0.001*	65 (96.1)	0.002	156 (84.8)
	1-4	7 (17.5)		23 (21.5)		18 (36.0)		29 (30.9)		28 (15.2)
	5-8	1 (2.5)		0 (0.0)		0 (0.0)		0 (0.0)		0 (0.0)
	>8	0		0 (0.0)		1 (2.0)		0 (0.0)		0 (0.0)
Total		40		107 (100)		50 (100)		94 (100)		184 (100)

* Fisher's Exact test

This difference is particularly evident in cases of pattern baldness and combined pattern baldness and TE, where a greater number of yellow dots were noted. No statistically significant association between the grading of pattern hair loss and the number of yellow dots was found p-value >0.05.

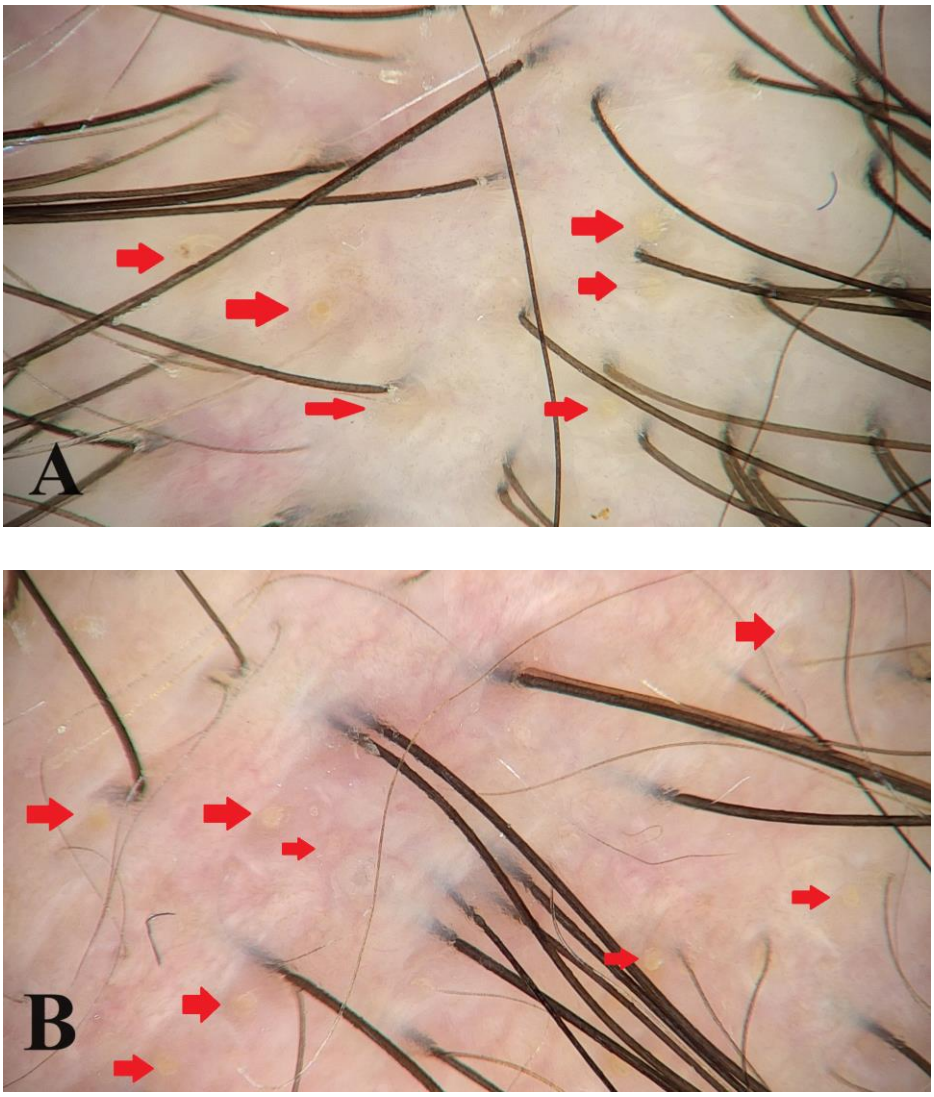

Figure 1. A 32 years old female with the diagnosis pattern baldness. A: Trichoscopy of scalp area, 40X. The red arrows showing multiple yellow dots. B: Trichoscopy of parietal area, 40X. The red arrows showing multiple yellow dots.

Regarding the highest cutoff values of yellow dots, frontal area exhibited the highest cutoff value of yellow dots across all diagnoses. Specifically, this value was 3 for acute and chronic TE and 4 for pattern baldness and combined cases. Notably, this result was highly significant for the last two conditions (pattern baldness and combined cases of pattern baldness a TE) (Table 3).

After analysing the sensitivity and sepcifity of yellow dots in relation to the given hair loss diagnosis we found ou the following (Table 3):

Table 3. Sensitivity and specificity of yellow dots and ROC curve vlues

Type of hair loss	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	The smallest cutoff value*	AUC**	P-value
Acute TE							
Frontal area	17.5	89.1	25.9	83.2	3	0.495	0.914
Temporal area	32.5	84.2	31	85.2	2	0.565	0.200
Vertex area	32.5	85.9	33.3	85.4	2	0.580	0.115
Occipital area	20.0	84.8	22.2	83	1	0.524	0.637
Chronic TE							
Frontal area	23.4	89.1	55.6	66.7	3	0.607	0.002
Temporal area	29.9	84.2	52.5	67.4	2	0.584	0.017
Vertex area	18.7	97.3	80	67.3	3	0.604	0.003
Occipital area	21.5	84.8	45.1	65	1	0.533	0.354
Combined pattern baldness and TE							
Frontal area	76.6	96.2	91.1	88.9	4	0.909	<0.001
Temporal area	55.3	84.2	64.2	78.7	2	0.741	<0.001
Vertex area	61.7	85.9	69	81.4	2	0.787	<0.001
Occipital area	30.9	84.8	50.9	70.6	1	0.580	0.029
Pattern baldness							
Frontal	62.0	96.2	81.6	90.3	4	0.845	<0.001

area							
Temporal area	58.0	84.2	50	88.1	2	0.735	<0.001
Vertex area	50.0	85.9	49	86.3	2	0.673	<0.001
Occipital area	38.0	84.8	40.4	83.4	1	0.615	0.012

ROC analysis results yields *the smallest cutoff value and **AUC (Area under the curve), which indicates the power of significance of the sensitivity and specificity with higher values toward 1.

1. In acute TE: a low sensitivity and a high specificity in the frontal area, 17.5% and 89.1% respectively. Highest sensitivity (32.5%) with lower specifity ,84.2% and 85.9%, was for the parietal and vertex areas respectively.
2. In chronic TE: the highest sensitivity for yellow dots was found in the parietal area of 29.9%, while the frontal area had a sensitivity of 23.4%, the corresponding specificities were 84.2% and 87.1%. A high positive predictive value was achieved in the vertex area of 80%.
3. In pattern baldness and combined cases of pattern baldness and TE: the frontal area showed a sensitivity of 62% (which was higher than acute and chronic TE) and specificity of 96.2%, and a similar specificity was calculated in cases with combined TE and pattern baldness with a higher sensitivity of 76.6%. A positive predictive value of 90.1% was found in the frontal areas of combined cases and 81.6% in pattern baldness.

Discussion

Yellow dots are empty follicular infundibula, they can be round or polycyclic, yellow to yellow-pink, and may lack or contain miniaturized, regrowing, cadaverized, or dystrophic hairs. On reflectance confocal microscopy a marked decrease in follicular adnexal structures and empty adnexal lumens filled with highly refractile material is seen corresponding to the yellow dots observed on dermoscopy (Ardigò et al., 2011). Yellow dots have been identified in different conditions. According to Sukanya et al. (2023), yellow dots were identified in 95% of alopecia Areata, 66.6% of discoid lupus erythematosus, and 100% of both androgenetic alopecia and seborrheic dermatitis (Sukanya et al., 2023). Yellow dots are an important trichoscopy feature that differentiates pattern baldness from chronic TE and is a major criterion for FPHL. These

criteria have a diagnostic sensitivity of 72% and a specificity of 98% for FPHL (Rakowska et al., 2009).

We noticed the highest number of yellow dots in the frontal area in patients with combined pattern baldness and TE (5.4043±2.95238) and next comes pattern baldness, while Rakowska et al. (2009) found the highest number of yellow dots in the frontal area of patients with female pattern baldness (8.86 ± 4.8) (Rakowska et al., 2009). This could be because the combination of two pathologies may enhance the findings, meanwhile, the difference in number could be due to the higher magnification they applied.

Yellow dots have been identified as a sensitive marker for the diagnosis of alopecia areata, though their sensitivity increased from 89.6% to 97.4% when associated with short vellus hairs according to Bapu et al. (2006) (Ross et al., 2006; Bapu et al., 2014).

Yellow dots have been identified in male and female pattern baldness. Being more predominant in the frontal region than the occipital area, they are of irregular size and distribution and are less numerous than is found in alopecia areata (Lima et al., 2017).

Park et al. (2015) found yellow dots in patients with diffuse alopecia in 11.8% of pattern baldness and 9.4% of TE (Park et al., 2015). Different studies reported variable yellow dot percentages, according to Ummiti et al. (2019) they were found in 92.4% of males and 88% of females with pattern baldness (Ummiti et al., 2019), Mani et al. (2018) found them in 18% of males pattern baldness patients and no patient with FPHL exhibited yellow dots (Mani et al., 2018). Vora et al. (2019) found them in 74.63% of male patients (Vora et al., 2019). Hu et al. (2015) noticed them in 20.1% of males and 24.0% of females with pattern baldness (Hu et al., 2015). Another study identified yellow dots in 52.88% of patients with pattern baldness with no significant differences between female and male androgenic alopecia (Kasumagic-Halilovic, 2021). We observed no correlation between the grading of pattern baldness and the number of yellow dots. This contrasts with other studies in which they were identified in more advanced stages of the condition (Bhat et al., 2020; Hu et al., 2015).

A total number of two yellow dots in the temporal and one in the occipital in pattern baldness and much lower values in TE and controls were found by Rakowski, et al. (2009), their results were comparable to ours (Rakowska et al., 2009). We noticed a significant number of yellow dots in the frontal and vertex areas of chronic TE and those patients did not fit the criteria of pattern baldness. In TE empty hair follicles appearing as yellow dots are a common finding (Lacarrubba et al., 2015). Yellow dots in these two areas have high specificity and low

sensitivity with the vertex area having a high PPV. The minimum number of yellow dots required to give a positive diagnosis was four in pattern baldness and combined pattern baldness and TE in the frontal area which was concordant with other investigators, the corresponding number for TE was three which supports the diagnosis of TE by eliminating one of the major criteria of pattern baldness (Rakowska et al., 2009). Here comes the importance of having a global assessment of the scalp by examining five scalp areas as the vertex area is not routinely part of the trichoscopic examination. In acute TE the level of significance was not reached in any scalp area indicating that chronic hair loss is a factor for the development of yellow dots. No study has evaluated the significance of yellow dots in TE we suggest that they should be investigated because of the probability of the concomitant existence of pattern baldness. Several studies have evaluated the validity of trichoscopy in the diagnosis of hair loss disorders (Saqib et al., 2021; Kowalska-Oledzka et al., 2012; Al-Refu, 2018; Dhurat, 2018; Ross et al., 2006). Bhamla et al. (2013) stated that trichoscopy is 75% sensitive and 61.54% specific in the diagnosis of early FPHL (Bhamla et al., 2013) but very few studies are found evaluating individual trichoscopic features. A study found the sensitivity and the specificity of yellow dots in FPHL in the frontal scalp to be 74% and 100% respectively compared to controls (Nagar & Dhudshia, 2019), which is comparable to our results. High sensitivity was found for yellow dots in the frontal area in combined pattern baldness and TE and slightly lower results for pattern baldness with a PPV of 91.1% and 81.6 % respectively. In light of the high sensitivity of yellow dots in some types of alopecia, a negative result would suggest absence of the hair loss condition. However, with a high specificity, a positive result confirms the presence of the hair loss condition.

Conclusion

The presence of yellow dots is a highly significant trichoscopic feature that can be used to accurately diagnose pattern baldness and combined pattern baldness from telogen effluvium cases. Specifically, in the frontal area, trichoscopic identification of yellow dots has statistically the most significant highiest values of sensitivity and specificity in the diagnosis of pattern baldness and cases of combined pattern baldness and TE, in which the sensitivity of 62.0% and 76.6%, and a specificity of 96.2% in cases of pattern baldness and combined conditions of pattern baldness and TE, respectively. This significant trichoscopic feature can be used to

accurately identify subtle conditions, determine prognostic factors, and predict potential outcomes.

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