

Alternating and coexisting skin diseases: Are they real concepts?

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Abstract

Background coexisting diseases are diseases that coexist with each other while alternating ones is the condition where one disease give place to another. In daily clinical practice, an increasing numbers of such conditions were seen. The exact pathogenesis is not fully understood.

Objective To find out if alternating and coexisting diseases are present in the clinical practice and to assess the frequency and various clinical aspects of common coexisting and alternating skin diseases among a sample Iraqi patients.

Methods A cross sectional analytical study that was designed to include (4390) patients, with dermatological diseases regardless their types, but conditionally to be existed with two or more diseases, focusing on the main four entities namely psoriasis, vitiligo, lichen planus and alopecia areata. The period of the study extended from January 2019 until February 2020. The included patients were collected from dermatology outpatient clinic in Al-Sadr teaching hospital, Basra - Iraq. The patient were subjected to full medical history and physical examination, skin biopsy was done in suspicious cases to confirm the diagnosis.

Results From the total number of attendants to outpatient clinic, 53 patients have coexisting dermatological diseases, which constitute about 1.2% of the total, 62.3% of them were males, while 37.7% were females. The most frequent coexisting diseases were vitiligo and psoriasis which accounted for 28 (52.83%) of the total, followed by vitiligo and lichen planus which were 9 (16.98%), while psoriasis and lichen planus were 7 (13.2%), psoriasis and alopecia areata were 4 (7.55%), vitiligo and alopecia areata were 3 (5.67%) and finally lichen planus and alopecia areata were 2 (3.77%) of the total. Regarding the distribution of the cases according to their age, there is no significant statistical difference between males and females, p-value = 0.636, while according to onset of the first disease and second coexisting disease, there is significant statistical difference between males and females, p-value= 0.027, 0.001 respectively.

Conclusion Coexisting and alternating skin diseases are really present in clinical practice, although the exact pathogenesis is not well known, but we thought that one disease may trigger or alternate with others because they share immunological and or genetic predispositions so that another study on larger sample size and thorough immunological and genetic investigations are advisable to clarify this issue.

Key words

Coexisting diseases; Psoriasis; Vitiligo; Lichen planus; Alopecia areata.

Introduction

Coexisting disorders mean the presence of more than one disorder in an individual patient at the same time.¹ Many terms have been used in medical literature in English to describe the

presence of multiple disorders in a single patient at the same time.² The most frequent term used is called comorbidity.³ Multi-morbidities or coexisting disorders represent the second highest frequently term used to describe the existence of more than one or multiple chronic or long-term

conditions in an individual patient.⁴ Many published cases reported the coexistence of two or more skin diseases at the same time in one patient.^{2,5-8} In addition a study with a large sample size, 390 patients admitted to medical wards in Dar es Salaam, Tanzania, reported many co-existing skin disorders and most of them being non-infectious conditions (142/390), whereas, (123/390) cases were infectious dermatoses.^{6,9} On the other hand, the term alternating diseases refer to the condition where one skin disease gave place on resolution to another one. The most common coexisting skin diseases that were reported in literature are psoriasis, vitiligo, lichen planus and alopecia areata. The exact pathogenesis of coexisting or alternating diseases is not clear, but it has been thought that genetic predisposition and environmental factors may possibly play a role in their pathogenesis. In daily practice, we noticed an increasing number of coexisting or alternating diseases, so that this study was designed to highlight this issue and to find out whether they are a true concepts and the frequency of their occurrence.

Methods

A cross sectional analytical study was designed to include (4390) patients, with dermatological diseases regardless of their types, but conditionally to be existed with two or more diseases. The period of the study extended from 1st week of January 2019, until last week of February 2020. The included patients were collected from dermatology outpatient clinic in Al-Sadr teaching hospital, Basra City, southern of Iraq.

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Inclusion criteria Any patient regardless of his age, gender, residence and occupation with simultaneous two or more dermatological diseases.

Exclusion criteria Any patient with single dermatological disease.

Ethical considerations An ethical approval was obtained from Arab board of dermatology-Basra training center directorate to perform the study. An informed consent was also taken from all participants or their parents (regarding the children).

Definition of variables of interest:

- 1- **Age:** age groups were classified accordingly, where the age subcategorized into six age groups:
 - a) Preschool children less than 6 years as preschool age group.
 - b) 6-12 years as primary schooling age.
 - c) Teenage: those between 12-18 years as intermediate and secondary schooling age.
 - d) Young adult (18-35 years)
 - e) Adults (35-45 years)
 - f) Old adults (45-64 years)
 - g) Elderly (64 years and more)
- 2- Sex that was sorted into male and females.
- 3-Date of development of each disease.
- 4- Types of dermatological diseases as listed in introduction.

Tools of the study:

1. Structured questionnaire: which was focused on:

- a) Personal identity: Name, age, gender.
 - b) Medical history: The patients were subjected to full medical history regarding current illnesses, duration of each, progression, family history of the diseases of interest, social history and drug history.
2. Physical examination for type of disease, area of involvement and severity of involvement.
3. Investigations: some of the patients were sent for skin biopsy to confirm the diagnosis.
4. Camera type: iPhone Xs Max.

Procedures of recording, coding and checking of data The data directly registered in the questionnaire form at the work field and checked on Monday and Wednesday weekly through the period of the study. A quantitative approach was used for coding and the questionnaire data was pre-coded by using of statistical package for social science (SPSS) version (25).

Statistical analysis:

SPSS version (25) was used for data analysis. Descriptive statistic in forms of frequencies, percentages and graphical presentation, test of significance (chi-square) was used for analysis of variables. Means and standard deviations were used to present data of continuous variables. A P-value <0.05 was considered statistically significant.

Results

The over-all number of attendances to dermatology outpatient clinic was (4390), from this total, 53 patients have coexisting dermatological diseases, which constitute about

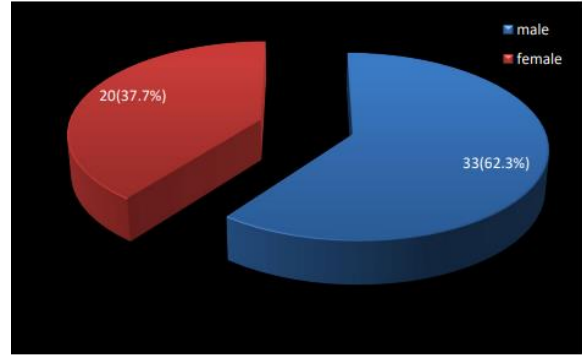


Figure 1 Distribution of coexisting diseases according to gender.

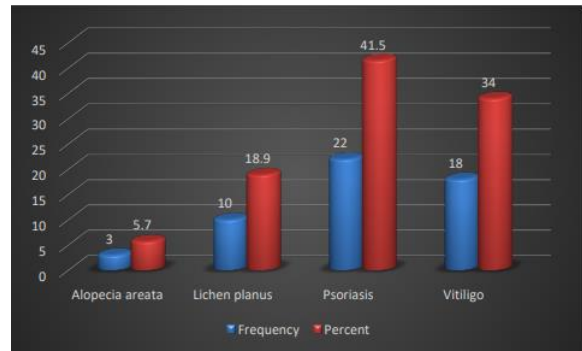


Figure 2 Distribution of the first disease.

1.2% of the total, 62.3% of them where males, while 37.7% were females as shown in **Figure 1**.

Regarding the disease that's considered as first disease of presentation, psoriasis and vitiligo representing the majority of cases, where they represent 41.5% and 34% respectively, followed by lichen planus which constitutes 18.9%, while alopecia areata representing 5.7% as shown in **Figure 2**. For second disease of presentation, vitiligo and psoriasis also representing the majority of cases, where they represent 41.5% and 32.1% respectively, followed by lichen planus which constitutes 15.1%, while alopecia areata representing 11.3% as shown in **Figure 3**.

As shown in **Table 1**, the most frequent coexisting diseases were vitiligo and psoriasis which accounted for 28 (52.83%) of the total,

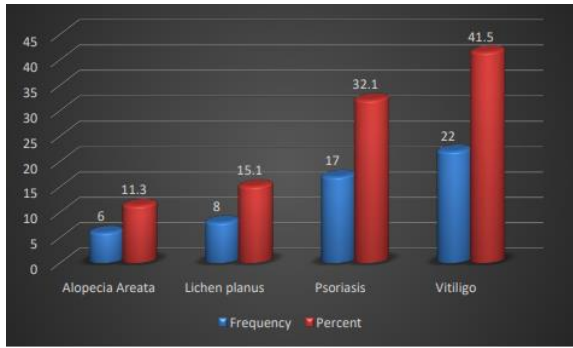


Figure 3 Distribution of the second disease.

followed by vitiligo and lichen planus which were 9 (16.98%), while psoriasis and lichen planus were 7 (13.2%), psoriasis and alopecia

areata were 4 (7.55%), vitiligo and alopecia areata were 3 (5.67%) and finally lichen planus and alopecia areata were 2 (3.77%) of the total as shown in **Figure 4-8**. Regarding the distribution of the patients according to their age, there is no significant statistical difference between males and females, p value = 0.636, while regarding the duration of starting of the first dermatological disease and second coexisting disease, there is significant statistical difference between males and females, p-value = 0.027, 0.001 respectively where the second disease occurred earlier in females in comparison with males as shown in **Table 2**.

Table 1 Cross tabulation of the first disease and second coexisting disease.

First disease		Second disease				Total	X ² , P
		AA	LP	Ps	Vt		
AA		0	0	1	2	3	32.6
		0.0%	0.0%	33.3%	66.7%	100.0%	
LP		2	0	4	4	10	0.001
		20.0%	0.0%	40.0%	40.0%	100.0%	
Ps		3	3	0	16	22	0.001
		13.6%	13.6%	0.0%	72.7%	100.0%	
Vt		1	5	12	0	18	0.001
		5.6%	27.8%	66.7%	0.0%	100.0%	
Total		6	8	17	22	53	0.001
		11.3%	15.1%	32.1%	41.5%	100.0%	

Table 2 Distribution of cases according to age, sex and duration of first and coexisting diseases.

	Gender	Mean	Std. Deviation	P value
Age by years	Male	31.2	16.6	0.636
	Female	29	19	
Duration of 1 st disease by years	Male	6.1	9.5	0.027
	Female	3.1	2.5	
Duration of 2 nd disease by years	Male	0.57	0.37	0.001
	Female	1.2	0.9	



Figure 4 Coexistence of Vitiligo and Psoriasis in a 25 years old female. (Author photo)



Figure 5 Coexistence of Psoriasis and Alopecia areata in a 35 years old male. (Author photo)



Figure 6 Coexistence of Lichen planus and Vitiligo in a 58 years old female. (Author photo)



Figure 7 Coexistence of Vitiligo and Lichen planus in a 32 years old male. (Author photo)



Figure 8 Coexistence of Alopecia areata and Vitiligo in a 23 years old female. (Author photo)

Discussion

In the current study and throughout one year, the frequency of coexisting or alternating diseases was 1.2% among the attendance of the dermatology clinic indicating that this combination is a real problem in dermatological practice. The study was also showed that there is no statistically significant differences between males and females, but regarding the onset of first and second diseases there is a significant statistical difference between males and females as the second was reported to occur earlier in females, the exact cause behind this is not well understood, but possibly it can be attributed to the nature of hormonal changes in females that increases the likelihood of having autoimmune and immunologically mediated diseases earlier.

These findings were inconsistent with that of other studies, which can be attributed to the difference in sample size and the diseases included in this study where four diseases were included in the present study instead of only two that had been reported by other studies.^{10,11} According to the onset of the first dermatological disease and second coexisting disease, there was significant statistical difference regarding to age, gender and types of diseases, these findings are similar to many other studies.¹²⁻¹⁴ In summary for our findings regarding the duration of the diseases, we can't predict which disease might coexist with other, and when that coexistence might occur; as the cause for this coexistence is still not clear, also the autoimmune diseases are unpredictable in their courses. Regarding the disease that's

considered as first disease of presentation, vitiligo and psoriasis representing the majority of cases, where collectively representing about 75% of the total number of cases, followed by lichen planus which constitutes about 20% of the total, while alopecia areata representing about 5%, while regarding the second disease of presentation, vitiligo and psoriasis also representing the majority of cases, where collectively representing about 74% of the total number of cases, followed by lichen planus which constitutes about 15% of the total, while alopecia areata representing about 11%. This differs from other studies that assessed the frequency and prevalence of the dermatological diseases and systemic diseases,^{15,16} because this study was intended for the chronic diseases rather than acute ones. The concept of coexisting diseases means the presence of more than one skin disease sharing the same site or different sites at the same time. It differs from the concept of alternating diseases, in which, one disease gives place to another unrelated disease.⁵ Among the studied group, many patients had the second disease while the first one is still present, i.e. both diseases are present at the same site of the same patient, which means that they are coexisting diseases (69.8%), while in the remaining (30.1%) patients, the second disease presented when the first one is completely resolved. The time when the second disease appear is variable ranging from 1 week to 2 -3 months. The latter group is considered as alternating diseases. From these findings, one can conclude that the concept of coexisting and alternating diseases are really present in daily clinical practice as it was reported in about 1.2% of outpatient dermatological clinic. The exact mechanism behind these two concepts is not well established, although they are seen in clinical practice and have been mentioned in literature, but the included diseases are possibly sharing same immunological and genetic predisposition that may be modified by

environmental factors and one disease may trigger the other at the same time or after its resolution. In addition, it has been suggested that this might occur because what is called Wolf's isotopic phenomenon, in which one disease give rise to another unrelated disease, this differs from Koebner's isomorphic phenomenon, where trauma give rise to the appearance of the same disease in the traumatized site, in the presence of the same lesion elsewhere.¹⁷ On the other hand, renbök phenomenon stated that the appearance of a new unrelated disease at the site of resolved lesion of other disease.¹⁸ Ovcharenko, Yuliya *et al.* describe a 23-year-old female patient with psoriasis, who underwent improvement of a psoriatic plaque on the scalp simultaneously with the development of a patch of alopecia areata.¹⁸ To the best of our knowledge, this is the first study that found out the frequency of coexisting and alternating skin diseases among a relatively large number of those patients attending dermatology outpatient's clinic rather than case reports of one patients as in previous studies.

Limitations of the study

1. The duration of the two diseases in the study, mainly depending on memory of the patient regarding the onset of the first disease and the duration of the development of coexisting disease.
2. Pandemicity of COVID-19 that interrupted the outpatients work, so remarkably affected the collection of data throughout the last 8 months of 2020.

Conclusions

1. The frequency of alternating and existing diseases was 1.2% of the dermatological outpatient attendances.

2. The most frequent combination was psoriasis and vitiligo, as they were reported in 28 (52.83%) of the total coexisting cases.

3. Coexisting and alternating skin diseases are really present in clinical practice, although the exact pathogenesis is not well known, but we thought that one disease may trigger or alternate with others because they share immunological and or genetic predispositions so that another study on larger sample size and thorough immunological and genetic investigations is advisable to clarify this issue.

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