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Original Article

Epidemiological aspects and disease association of childhood vitiligo

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Abstract

Objective To determine, for the first time in Iran, different epidemiological aspects and association of vitiligo with diseases between children and adults.

Methods This was a cross-sectional study with 324 participants, divided into 3 groups, each consisting of 108 of cases. The first group consisted of sex matched adults with vitiligo, second group were children between 2 and 18 years old with vitiligo (case group) and the third group were children with other skin disorders being matched for age and sex. Laboratory tests such as FBS, thyroid function test, CBC/Differentials and anti TPO antibody obtained from the participants and the type of the vitiligo was recorded.

Results Our findings showed that thyroid abnormalities were seen in 4.5% of children of the case group. FBS was higher in only one child with vitiligo. Family history of vitiligo was significantly different between children with vitiligo and those with other skin disorders (p=0.001).

Conclusion In our research, most of the children with vitiligo had positive anti-TPO antibody, confirming the importance of anti –TPO screening test in vitiligo patients.

Key words
Vitiligo, thyroid abnormality, children

Introduction

Vitiligo is an acquired pigmentary and occasionally familial skin disorder that affects melanocytes of the hair and skin.[1] Prevalence of vitiligo is 1-2%, without any sex, racial and regional differences.[2-7] In almost half of the patients, it starts before the age of 18 years old and congenital forms are uncommon.[8]

Although etiology of the disease is unknown, but there are several theories including autoimmune and neurologic mechanisms, genetic factors, role of oxidative stress or toxic metabolites and absence of melanocyte growth factor.[9-12] Autoimmune theory is supported by the association of vitiligo with other autoimmune disorders especially thyroiditis with hypothyroidism that is the most common association in adults with vitiligo (30%). On the other hand there is not enough data about the prevalence of thyroiditis in children with vitiligo.[9,10]

There are several types of clinical presentation in vitiligo patients, including: a) focal: one or more depigmented macules (2%); b) vulgaris: scattered macules (2%); c) segmental: unilateral few macules; d) universalis: total or near total body involvement; e) mucosal and mixed: a combination of above types.[13,14]

Vitiligo in children is different in some aspects from the adult forms: a) according to the literature segmental type of the vitiligo is more common in children than adults; b) there is stronger association between vitiligo in children and autoimmune-endocrine disorders; c) the response to treatment in children with vitiligo is different from adults; and d) some of

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the treatment modalities used routinely in adults are contraindicated in children.[15]

There are a few studies that assess clinical features and epidemiological aspects and association of the vitiligo with other diseases in children, and nearly most of them have been done in Western countries and far east, but there is no studies in Iran so far and because of the difference between racial and cultural issues in these regions that can affect clinical and laboratory results, we decided to study the clinical and epidemiologic aspects of vitiligo and association of the disease in children with other abnormalities in Kerman, a city situated in the southeast part of Iran.

Methods

In this cross sectional study, a total of 324 participants were enrolled, as 3 groups each consisting of 108 cases, including: 216 children between 2 and 18 years old (half of them i.e. 108 had vitiligo, and rest of them i.e. 108 that were age- and sex-matched had other skin disorders such as psoriasis, lichen planus, warts, pityriasis rosea, pityriasis alba, tinea, acne that did not predispose patients to autoimmune disorders like pernicious anaemia, diabetes mellitus, connective tissue diseases and allergic diseases) and finally 108 sex-matched adults with vitiligo.

Clinical diagnosis of Vitiligo was approved with wood's lamp examination, and in case of doubt with the diagnosis, skin biopsy was done followed by staining with Fontana-Mason method.

Written informed consent was obtained from the patients or parents. A questionnaire including family history of vitiligo, autoimmune and endocrine diseases such as pernicious anemia, diabetes mellitus, connective tissue disease, Addison disease and leukotrichia (before the age of 30), was prepared and completed.

Demographic information including skin type, age, mean duration of the disease and positive Koebner phenomenon was collected. Patients with vitiligo were divided to 5 clinical subtypes including: focal, vulgaris, segmental, universal, mucosal and mixed types.

Following laboratory tests were carried out in all subjects including: fasting blood sugar, T3, T4, TSH, anti-thyroid peroxidase (TPO) antibody, complete blood count/differential count. If the patients with vitiligo already had received any treatment, treatment modalities and rate of the response to the treatments were recorded.

According to the literature the response rate to treatments was categorized to: Complete (100%) response; excellent (75-99% reduction in size of the lesion); good (50-75% reduction in size); moderate (25-49% reduction in size); and no response or minimal response (less than 25% reduction in size), follicular repigmentation.

Statistical analysis

The data assessed using chi square test and the variables in the groups were compared by regression logistic using SPSS software version 20.

Results

Altogether, 108 children with vitiligo were enrolled in the study, 44 (40.7%) male, 64 (59.3%) female and we found no significant difference statistically in males and females (p=0.86). Mean age of the children with vitiligo was 11.52±4.78 years, and mean age of the incidence of the disease was 8.3±4.85 years. Mean body surface area of the involvement was 9.63±15.29 cm^2. The difference in the mean surface area of involvement and occurrence of Koebner phenomenon between children and adults with vitiligo was not significant (p=0.25). Majority of patients were of either skin type 3 or 4.

There was a meaningful relationship between positive family history of vitiligo in both adults and children with vitiligo in comparison to patients with other skin disorder (**Table 1**), but there was no significant association of history of the autoimmune disorder in vitiligo patients in our study (p=0.46).

Clinical features of patients with vitiligo including different subtypes of vitiligo, distribution of the lesions and association with other skin disorder are showed in **Tables 2**, **3** and **4**.

Regarding treatment of disease, topical steroids, calcineurin inhibitors, phototherapy and excimer laser had been used. Treatment response to steroid in children was rated as moderate, similar to adults, while calcineurin

Table 1 Prevalence of family history of vitiligo in each group

Family history	*Grade*	*Adults with vitiligo (n=108)*	*Children with vitiligo (n=108)*	*Children without vitiligo (n=108)*	*p value*
Yes	1	6 (5.6%)	2 (1.8%)	2 (1.8%)	0.464
	2	6 (5.6%)	4 (3.8%)	5 (4.7%)	
	3	0 (0)	1 (0.9%)	0 (0)	
	1 & 2	0 (0)	1 (0.9%)	0 (0)	
No		96 (88.9%)	100 (92.6%)	101 (93.5%)	

Table 2 Clinical subtypes of vitiligo in two groups, adults (n=108) and children (n=108).

Type of vitiligo	*Adults with vitiligo*	*Children with vitiligo*	*Total*	*p value*
Focal	10 (9.2%)	19 (17.6%)	29 (13.4%)	0.204
Vulgaris	57 (52.8%)	59 (50.9%)	16 (53.7%)	
Segmental	7 (6.5%)	9 (8.3%)	16 (7.4%)	
Universalis	12 (11.1%)	9 (8.3%)	21 (9.7%)	
Mucosal	3 (2.8%)	4 (3.7%)	7 (3.2%)	
Acrofacial	18 (16.7%)	8 (7.4%)	26 (12%)	
Mixed	1 (0.9%)	0 (0)	1 (0.5%)	

Table 3 Sites of involvement in vitiligo patients, adults (n=108) and children (n=108).

Sites of involvement	*Adults with vitiligo*	*Children with vitiligo*	*Total*	*p value*
Limb	81 (48.2%)	89 (51.8%)	168	0.322
Trunk	72 (50%)	72 (50%)	144	0.519
Head and neck	79 (73.1%)	74 (48.4%)	153	0.550
Mucous	8 (7.4%)	9 (52.9%)	17	0.577

Table 4 laboratory test results in three groups, each comprising of 108 patients.

		Adult with vitiligo	*Children with vitiligo*	*Children without vitiligo*	*p value*
WBC	Normal	108 (33.4%)	108 (33.4%)	108 (33.1%)	0.135
ESR	Normal	106 (33%)	108 (33.6%)	108 (33.3%)	
	High	2 (100%)	0 (0)	0 (0)	
TSH	Normal	104 (33.1%)	103 (32.8%)	108 (34.1%)	0.099
	High	4 (57.1%)	3 (42.9%)	0 (0)	
	Low	0 (0)	2 (100%)	0 (0)	
AntiTPO	Normal	102 (32.9%)	101 (32.6%)	108 (34.5%)	0.033
	High	6 (46.2%)	7 (53.8%)	0 (0)	
FBS	Normal	105 (33.1%)	107 (33.8%)	106 (33.1%)	0.602
	High	3 (50%)	1 (16.7%)	2 (33.3%)	
T_4	Normal	104 (32.9%)	105 (33.2%)	108 (33.9%)	0.400
	High	2 (50%)	2 (50%)	0 (0)	
	Low	2 (66.7%)	0 (0)	0 (0)	
HB	Normal	108 (33.4%)	108 (33.4%)	108 (33.1%)	
PLT	Normal	108 (33.4%)	108 (33.4%)	108 (33.1%)	

Anti TPO=anti-thyroid peroxidase antibody, FBS=fasting blood sugar, PLT=platelet count.

Table 5 Associated skin disorders in different groups.

	Adult with Vitiligo (N=108)	*Children with vitiligo (N=108)*	*Children without vitiligo (N=108)*	*p value*
Alopecia	3 (18.8%)	7 (43.8%)	6 (37.5%)	<0.423
Early whitening of hair	55 (69.6%)	22 (27.8%)	2 (2.5%)	0.001
Leukotrichia	78 (61.3%)	43 (38.7%)	0 (0)	0.001
Halo nevi	6 (27.3%)	10 (45.5%)	6 (27.3%)	0.465

Table 6 Prevalence of associated systemic disorder in different groups

Associated systemic diseases	*Adult with vitiligo (N=108)*	*Children with vitiligo (N=108)*	*Children without vitiligo (N=108)*	*p value*
Diabetes mellitus	3 (2.8%)	3 (2.8%)	2 (1.9%)	0.025
Eye involvement	1 (0.9%)	0 (0)	0 (0)	
Allergic disease	12 (11.1%)	23 (21.3%)	35 (32.7%)	
Deafness	0 (0)	1 (0.9%)	0 (0)	
Hypothyroidism under treatment	3 (2.8%)	0 (0)	0 (0)	
Hypothyroidism	1 (0.9%)	0 (0)	0 (0)	
Iron deficiency	1 (0.9%)	0 (0)	0 (0)	

inhibitors showed good response. Response to phototherapy (both PUVA and NBUVB) and excimer laser was minimal to moderate and moderate to good, respectively with no meaningful difference with adults.

The results of CBC and ESR studies were in normal ranges in children and adults. Fasting blood sugar was high in only one child and TSH was high in 2.2% and low in 2.3% of children (**Table 4**). The associated dermatoses and systemic diseases are shown in **Table 5** and **6**, respectively.

Discussion

In our study the prevalence of vitiligo in children was equal in both sexes, and there were no differences with adults. Also, the mean surface area of the involvement was similar in adults and children, which can be due to relative similar severity of the disease in both groups of ages.

The percent of involvement in skin type 3 and 4 was meaningfully higher than other types. This can be related to higher prevalence of these skin types in our country and because of the greater contrast between darker skin phenotype than other types that can lead to higher search for treatment. The prevalence of the Koebner phenomenon in children with vitiligo was 50% which is similar to adults. This showed the importance of avoidance of trauma in children like adults.

Family history of vitiligo in children with vitiligo was meaningfully higher than children with other skin disorders (p=0.001). These results were similar to the study accomplished by Almutairi *et al.* in Kuwait[14] additionally prevalence of positive family history was equal in both children and adults.

In our research, family history of autoimmune disorders in children with vitiligo was similar to other groups. Family history of leukotrichia was similar to adults with vitiligo, but it was different from children with other dermatosis.

In our study the most common form of vitiligo was vulgaris, which was similar to adults. This is compatible with study by Almutairi *et al.* in Kuwait[14] and Esfandiarpour and Farajzadeh in Iran,[17] but different from the study by Halder *et al.*[1] in USA, in that segmental type was the most common type. This can be related to the role of racial and geographical factors, but needs more research to confirm.

In our study common sites of involvement in children were limbs, head and neck, trunk and

mucosal surface in descending order, which was similar to adults and compatible with study by Esfandiarpour and Farajzadeh,[17] while different from study by Dogra *et al.*[18] in which head and neck was the most common site of involvement. This can be explained by 50% prevalence of Koebner phenomenon in more common types of the disease.

In our study, response to phototherapy (both PUVA and NBUVB) and excimer laser was minimal to moderate and moderate to good, respectively with no meaningful difference with adults. Because of the small number of subjects the effect of these treatment methods on vitiligo in children could not be assessed. These results were compatible with Halder *et al.*[1] study in USA.

Treatment response to topical steroid, the most common treatment modality used in children was of moderate level, similar to adults.[19] Also, treatment response to topical calcineurin inhibitors in both children and adults was of good level, and because of the better response rate with topical steroid and the higher cost of topical calcineurin inhibitors, it can be concluded that topical calcineurin inhibitors are best reserved for resistant cases and in anatomical areas with more cosmetic importance.

In our study, thyroid abnormality in children with vitiligo was greater than children with other skin dermatosis, but it was similar to adults. Also the frequency of anti-TPO antibody in children with vitiligo was higher than other children, but there was no difference with adults, and these results were compatible with Lacovelli *et al.*[16] research in Italy that demonstrated the importance of the anti-TPO antibody screening as the most sensitive and specific marker[20] for autoimmune thyroid disease in subjects with vitiligo. Prevalence of other skin disorder such as alopecia, leucotrichia and autoimmune disorder was similar in children and adults with vitiligo, but higher than children with other dermatosis.

Summary

In our study the most common type of vitiligo and the most common sites of involvement in children were vulgaris and extremities, respectively. Anti-TPO antibody titer was higher in children with vitiligo than those children with other dermatosis. Also there was no difference in response to treatment modalities such as PUVA and topical steroid and topical calcineurin inhibitors between children and adults.

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