

A Study on Vitiligo- An Association with Endocrine Disorders, Audiological and Ocular Defects

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ABSTRACT

Background: Vitiligo is a disorder of unknown etiology characterized by the development of milk white macules due to destruction of melanocytes. There is high frequency of association of vitiligo with various autoimmune diseases which favors autoimmune origin of vitiligo. Since melanocytes are destroyed in vitiligo melanocytes present in the retina and in the inner ear could also be affected in vitiligo.

Aim: To evaluate any association of vitiligo with endocrine disease, audiological and ocular defects.

Method: This study comprised of 285 vitiligo patient and age and sex matched 100 control cases without vitiligo. History of onset, duration, family history was taken. Relevant laboratory tests were done. Thorough ocular examination, audiometry was also done.

Result: Incidence of vitiligo was 1.1%, male and female ratio was 1:1.11. High incidence was recorded among early age group, below 30 years of age. Generalized vitiligo was highest in number 69.12%; hearing loss and ocular defects were significantly high among generalized and long duration of vitiligo.

Limitation: Larger and longer follow up studies are needed to establish the precision of our observation.

Conclusion: Vitiligo affects the pigment cell throughout the body. Generalized type of vitiligo, with leucotrichia indicates more destruction of melanocytes which can lead to ocular defect, sensorineural damage and hearing loss. The early recognition of these clinical markers may help patient to halt the further damage.

Keywords: vitiligo, melanocyte, endocrine, ocular, audiological, sensorineural, hypoacusis

INTRODUCTION

Vitiligo is an acquired, multifactorial, depigmenting disorder of the skin characterized clinically by the development of milk white macules and histologically by the loss of melanocytes from the epidermis and its appendages. The disease being so conspicuous, especially in skin of colour, is a matter of major socio-psychological concern.

There is a positive family history in 30% to 40% of vitiligo cases and it is thought that the mode of inheritance is

either polygenic or autosomal with an incomplete penetrance and variable expression.^{1,2} Of the many hypothesis regarding the etiopathogenesis of vitiligo, the autoimmune is important as there is a high frequency of association of vitiligo with various autoimmune diseases and with the presence of autoantibodies against thyroid, adrenals, parietal cells etc.^{3-5,6} Moreover, various studies suggest a strong association of vitiligo with endocrine disorders like hypothyroidism, hyperthyroidism, diabetes and

adrenocortical insufficiency which are often considered to be autoimmune in nature.^{3,4,7,8,9}

The key event in the pathogenesis of vitiligo is the destruction of melanocytes in the skin. Therefore, melanocytes present in the retinal pigment epithelium and in the inner ear could also be affected in vitiligo. One third patients with vitiligo were reported to have defects of the retinal pigment epithelium and/or the choroid.¹⁰ Also, a higher incidence of sensory neural deafness in vitiligo has been reported in some studies.^{3,11,12,13} Hence, vitiligo may be considered a systemic autoimmune disorder affecting the entire pigmentary system.

The present study is, therefore, an attempt to identify systemic nature of vitiligo by assessing the associations of vitiligo with hearing abnormalities, ocular pigmentary disturbances and endocrine disorders and the clinical characteristics of vitiligo that may indicate any such association.

METHODS

The present study consisted of all new patients of vitiligo, compared with an age and sex matched control group of 100 non vitiligo patients attending the Dermatology OPD in a tertiary referral center of Assam for a period of one year, who consented for the study. Ethics committee approval was taken prior to the initiation of the study. Vitiligo was diagnosed clinically and by Wood's lamp examination. Patients with depigmentation caused by chemicals, trauma or any other disease were excluded. Both the groups were subjected to a detailed history including age of onset, initiating factors, treatment taken, family history, presence of co-morbid conditions, deafness, ocular complaints, occupational history and history of exposure to factors causing deafness or ocular disease. A thorough clinical examination was done. Analysis of auditory function was done using the tuning fork tests, pure tone audiometry for ages 5 years

and above, conditioned audiometry for ages 2 to 5 years and brainstem auditory evoked potential examination in children aged 3 months to 2 years. Hearing loss was graded according to the Goodman's classification of deafness.

A thorough ocular examination was done in all patients including slit lamp and ophthalmoscopy to detect iris and retino-choroidal pigmentary defects. Laboratory investigations included complete blood count, liver and renal profile, fasting and post prandial plasma glucose, thyroid function tests, basal cortisol secretion at 8AM and 4 PM, serum electrolytes.

Microsoft Word Excel was used to generate data and software SPSS version 16.0, the InStat 3 was utilized along with unpaired t test and Fisher's exact for data analysis. A p value of less than 0.05 was considered significant.

RESULTS

The total number of new patients attending the outpatient department during one year was 25795. Of this, 285 were new vitiligo cases with an incidence of 1.1% among the dermatology OPD attendance. The male to female ratio was 1: 1.11. The control group was comparable with 46 males and 54 females.

The ages at onset of vitiligo ranged from 2 months to 69.5 years of age, most patients are below 30 years of age (Table 1). A positive family history of vitiligo was obtained in 52 (18.25%) of the vitiligo patients of which 33 (11.5%) had a first degree relative affected and 22 (7.7%) had a second degree relative affected with vitiligo.

Generalized type of vitiligo was present in 197 (69.12%); with vitiligo vulgaris 164 cases, (57.54%) followed by acrofacial 32 cases (11.23%) and one case (0.35%) of universal vitiligo. Out of total 88 (30.88%) localized type, 67 (23.5%) cases comprised of focal, 10(3.5%) segmental and 11 (3.8%) mucosal vitiligo (diagram 1).

Seventy three (25.6%) cases had leucotrichia including poliosis of hair on the scalp and/or of eyebrows and eyelashes.

Endocrine disorders were documented among 36 (12.63%) cases and only 5 (5%) had endocrine disorder in the control group. The difference was significant (p value 0.0374) [Table 1].

TABLE 1: Endocrine disorders in vitiligo

TYPE OF ENDOCRINE DISORDER	IN VITILIGO PATIENTS	IN CONTROLS	DIFFERENCE
Diabetes	8 (2.8%)	2 (2%)	not significant (p value 1)
Thyroid Disorder	31 (10.87%)	3 (3%)	significant (p value 0.0141)

TABLE 2: Ocular defects in vitiligo

OCULAR FINDINGS	NO. OF CASES
Iris hypopigmentation	25
Patchy retino-coroidal hypopigmentation/atrophy	14
Tesselated fundus	17
Both iris and retinal hypopigmentation	5

TABLE 3: Ocular defects and age of presentation of vitiligo

AGE GROUPS (YRS)	TOTAL NUMBER OF CASES	CASES WITH OCULAR DEFECTS
0-9	44	5 (11.4%)
10-19	76	11 (14.5%)
20-29	59	9 (15.25%)
30-39	44	7 (15.9%)
40-49	36	7 (19.5%)
50-59	16	5 (31.25%)
60-69	7	4 (57.14%)
70-79	3	3 (100%)
TOTAL	285	51 (17.89%)

TABLE 4: Ocular defects and type of vitiligo

TYPE OF VITILIGO		WITH OCULAR DEFECTS	WITHOUT OCULAR DEFECTS
GENERALIZED	Vitiligo Vulgaris	42 (82%)	122 (52.5%)
	Acrofacial	3 (6%)	29 (12.5%)
	Universal	1 (2%)	0 (0%)
LOCALIZED	Focal	4 (8%)	63 (27%)
	Segmental	0 (0%)	10 (4%)
	Mucosal	1 (2%)	10 (4%)

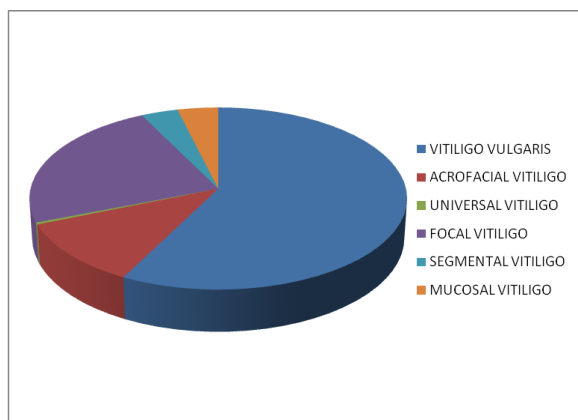


Diagram 1: Distribution of cases according to type of disease

Among the thyroid disorders, hypothyroidism (9.47%) occurred in a significantly higher proportion of cases compared to the controls (p value 0.0487). A case of toxic multinodular goiter had hyperthyroidism.

Sensorineural (SN) hypoacusis was detected in 63 (22.1%) patients in the vitiligo group and 9 (9%) subjects in the

control group and difference was statistically significant (p value 0.0029). Out of the 63 vitiligo patients with sensorineural hypoacusis, 43 (68.25%) patients had mild degree hearing loss (diagram 2).

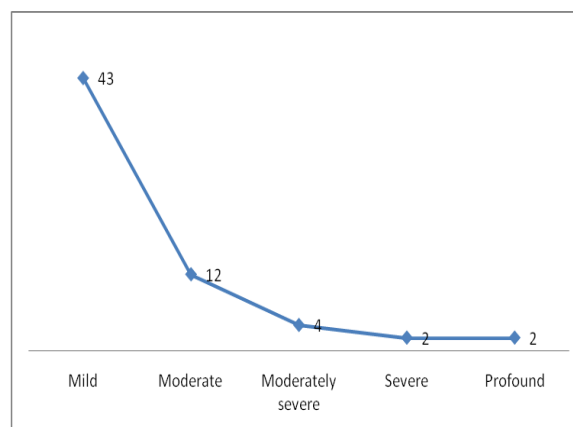


Diagram 2: Degree of deafness in vitiligo patient

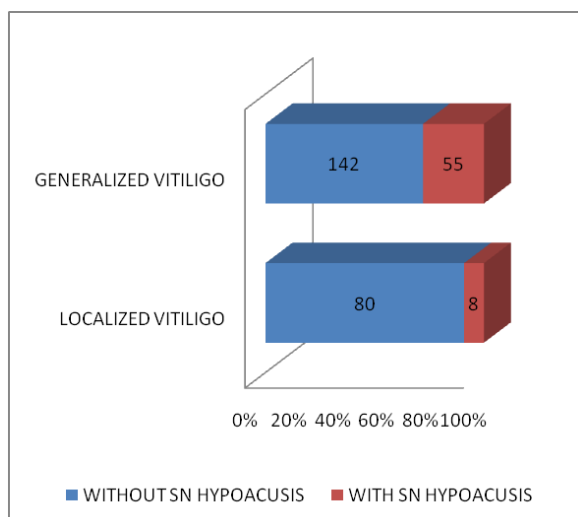


Diagram 3: Sensorineural hypoacusis and type of vitiligo

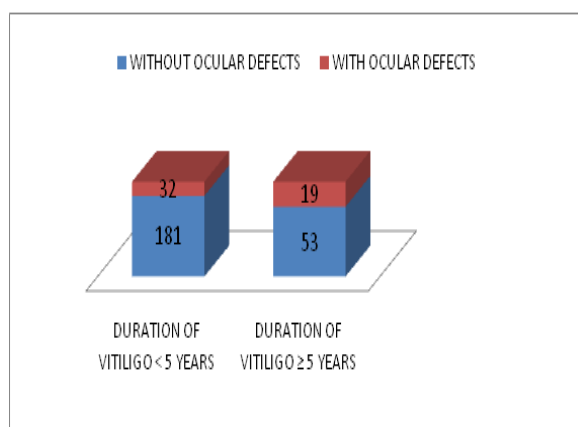


Diagram 4: Ocular defect and duration of vitiligo

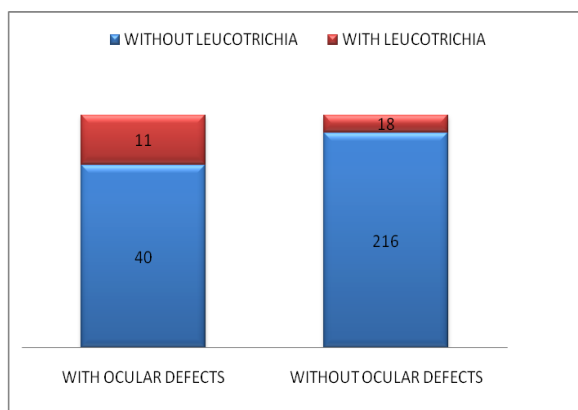


Diagram 5: Ocular defect and vitiligo in the periorbital area with leucotrichia

There was a statistically significant difference (p value 0.0112) in the mean age at presentation of vitiligo patients with hypoacusis (30.5 ± 2.25 years) and the mean age at presentation of vitiligo patients without hypoacusis (24.82 ± 1 years). There was no significant difference in the mean duration of vitiligo in patients with hypoacusis and in those without hypoacusis.

The prevalence of sensorineural hypoacusis in vitiligo patients was seen to increase with increasing age at presentation. The difference in occurrence of sensorineural hypoacusis in vitiligo patients with generalized vitiligo was higher and statistically significant (p value 0.0003) as compared to that in patients with localized vitiligo (diagram 3). Further, 36.5% of vitiligo patients with sensorineural hypoacusis had leucotrichia compared to only 22.52 % in the group of vitiligo patients without hypoacusis, which was significant (p value 0.0330). Of the 63 vitiligo patients with sensorineural hypoacusis 9 (14.28%) patients had ear and/or periauricular lesions and the difference was not statistically significant when compared with the occurrence of such lesions in cases without hypoacusis (p value 0.3506).

Ocular pigmentary abnormalities were observed in 51 (17.9%) patients in the vitiligo group which was significantly higher (p value 0.008) as compared to that in the control group (7%). The ocular abnormalities detected were iris hypopigmentation, patchy retino-choroidal hypopigmentation/atrophy and tessellated fundus (table 2).

The mean age at presentation of vitiligo patients with ocular defect was 33.39 ± 2.70 years (Mean \pm SEM) which was significantly higher (p value 0.0002) than that of vitiligo patients without ocular defects (24.48 ± 0.90 years) [Table 3]

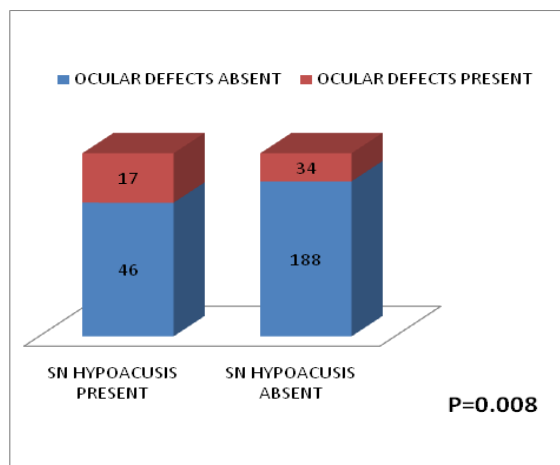


Diagram 6: Sensorineural hypoacusis and ocular abnormalities.

There was a statistically significant difference (p value 0.0340) between the presence of ocular defects in vitiligo patients with duration of vitiligo less than 5 years and more than or equal to 5 years (diagram 4).

Ocular defects were significantly higher (p value 0.0002) in patients with generalized vitiligo as compared to those in patients with localized vitiligo (table 4). No significant relationship was seen between the presence of ocular defects and leucotrichia. A significantly higher proportion (23.5%) of vitiligo patients with ocular defects were seen to have depigmentation on the periorbital area as compared to patients without ocular defects (diagram 5).

A higher proportion (27%) of cases with sensorineural hypoacusis had ocular changes which were statistically significant when compared to cases without hypoacusis (p value 0.008) [diagram 6]

DISCUSSION

In our study of 285 vitiligo patients, females slightly outnumbered males which conform to the sex incidences reported by other authors.^{14,15,16} Female patients probably tend to report more. In this study most vitiligo patients had onset of vitiligo below 30 years of age with the highest number in the age group of 10-19 years which is in agreement with studies from Calcutta¹⁷ and South India^{9, 18} suggesting that although vitiligo can occur at any age, but most cases develop during the active growth phase.¹⁹

Vitiligo is regarded as a genetic disease with familial occurrence reported up to 36%.^{9,15,19,18} We found a positive family history of vitiligo in 18.25% cases. The pattern of vitiligo was similar to that of published reports with a higher proportion of generalized type of vitiligo, vitiligo vulgaris being the commonest type.^{17, 20, 21} Leucotrichia was seen in 25.6% patients.

A higher prevalence of autoimmune diseases in vitiligo like hypothyroidism, hyperthyroidism, diabetes and

adrenocortical insufficiency which are often considered to be autoimmune in nature supports autoimmune origin of vitiligo. In our study 12.63% patients had one or more endocrine disorders which are significantly higher than in controls. Which supports the previous suggestion that vitiligo could be a marker of certain endocrine diseases.²³ Although diabetes was diagnosed in 2.8% vitiligo patients, this study could not establish an association with diabetes. This finding is consistent with Schallreuter et al.²⁴ and Garg et al.²⁵ Of the 31 cases with thyroid disorders, one had hyperthyroidism and the rest had hypothyroidism. An increased incidence of thyrotoxicosis in vitiligo has been suggested by Schallreuter et al. The lack of such evidence in our study could be attributed to the region (north east India) being iodine deficient. On the other hand 9.47 % cases had hypothyroidism which was significantly higher and consistent with other studies.^{9,20} In accordance with a Hamburg study²⁴, we failed to find an association of hypothyroidism in vitiligo with the age of the cases.

Sensorineural hypoacusis, mostly of mild degree and at high frequency was seen in 22.10 % case which was statistically higher and is consistent with other studies.^{12,13,14} Old age, generalized vitiligo and the presence of leucotrichia were statistically associated with the occurrence of sensorineural hypoacusis. It is likely that systemic autoimmunity directed against melanocytes in the inner ear fail to protect and predispose to damage by environmental factors over time leading to deafness.^{26, 27}

Ocular pigmentary defects were detected in a statistically higher proportion of cases (17.9%) conforming to other studies.^{13,14} Older age at presentation, generalized vitiligo and proximity of vitiligo lesions to the eyes significantly increased the occurrence of ocular defects. Ocular defects were also seen in a significantly higher proportion (27%) of vitiligo patients with sensorineural hypoacusis. All extracutaneous melanocytes in the body

including those in the uveal tract, retinal pigment epithelium, the leptomeninges and the inner ear may get destroyed or degenerated in patients with vitiligo.

Limitation: Larger sample size and longer follow up studies are necessary to establish the precision of our observations which is lacking in our study.

CONCLUSION

Vitiligo is a fairly common disorder with a significant degree of familial aggregation. There is a higher frequency of occurrence of hypothyroidism, sensory neural hypoacusis and ocular pigmentary defects supporting the notion that vitiligo is a systemic autoimmune disorder affecting the pigment cells throughout the body and is not confined to cutaneous problem.

Generalized type of vitiligo and leucotrichia may suggest a more generalized destruction of melanocytes in the body to involve the eyes and inner ear. The identification of these clinical signs could help in the early detection of ocular and audiological defects to prevent the development of functional impairment of these organs.

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