# A study on the clinico-epidemiological profile of vitiligo patients and its association with endocrine, audiological and ocular abnormalities

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**Background:** Vitiligo is an acquired condition resulting from the progressive loss of melanocytes. It may be associated with disorders of pigmented tissues of the eyes and ears, and with disorders of the endocrine organs.

**Aim:** To study the clinico-demographic profile of vitiligo patients and its association with endocrine disorders and audiological and ocular abnormalities.

**Materials and Methods:** This was a case-control study conducted at a tertiary care hospital; 261 vitiligo patients were enrolled together with 100 age- and gender-matched healthy individuals without vitiligo as the controls. A detailed history and clinical examination, including audiological and ocular examination, was undertaken; blood investigations like random blood sugar, thyroid function tests, and serum cortisol levels were requested for all subjects.

**Results:** Vitiligo vulgaris was the most common type of disease detected in 146 (55.93%) patients, followed by focal vitiligo in59 (22.60%), mucosal vitiligo in 31 (11.87%), acrofacial vitiligo in 16 (6.13%), segmental vitiligo in 8 (3.06%), and universal vitiligo in one (0.38%) patient. Endocrine disorders were noted in 40 (15.32%) patients, which included hypothyroidism in 27, hyperthyroidism in 5, and diabetes in 8 patients. Sensorineural hypoacusis and ocular abnormalities were noted in 56 (21.45%) and 49 (18.77%) vitiligo patients respectively. The association of hypothyroidism, sensorineural hypoacusis, and ocular abnormalities with vitiligo was statistically significant.

**Conclusion:** Vitiligo is not limited to cutaneous melanocytes; it also affects pigment cells throughout the body. Patients with increased age, prolonged duration of disease, and greater body surface area involvement are at increased risk for systemic associations. A thorough clinical evaluation seems necessary for all vitiligo patients.

**Keywords:** hypothyroidism, hyperthyroidism, hypoacusis, vitiligo

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## INTRODUCTION

Vitiligo is an acquired depigmenting disorder of the skin resultingfrom the progressive loss of melanocytes [1]. It affects 0.5–2% of the world's population and is considered as a multifactorial

disorder [2]. The theory of autoimmune-mediated destruction of melanocytes is well accepted and seems to have become the leading hypothesis regarding the pathogenesis of vitiligo. Various studies suggest that patients with vitiligo have an increased risk of developing autoimmune diseases such as thyroid disease, Addison's disease, pernicious anemia, etc. [3-5]. The embryonic origin of human melanocytes is from the neural crest [6]. Melanocytes are located in the epidermis, hair bulbs, uveal tract, retinal pigment epithelium, inner ear, and leptomeninges [7]. The mechanism behind melanocyte destruction in the skin could also affect other melanocytic organs [8]. Several ocular and audiological abnormalities have been reported in patients with vitiligo [9,10]. This has prompted some researchers to believe that vitiligo is a systemic disorder affecting the entire pigmentary system or is a marker for certain diseases [11,12]. The appendages of the skin like the nails may also be involved in vitiligo patients due to an autoimmune attack. Nail abnormalities are also found in patients with vitiligo, especially among those with alopecia areata [13].

Vitiligo, as the most common pigmentary disorder, affects the quality of life and exerts an important emotional and psychological impact on patients, especially women and younger adults. Vitiligo patients suffer from a lack of self-confidence, an unpleasant body image, unsuccessful social relationships, and a lower quality of marital relations; they are also at higher risk of social discrimination and stigma, which is why vitiligo is considered as a psychosomatic disorder [14].

The present study was conducted to determine the clinico-demographic profile of vitiligo patients and to evaluate the association of the disease with endocrine disorders and audiological and ocular abnormalities.

## MATERIALS AND METHODS

This was an observational case-control study conducted at the Outpatient Department (OPD) of Dermatology, Venereology and Leprosy in a tertiary care hospital. The study period was from July 2015 to June 2016. A total of 261 cases of vitiligo and 100 controls were included in the study. Prior approval of the institutional ethical committee was obtained. Informed consent was taken from the study subjects or their guardians before including them in the study.

### Inclusion criteria

1. Cases: All patients with a clinical diagnosis of vitiligo irrespective of age and sex.
2. Controls: One hundred patients attending the dermatology clinic with disorders other than vitiligo and of similar age and sex as the vitiligo patients.

### Exclusion criteria

1. Patients with depigmentation caused by chemicals, burns, or any other disease.
2. Patients who had received topical or systemic treatment prior to attending the dermatology clinic.

A detailed clinical history was taken for all cases including age, sex, occupation, site of onset, duration of the disease, family history, and treatment history. Patients were also asked regarding the presence of comorbid conditions like endocrine disorders, deafness, photophobia, night blindness, and any other ocular or audiological complaints. A thorough cutaneous and systemic examination was done for all study subjects, including examination of the site of involvement, the border of the lesion, the skin texture, Koebner's phenomenon, leucotrichia, and areas of repigmentation. Based on the site and extent of involvement, vitiligo was classified into generalized and localized vitiligo. Generalized vitiligo includes vitiligo vulgaris, acro-facial vitiligo, and universal vitiligo; localized vitiligo includes focal vitiligo, segmental vitiligo, and mucosal vitiligo. The distribution of lesions was recorded with special mention of lesions in proximity to the eyes and ears. The total body surface area (BSA) involved by vitiligo was recorded with the help of the "rule of nine" formula.

Analysis of auditory function was done in all patients via the tuning fork test, pure tone audiometry, conditioned audiometry, and brain stem evoked response audiometry (BERA). Ocular examination was done with direct ophthalmoscopy and slit-lamp examination.

Laboratory investigations including thyroid function tests, adrenal function tests, and random blood sugar were requested for all participants.

Complete blood count, liver function tests, renal function tests, fasting blood sugar level, post-prandial blood sugar level, and glycosylated hemoglobin level assays were requested if necessary.

Statistical analysis was done using the SPSS software, version 20.0, and the Instat 3 software. Statistical significance was determined by the unpaired t-test,Fisher's exact test, and Chi-squared test.

## RESULTS

A total of 261 patients of vitiligo were included in the study, of which 128 (49.0%) were male and 134 (51.34%) were female. The female to male ratio was 1.04:1. The prevalence of vitiligo among attendees of the clinic was 1.2%. The age of onset of vitiligo ranged from 1 month to 81 years (mean = 25.95 ± 1.08 years). The prevalence of vitiligo was highest in the age group of 20to 29 years. Out of 261 patients, 57 were in the age group of 0-9 years, 46 in 10-19 years, 61 in 20-29 years, 40 in 30-39 years, 26 in 40-49 years, 19 in 50-59 years, 9 in 60-69 years, 2 in 70-79 years, and 1 in 80-89 years. Duration of vitiligo ranged from 15 days to 25 years (mean = 3.33 ± 0.28 years). Positive family history was noted in46 (17.62%) patients, of which 36 (13.79%) had first-degree relatives and 13 (4.98%) had second-degree relatives with vitiligo. Vitiligo vulgaris was the most common presentation (146 patients; 55.93%), followed by focal vitiligo in 59 (22.60%), mucosal vitiligo in 31 (11.87%), acrofacial vitiligo in 16 (6.13%), segmental vitiligo in 8 (3.06%), and universal vitiligo in one patient (0.38%). Most of the patients had a BSA involvement of < 20% (95.40%). Vitiligo was stable for at least one year in 57 (21.83%) patients. Seventy-three vitiligo patients (24.13%) had leucotrichia including the poliosis of hair on the scalp, eyebrows, and eyelashes.

### Endocrinal association of vitiligo

Endocrine disorders were noted in 40 (15.32%) vitiligo patients and 6 (6%) individuals in the control group (Table 1). Out of 40 vitiligo patients with endocrine disorders, 27 had hypothyroidism, 5 had hyperthyroidism, and 8 had diabetes. The association between hypothyroidism and vitiligo was statistically significant (P = 0.0309). There was no significant statistical association of hyperthyroidism and diabetes with vitiligo. In our study, none of the patients had adrenal dysfunction.

Of the 27 vitiligo patients with hypothyroidism, 11 (40.74%) belonged to the age group of above 40 years and 16 (59.25%) were below 40 years of age. The difference in the occurrence of hypothyroidism in the two age groups was significant (P = 0.0237).

### Audiological association of vitiligo

Sensorineural hypoacusis was noted in 56 (21.45%) vitiligo patients and 5 (5%) individuals of the control group; this difference was found to be statistically significant (P = 0.0001) (Table 2). The degree of hearing loss was quantified into mild, moderate, moderately severe, severe, and profound deafness based on Goodman's classification. Out of 56 patients with sensorineural hypoacusis, 48 (85.71%) had high-frequency, 5 (8.92%) had mid-frequency, and 3 (5.35%) had low-frequency hearing loss (Table 3). Hypoacusis was found in

**Table 1.** Endocrine disorders in vitiligo patients and control group.

| Sl. No. | Endocrine disorder | Vitiligo patients (n=261) | Control group (n=100) | *P*-value |
|---|---|---|---|---|
| | Hypothyroidism | 27 | 3 | 0.0309 |
| | Hyperthyroidism | 5 | 1 | 1.000 |
| | Diabetes | 8 | 2 | 0.732 |
| | Adrenal dysfunction | 0 | 0 | |
| Total | | 40 | 6 | |

**Table 2.** Sensorineural hypoacusis in vitiligo patients and control group.

| | Vitiligo patients | Control group | *P*-value |
|---|---|---|---|
| Sensorineural hypoacusis present | 56 (21.45%) | 5 (5%) | 0.0001 |
| Sensorineural hypoacusis absent | 205 (78.54%) | 95 (95%) | |

**Table 3.** Degree of hearing loss in vitiligo patients.

| Sl. No. | Degree of hearing loss | No. of vitiligo patients (n=261) |
|---|---|---|
| 1 | Mild (26-40 dB) | 38 (14.5%) |
| 2 | Moderate (41-55 dB) | 7 (2.6%) |
| 3 | Moderately severe (56-70 dB) | 4 (1.5%) |
| 4 | Severe (71-90 dB) | 4 (1.5%) |
| 5 | Profound (>90 dB) | 3 (1.1%) |
| Total | | 56 |

29 of 74 (39.18%) vitiligo patients of age ≥ 40 years and 27 out of 187 (14.43%) vitiligo patients of age < 40 years. Hypoacusis was found to be significantly more prevalent among vitiligo patients aged ≥40 years compared to those who were below the age of 40 years(P = 0.0001). The mean BSA involvement in the 56 vitiligo patients with sensorineural hypoacusis was 5.09 ± 1.62 and in the 205 vitiligo patients without sensorineural hypoacusis was 4.42 ± 0.73;this difference was not significant (P = 0.6819).

Out of 56 patients with sensorineural hypoacusis, 36 had vitiligo vulgaris, 4 had acrofacial vitiligo, 12 had focal vitiligo, 3 had mucosal vitiligo, and 1 had segmental vitiligo. There was no statistical significance between the type of vitiligo and sensorineural hearing loss (P = 0.1232). Leucotrichia and periauricular vitiligo were noted in 15 (26.78%) and 8 (14.28%) of patients, respectively, and were not significantly associated with sensorineural hypoacusis. Eleven patients had both sensorineural hypoacusis and thyroid dysfunction.

### Ocular abnormalities in vitiligo

Ocular abnormalities were observed in 49 (18.77%) vitiligo patients and 4 (4%) individuals in the control group (P = 0.0002) (Table 4). The mean age at presentation of vitiligo patients with ocular abnormalities was 36.73 ± 2.57 years. The mean duration of vitiligo in patients with ocular abnormalities was 5.50 ± 0.87 years, compared to 2.83 ± 0.27 years in those without ocular abnormalities; this difference was statistically significant (P = 0.0002). The mean BSA involvement was significantly higher among vitiligo patients with ocular abnormalities (10.38 ± 3.06%) relative to those without ocular abnormalities (3.22 ± 0.39%; P = 0.0001). Leucotrichia was present in 14 vitiligo patients with ocular abnormality (P = 1.0654). Out of 49 patients with ocular abnormalities, 16 (32.6%) had a vitiligo patch around the eye. A statistically significant association was found between periorbital vitiligo and ocular abnormalities (P = 0.0001). Both sensorineural hypoacusis and ocular abnormalities were noted in 22 vitiligo patients (P = 0.0001).

## DISCUSSION

Vitiligo affects 1%–2% of the world population [16-22]. In the present study,the prevalence of vitiligo was noted to be 1.2%. The variations in prevalence observed may be due to the varying ethnic backgrounds of the population residing in different geographic regions with varying environmental conditions. In our study, most of the vitiligo patients were in the age group of 20-29 years. This finding is consistent with other studies [22,23]. The higher proportion of younger patients in the present study may be due to early reporting. Females were more predominantly affected. This finding is similar to previous studies [17,24,25]. Such female preponderance can be attributed to the high level of cosmetic concern among young women. In contrast, male predominance was noted in the studies done by Handa *et al.* [26] and Castro *et al.* [27] The mean duration of disease in the vitiligo patients was 3.33 ± 0.28years, which is consistent with that of other studies [23,28]. Genetic factors play an important role in the manifestation of vitiligo. The rate of positive family history in

**Table 4.** Ocular abnormalities in vitiligo patients and control group.

| Sl. No. | Ocular abnormalities | Vitiligo patients (n=261) | Control group (n=100) | *P*-Value |
|---|---|---|---|---|
| 1 | Iris hypopigmentation | 22 (8.4%) | 0 | |
| 2 | Patchy retinal hypopigmentation and atrophy | 12 (4.59%) | 3 (3%) | |
| 3 | Tessellated fundus | 11 (4.21%) | 1 (1%) | |
| 4 | Iris and retinal hypopigmentation | 4 (1.53%) | 0 | |
| Total | | 49 (18.77%) | 4 (4%) | 0.0002 |

vitiligo patients varies from 5-37.5% [25,29-35]. In the present study, positive family history was noted in 17.62% of patients.

Vitiligo vulgaris was the most common presentation (55.93%); a similar finding was noted in other studies [25,36]. This indicates that the process of depigmentation, either immune-mediated or toxic, may occur simultaneously or subsequently at various unrelated distant sites [25]. The higher proportion of focal vitiligo in our study can be explained on the basis of a higher number of patients with the disease presenting early for treatment and increasing awareness among the general population, leading to early treatment-seeking behavior. We found that 95.40% of vitiligo patients had < 20% BSA involvement. A similar finding (94.4%) was noted by Handa *et al.* [26]. In our study, most of the patients had unstable vitiligo (204; 78.16%). Dave *et al.* [37] noted unstable vitiligo in 76% of patients in his study. Leucotrichia in vitiligo patients varied between 9-25% in different studies [23,25,26,38,39]. In our study, it was noted in 25.13% of vitiligo patients.

Nail abnormalities in patients with vitiligo have been reported by various authors and maybe the result of an autoimmune trigger. Leukonychia, longitudinal ridging, absence of lunula, longitudinal ridging nail dystrophy, and red lunula are the main abnormalities that have been noted and should be assessed [13].

## Association of vitiligo withendocrine disorders

The prevalence of thyroid disease in vitiligo patients has been reported to vary from 0.7-7.8% [23,25,40]. In our study, hypothyroidism and hyperthyroidism were seen in 27 (10.34%) and 5 (1.91%) vitiligo patients, respectively. A statistically significant association was noted between vitiligo and hypothyroidism (P = 0.0309); this association was stronger among patients below 40 years of age. A similar finding was noted in the Shajil *et al.* study [23]. Most of the vitiligo patients with thyroid disease were asymptomatic except one patient who presented with exophthalmos. Vitiligo can be associated with autoimmune disorders, most commonly Hashimoto's thyroiditis or Grave's disease [41]. It is now recommended that all patients with vitiligo should be screened for thyroid disease and thyroid autoantibodies to detect undiagnosed thyroid disease or to assess the risk of future onset. Colucci *et al.* noted that 77 out of 79 vitiligo patients had anti-thyroid hormone antibodies [42]. Facilities for the detection of thyroid hormones antibodies were not available in our institution and thus formed a limitation of our study.

The rate of association of diabetes with vitiligo varies from 0.6-1.7% in different studies [23,27,40]. Diabetes was noted in 8/261 (3.0%) vitiligo patients and 2/100 (2%) individuals in the control group. Diabetes was not significantly associated with vitiligo in our study. A similar finding was noted by Schallreuter *et al.* [40]. Vora *et al.* [25] noted that diabetes mellitus was the most common systemic condition associated with vitiligo. No case of Addison's disease was noted in our study.

## Association of vitiligo with audiological defects

Previous studies reported sensorineural hypoacusis in 4–18.9% of vitiligo patients [43-50]. In our study, none of the patients complained of hearing loss, but audiological examination revealed sensorineural hypoacusis in 56 (21.45%) vitiligo patients and 5 (5%) controls,which was statistically significant (P = 0.0001). Sharma *et al.* noted a significant association between vitiligo and hypoacusis [47]. The researchers studied 200 vitiligo patients and 60 controls, of which 34 (17%) vitiligo patients and 2 (3.3%) controls had hypoacusis on audiological examination [47]. Moghaddam *et al.* could not find a significant association between sensorineural hypoacusis and vitiligo [51]. Prabha *et al.* studied 52 vitiligo patients of which 10 (19.2%) had hypoacusis [9]. There was no significant association between hypoacusis and the type of vitiligo in our study. Prabha *et al.* noted that most cases of sensorineural hypoacusis were in the age group of 41 to 60 years among vitiligo patients (63.6%), which was statistically significant [9]. In our study, hypoacusis was found to be significantly more prevalent in the age group of ≥ 40 years (39.18%) compared to the age group of < 40 years (14.43%) (P = 0.0001). This may be because of increased exposure to environmental hazards with increased age. There was no significant association between BSA involvement and hypoacusis in vitiligo patients. A similar finding was noted by Rahimi *et al.* [7].

### Association of vitiligo with specific ocular abnormalities

In the present study, ocular abnormalities were noted in 49 (18.77%) vitiligo patients. Bulbul *et al.* [52] and Mehran *et al.* [53] noted ocular abnormalities in 22.23 and 20.7 percent of vitiligo patients, respectively. The specific ocular abnormalities detected in our study were iris hypopigmentation in 22 (8.4%), patchy retinal hypopigmentation and atrophy in 12 (4.59%), tessellated fundus in 11 (4.21%), and iris and retinal hypopigmentation in 4 (1.53%) patients. Pai *et al.* [54] noted iris hypopigmentation in 33.3%, fundus changes in 30.6%, and anterior angle changes in 20% of vitiligo patients. In our study, iris and retinal hypopigmentation were the major ocular manifestations in vitiligo. Similar findings were noted by Biswas *et al.* [55]. Previous studies reported uveitis and chorioretinal scars in vitiligo patients, which were not found in our study [53,56,57].

The duration of vitiligo in patients with ocular abnormalities was significantly higher than in vitiligo patients without ocular abnormalities ($P = 0.0002$). However, Prabha *et al.* [9] found no association between ocular abnormalities and the duration of vitiligo. No predisposition of ocular abnormalities in vitiligo related to sex was found; a similar finding was reported by Mehran *et al.* [53] and Pai *et al.* [54].

Out of 49 vitiligo patients with ocular abnormalities, 43 (87.75%) had the generalized type of vitiligo and 6 (12.24%) had localized vitiligo; this difference was significant ($P < 0.05$). Biswas *et al.* noted that ocular abnormalities were present more in patients with generalized vitiligo than localized vitiligo [55]. This indicates that ocular pigment cells are more vulnerable in generalized vitiligo compared with localized vitiligo.

In our study, periorbital vitiligo was associated with a high prevalence of ocular abnormalities (32.65%). This may be due to the embryological relation between periorbital epidermal melanocytes and ocular melanocytes. Pai *et al.* noted that 30.6% of patients with periorbital vitiligo had ocular abnormalities [54]. Bulbul *et al.* noted similar findings in their study and concluded that periorbital vitiligo could be the most probable alerting feature for ocular abnormalities [52].

Our study was a modest effort to identify clinical characteristics and associations of vitiligo. However, larger follow-up studies are necessary to establish the precision of our observations, which suggest that vitiligo is a systemic disorder, and to determine the progress and prognosis of the abnormalities associated with this cutaneous disorder.

## CONCLUSION

Vitiligo is a common pigmentary disorder with a significant degree of familial aggregation. There is a significantly high association of hypothyroidism, sensorineural hypoacusis, and ocular pigmentary defects with vitiligo. We suggest that all patients with vitiligo should be routinely subjected to thyroid screening as it is important to avoid the negative impact of hypothyroidism on the health status of the patients. In addition, aging and duration of vitiligo can increase the risk of audiological and ocular abnormalities, suggesting more generalized destruction of melanocytes throughout the body. Also, increased BSA involvement and periorbital lesions could point towards extensive involvement of the ocular pigment cells. Thus, identification of these clinical signs and further evaluation of ocular and audiological defects in asymptomatic patients with no audiological or ocular complaints could help in prompt intervention in all detected cases, hence preventing long-term morbidity and complications. It is reasonable to consider that vitiligo is more than a skin disease and affects pigment cells throughout the body.

**Conflict of interest:** None declared.

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