Clinical patterns of vitiligo and its associated co-morbidities: A prospective controlled cross-sectional study in South India

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ABSTRACT

Aim: The purpose of this study is to assess the clinical patterns and associations of vitiligo, audiometric functions, and ocular involvement and to correlate the morphology, clinical behaviour and comorbidities associated with vitiligo. Settings and Design: For this prospective and cross-sectional study 80 self-reporting patients in the age group 7-75 years with vitiligo attending the outpatient department of Manipal hospital during the period August 2008 to February 2010 were selected and the data was analysed. Materials and Methods: The patients were subjected to detailed history, clinical examination and investigations [complete blood count (CBC), absolute eosinophil count (AEC), erythrocyte sedimentation rate (ESR), thyroid stimulating hormone (TSH), vitamin B12 estimation, fasting blood sugar (FBS), and post prandial blood sugar (PPBS), antibody titre estimations that is antithyroid peroxidase (ATPA), antithyroglobulin (ATA), antinuclear antibodies (ANA), urine analysis, audiometric evaluation and ophthalmic examination. Statistical Analysis Used: The Fisher exact test has been used to find the significance of study parameters on categorical scale between two or more groups. Results: In the present series of 80 cases, 41 (51.25%) were males and 39 (48.75%) were females. The male to female ratio was 1.05:1. In our study 20% cases gave definite family history of vitiligo and patients in the age group of 20 - 30 years were the most commonly affected. Generalized vitiligo (31.3%) was the most common type followed by segmental (30%), focal (18.8%), acrofacial (8.8%), and mucosal vitiligo (11.3%). In the present study there was a high incidence of autoantibodies (22.5%), vitamin B12 deficiency (30%), hypothyroidism (11.3%), elevated absolute eosinophil count (16.3%), hypoacusis (10%) and retinal changes (8.8%). This suggests multisystem autoimmunity in vitiligo.

Keywords: Deafness, retinal changes, thyroid disease, vitiligo, vitamin B12 deficiency

INTRODUCTION

Vitiligo is a commonly acquired, idiopathic, heritable depigmentary disorder of the skin and/or mucous membranes.[1] It is of major social and cosmetic concern in India, characterised by depigmented macules of varying size and shape.[2] There are no other textural changes besides loss of color.[3] Vitiligo occurs worldwide with an overall prevalence of 1%.[4,5] However, its incidence ranges from 0.1 to >8.8% across the country and other parts of the world.[3] Widespread prejudices, ignorance, taboos, lack of scientific appraisal about vitiligo and confusion with leprosy all make it a social embarrassment for the patient.[7,8] However, life expectancy is unaffected.[7,8] The present study was conducted to assess the clinical patterns of vitiligo and its associated co-morbidities, audiometric function, and ocular involvement.

MATERIALS AND METHODS

This study was conducted on 80 vitiligo successive patients reporting to the outpatient department at Manipal hospital during the period of August 2008 to February 2010. All patients diagnosed to be having vitiligo willing to enrol for the study and above the age of 5 years were included in the study. Unwilling patients, patients below the age of 5 years and patients with established auditory or ophthalmic abnormalities due to other causes were excluded from the study.

Details of dietary habits and family history were taken in each case. History of associated diseases such as diabetes mellitus, thyroid
disorders, pernicious anaemia and alopecia were noted. History of precipitating or initiating factors especially physical trauma, sun exposure, acute mental or emotional stress, contact with chemicals or synthetic footwear was noted.

Patients were subjected to a detailed history, clinical examination, and investigations which included complete blood count (CBC), absolute eosinophil count (AEC), erythrocyte sedimentation rate (ESR), thyroid stimulating hormone (TSH), vitamin B12 estimation, fasting blood sugar (FBS), postprandial blood sugar (PPBS), antibody titre estimations like antithyroid peroxidase (ATPA), antithyroglobulin (ATA), antinuclear antibodies (ANA), urine analysis, audiometric evaluation, and ophthalmic examination.

**RESULTS**

Of all patients included in the study, 41 (50.25%) were males and 39 (49.75%) were females and no gender preponderance as with other studies [Table 1]. The age of patients ranged from 7 - 75 years, with a mean age of 32.4 years. The duration of illness ranged from half a month to 60 years with a mean of 46.9 months [Table 2]. Twenty percent of patients gave a family history of vitiligo and first-degree relatives were most commonly affected [Table 3]. There were 59 (73.8%) cases of unstable vitiligo, and 21 (26.3%) stable patients. Stable vitiligo was statistically associated with a significant family history [Table 4]. Majority of cases were generalized type (31.3%) followed by segmental (30%), focal (18.8%), acro-facial (8.8%) and mucosal type (11.3%) [Table 5]. Complete audiological examination revealed that 8 (10%) patients were suffering from hypoacusis [Table 6]. Retinal examination showed that 7 (8.8%) patients had abnormal retinal findings such as lattice degeneration, retinal atrophy and pigmentation [Table 7]. A disease duration of less than 6 months was statistically associated with generalised vitiligo and duration of 6 -12 months with focal type of vitiligo [Table 8]. Disease duration of more than 6 months was associated with higher absolute eosinophil count (AEC) and higher PPBS. Patients with vitiligo aged more than 30 years were significantly associated with high PPBS, high incidence of autoantibodies (22.5%) [Figure 1], vitamin B12 deficiency (30%), hypothyroidism (11.3%), high AEC (16.3%) [Figure 2], hypoacusis (10%) and retinal changes (8.8%). Incidence of auditory (P=0.638) and retinal abnormalities (P=0.973) was not statistically associated with type of vitiligo.

**DISCUSSION**

Vitiligo is a commonly acquired, idiopathic, heritable depigmentary disorder of skin and/or mucous membrane.[1] Statistics about vitiligo are variable. Vitiligo occurs worldwide with an overall prevalence of 1%.[3,4] Patients suffer from a poor body image and low self-esteem and also experience a considerable level of psychological burden.[11] This disorder does not result in restriction of working capacity or life expectancy but it causes cosmetic disfigurement leading to psychological trauma to the patient. Since ancient times, patients with vitiligo have suffered the same mental abuse as patients with leprosy, and the two diseases have often been confused clinically.[11,12] Although vitiligo affects both sexes equally, [13] most of the studies show a female preponderance.[14,16] The cause of female preponderance is probably because of greater cosmetic awareness and the impact of the disease on their social life.[7] Our study had a male to female ratio of 1.05:1 and there was no gender preponderance. Vitiligo is considered to be a multifactorial disorder. An assortment of hypotheses, such as genetic, neural, biochemical (autocytotoxic), and autoimmune have been put forth to elucidate its aetiopathologic mechanism.[2] Three major factors seem to be involved in the destruction of melanocytes in patients of vitiligo.[16,17] The first is that vitiligo patients inherit a set of three vitiligo genes that predispose them to destruction of melanocytes.[16,18-20] The second factor is that melanocytes in vitiligo patients differ from that of normal persons. Melanocytes in vitiligo patients are more sensitive to phenolic chemicals and require different, more fastidious culture conditions than those of normal individuals.[21-23] The third factor is destruction of melanocytes occur due to activation of vitiligo genes by environmental agents, which in turn leads to activation of autointimmune and apoptosis of melanocytes.[16,24-30] Clinically, vitiligo is classified depending upon the site and extent of involvement into following types: generalized which is the most common, segmental, focal, acro-facial and mucosal type.[31] In our study, generalized vitiligo (31.3%) was the most common type followed by segmental and other types.

Various studies have shown family history ranging from 7-36% and first-degree relatives were the most commonly affected. About 20% of vitiligo patients have at least one first-degree relative with vitiligo and the relative risk of vitiligo for first-degree relatives (parents, children, siblings) is elevated 7-10 fold as per the observations made in other similar

| Parameters          | Our study (80 pts) | Gopal et al.[36] | Dave et al.[44] | Shajil et al.[46] | Shah et al.[49] | Moradi et al.[41] |
|---------------------|--------------------|------------------|-----------------|------------------|----------------|------------------|
| Males               | 51.25%             | 54%              | 51.2%           | 35.44%           | 31.6%          | 35%              |
| Females             | 48.8%              | 46%              | 46.8%           | 61.56%           | 68.4%          | 65%              |
| M : F               | 1.05:1             | 1.17:1           | 1.05:1          | 1.16             | 1.21           | 1.186            |
Table 2: Age distribution in comparison with other studies

| Parameters                      | Our study (80 pts) | Gopal et al.[36] | Shajil et al.[48] |
|---------------------------------|--------------------|-------------------|-------------------|
| Age (years)                     | 7-75               | 10-55             |                   |
| Mean age (years)                | 32.4               | 23                | 25.59             |
| Duration of disease (months)    | 0.5-720            | 0.5-372           | 0.5-720           |
| Mean duration (months)          | 46.9               | 43.2              | 39.6              |

Mean ± SD: 32.39±16.90

Table 3: Family history of vitiligo

| Parameters                      | Our study (80 pts) | Gopal et al.[36] | Dave et al.[34] | Shajil et al.[48] | Behl et al.[33] | Shah et al.[49] |
|---------------------------------|--------------------|-------------------|-----------------|-------------------|-----------------|-----------------|
| Family history                  |                    |                   |                 |                   |                 |                 |
| 1º degree                       | 20%                | 36%               | 7.5%            | 21.93%            | 8.4%            | 13.7%           |
| 2º degree                       |                    |                   |                 |                   |                 |                 |
| 3º degree                       |                    |                   |                 |                   |                 |                 |

First-degree relatives were most commonly affected

Table 4: Stable vitiligo and family history

| Family history of vitiligo | Number of patients | Stable |
|----------------------------|--------------------|--------|
| Absent                     | 66                 | 16 (24.2%) 50 (75.8%) |
| Present                    | 14                 | 5 (35.7%) 9 (64.3%)   |
| Total                      | 80                 | 21 (26.3%) 59 (73.8%) |

Stable vitiligo patients had significant family history with P=0.504

Table 5: Clinical types of vitiligo

| Parameters                      | Our study (80 pts) | Gopal et al.[36] | Martis et al.[7] | Shajil et al.[48] | Behl et al.[33] | Shah et al.[49] |
|---------------------------------|--------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Generalized                    | 31.3%              | 48              | 39              | 52.36           | 47.5            | 64.9            |
| Segmental                      | 30%                | 13.4            | 3               | 6.84            | 3.3             | 1.4             |
| Acro-facial                    | 8.8%               | 22.67           | 18              | 7.55            | 41.6            | 0.8             |
| Focal                          | 18.8%              | 16              | 27              | 28.54           | 18.6            |                 |
| Mucosal                        | 11.3%              | 0               | 5               | 2.83            | 5.6             | 14.8            |
| Universal                      | 1                  | 1.89            |                 | 8.2             |                 |                 |

Generalized type was the commonest in all studies and even in our study

Table 6: Age and audiological findings

| Age in years | Number of patients (n=80) | Audio logical findings |
|--------------|---------------------------|------------------------|
|              | Normal                     | Abnormal               |
| 1-10         | 8                         | (11.1%)                | 0                     |
| 11-20        | 9                         | (12.5%)                | 0                     |
| 21-30        | 23                        | (31.9%)                | 0                     |
| 31-40        | 21                        | (27.8%)                | 1 (12.5%)             |
| 41-50        | 5                         | (6.5%)                 | 1 (12.5%)             |
| 51-60        | 7                         | (6.9%)                 | 2 (25.0%)             |
| >60          | 7                         | (4.2%)                 | 4 (50.0%)             |
| Total        | 80                        | 72 (100.0%)            | 8 (100.0%)            |

Patients aged more than 30 years significantly associated with abnormal auditory findings with P=0.003**

Table 7: Age and retinal findings

| Age in years | No of patients (n=80) | Ocular findings |
|--------------|-----------------------|-----------------|
|              | Normal                | Abnormal        |
| 1-10         | 8                     | (10.9%)         | 0                |
| 11-20        | 9                     | (12.3%)         | 0                |
| 21-30        | 23                    | (31.5%)         | 0                |
| 31-40        | 21                    | (21.9%)         | 5 (71.4%)        |
| 41-50        | 5                     | (5.5%)          | 1 (14.3%)        |
| 51-60        | 7                     | (6.2%)          | 1 (14.3%)        |
| >60          | 7                     | (9.6%)          | 0                |
| Total        | 80                    | 73 (100.0%)     | 7 (100.0%)       |

Patients aged more than 30 years significantly associated with abnormal retinal findings with P=0.012*

Second-degree relatives also have significantly elevated relative risks. In our study, 20% of patients gave a definite family history of vitiligo, of which first-degree relatives were 8.75%, second degree relatives 7.5% and third degree relatives were 3.5%.

Younger people were more frequently affected and had active vitiligo compared to older people according to few studies.[33] In our study also the younger age groups were commonly affected. This suggests a genetic factor in vitiligo. The presence of a positive family history, mucosal involvement, the isomorphic Koebner’s phenomenon, nonsegmental vitiligo and mucosal vitiligo are associated with progressive disease as per the observation made by other authors and also in our study.[34] Autoimmunity seems to play a significant role in its causation in a considerable number of patients.[35-38] Various studies suggest that patients with vitiligo have an increased risk of developing autoimmune disease such as thyroid disease, Addison’s disease, pernicious anaemia, diabetes mellitus, pemphigus vulgaris and alopecia areata.[39-44] In the present study, there was a high incidence of autoantibodies (22.5%) and hypothyroidism (11.3%) favouring autoimmunity in vitiligo. Other conditions with proposed autoimmune mechanism such as alopecia areata, pernicious anaemia were however not found in any of our cases.

Vitiligo patients may present various pigment changes in the fundus, in particular atrophic spots in the retinal pigment epithelium or choriretinal scars, probably related to previous inflammatory events. Uveitis is the more common in patients with vitiligo.[50]
Deiciency of vitamin B12 associated with vitiligo was reported many years ago [45,46] probably due to defective absorption. Studies reported excellent repigmentation in patients with vitiligo after 1-2 years of treatment with oral folic acid, ascorbic acid and parental B12 (100 mg intramuscular). [46,47] Pteridine part of folic acid could interfere with the recycling of the reduced pterins in vitiligo. Vitamin B12 downregulates the formation of homocysteine, which appears to cause the depigmentation in vitiligo. [45] Systemic oxidative stress has a pathophysiological role in precipitating all clinical types of vitiligo. [48]

The incidence of audiological and retinal abnormalities were not statistically associated with type of vitiligo, which is in agreement with other studies.

**CONCLUSION**

Findings in our study correlate with other studies, and this clearly establishes that the pathophysiology of vitiligo is complex and systemic rather than focal. Therefore all vitiligo patients irrespective of the duration of illness or morphology must be investigated for hypothyroidism, thyroid and nuclear autoantibodies, vitamin B12 deficiency, hearing defects and retinal changes. Duration less than 6 months is statistically associated with generalized and 6-12 months with focal type of vitiligo. Age and gender is not associated with any specific type of vitiligo. Age of more than 30 years is significantly associated with abnormal audiometry, abnormal retinal findings, high AEC and high PPBS. Our study does not address adrenal disease and myasthenia gravis, which are rare but known associations of vitiligo. Notwithstanding this, we recommend that this short list of investigations and consultations be offered to all newly diagnosed adult patients of vitiligo, given the high diagnostic yield and its implications for general health. Our study underlines the fact that vitiligo is the skin manifestation of an internal disease.

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