



## EPIDEMIOLOGICAL PROFILE AND TREATMENT PATTERN OF VITILIGO IN A TERTIARY CARE TEACHING HOSPITAL

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### ABSTRACT

The objective of the present study was to assess the prevalence, precipitating factors, clinical features and management pattern of vitiligo patients. An observational, cross sectional descriptive study was carried out for a period of five months from a study population of 6250 outpatients who visited the dermatology department of a tertiary care hospital. The prescriptions of the individual patients were collected to assess the therapeutic management pattern. Prevalence of vitiligo was found to be 1.3%. The mean age at onset of the disease was  $29.6 \pm 20.6$  years. 18.8% of the patients had a family history of vitiligo. Lower limbs (42.5%) followed by face (27.5%) were the most affected parts. Major precipitating factor was found to be physical trauma (18.8%). Thyroid disorder was the most common autoimmune disorder observed (21.3%). Vitiligo vulgaris was the common clinical type (53.7%) followed by focal vitiligo (18.8%), acrofacial vitiligo (13.8%), segmental vitiligo, etc. Topical tacrolimus (68.8%), topical corticosteroids (53.7%), and topical psoralen (48.8%) were the first line treatments used in the study center. Systemic steroid pulse therapy was used in progressive vitiligo patients and the noted adverse effects of the treatments were gastric irritation (11.3%) and weight gain (7.5%). Autologous melanocyte transplantation (5%), epidermal suction blister grafting (2.5%) and narrow band ultra violet B phototherapy (27.5%) were other treatment modalities used. Similar studies covering large number of patients are needed to confirm our findings.

**Keywords:** Vitiligo, Clinical type, Precipitating factors, Treatment patterns.

### INTRODUCTION

Vitiligo is a depigmenting disorder of the skin of spontaneous onset. Occasionally, the loss of melanin (ie, hypopigmentation) is partial.<sup>1</sup> It is an acquired progressive disorder in which some or all of the melanocytes in the interfollicular epidermis, and occasionally those in the hair follicles, are selectively destroyed.

It presents in childhood or adult life. It often involves the hands, feet, wrists, axilla, periorbital, perioral and anogenital skin.<sup>2</sup> Based on a few dermatological outpatient records, the incidence of vitiligo is found to be 0.25-2.5% in India.<sup>3</sup> There is a stigma attached to vitiligo and affected persons and family, particularly girls are socially ostracized for marital purpose. This disorder does not result in restriction of capacity to work or expectancy of life, but it causes cosmetic disfigurement leading to psychological trauma to the patients. Most evidence support autoimmune etiology, focusing on the presence of circulating antibodies against melanocytes and the association of vitiligo with other autoimmune disorders such as pernicious anemia, Addison's disease, diabetes mellitus and autoimmune thyroiditis.<sup>1,2,4</sup>

Patients with vitiligo present with one to several amelanotic macules that appear chalk or milk white in colour. The macules are round and /or oval in shape often with scalloped margins.<sup>5</sup> Vitiligo is classified as focal, segmental, acrofacial, generalized, mucosal and universal vitiligo.<sup>6</sup> Topical therapy is employed as first-line treatment in localized vitiligo. Currently, several topical agents are available in many forms viz. methoxsalen (solution and cream), trioxsalen (solution), corticosteroids (gel, cream, ointment and solution) and calcineurin inhibitors (ointment and cream). Although topical therapy has an important position in vitiligo treatment, side-effects or poor efficacy affect their utility and patient compliance.<sup>7</sup>

Vitiligo occurs worldwide with an overall prevalence of 1%. The highest incidence of the condition has been recorded in Indians from the Indian subcontinent, followed by Mexicans and

Japanese.<sup>5</sup> Epidemiological studies on vitiligo have been rarely reported from South Kerala. So we conducted this study in a tertiary care centre in South Kerala, to learn more about the epidemiology, clinical features, precipitating factors and the treatment patterns of vitiligo.

### MATERIALS AND METHODS

#### Study design and settings

It was a non - experimental (observational), prospective, and cross sectional study done in the Department of dermatology, Amrita Institute of Medical Sciences (AIMS), a 1,200-bed multispecialty tertiary care teaching hospital located at Kochi, Kerala for a period of five months from Jan 15<sup>th</sup> to June 15<sup>th</sup> 2010. The study sample consists of all the eighty vitiligo patients (who had a confirmed diagnosis of vitiligo by the dermatologist and met the inclusion criteria) from a study population of 6250 outpatients who visited the dermatology department during the study period.

#### Data collection

The prescriptions of the individual patient's were collected to assess the therapeutic management pattern. The demographic and clinical data of the patients were collected using a data collection form and also from the medical records of patients. The data collection form included particulars like the name, age and sex of the patients, age of onset of vitiligo, duration of disease since first visit, whether the disease is stable or progressing, drug history, presence of koebner phenomenon, distribution of the vitiligo lesions, history of autoimmune diseases in association with vitiligo (thyroid, diabetes, Addison's disease, pernicious anemia, arthritis), family history of autoimmune diseases, family history of vitiligo, presence of any other cutaneous or systemic illness, drug and non drug therapy for vitiligo, and side effects if any with the current treatments etc.

Vitiligo was considered to be stable if there had been no progression of lesions for at least the last 2 years. A record was made of the precise distribution of lesions, and the cases were classified into six groups according to the standard working classification of clinical types of vitiligo.

History of associated diseases notably diabetes mellitus, thyroid disorder, pernicious anaemia, alopecia areata were noted. History of precipitating / initiating factors especially physical trauma, sun exposure, acute mental / emotional stress, contact with chemicals / synthetic footwear, disease like burns, herpes zoster etc were also noted. Detailed dermatological examination was performed to classify to note the presence of any other associated dermatological conditions like psoriasis, atopic dermatitis etc. Apart from the

results of routine blood and urine examination, blood sugar and thyroid function tests were also recorded.

The data obtained from the data collection form were entered in the Microsoft excel programme and analyzed. The values of quantitative variables were expressed as mean ± SD. An online statistical calculator was used for computing descriptive statistics.

**Study approval**

The study protocol was approved by the Research ethics committee of AIMS hospital, Kochi and all the patients gave written informed consent.

**RESULTS**

Of the 6250 patients, who attended the dermatology outpatient department of the study center over a period of five months, 80 had vitiligo and hence a prevalence of 1.3%. Females (52.5%) were affected more than males (47.5%) giving a male female ratio of 1.1:1. Among the total 80 patients 41 (51.2%) were from urban areas and the remaining 39 (48.7%) were from rural areas.

Of the 80 patients, 32.5% of the study population was within the age group of 41-60 years while 31.3% were with the age group of 21 – 40 years age group .The youngest patient was 4 years old and the oldest was 78 years. The Mean ± SD age at onset of the vitiligo was 29.6 ± 20.6 years. The earliest onset was 2 years of age, whereas the latest was 75 years of age. Majority of the patients (45%) were in the age group of 2 – 20 years. The distribution of age at onset of vitiligo patients are listed in table 1.

**Table 1: Distribution of age at onset of vitiligo patients**

Age group (Yrs)	Number	Percentage
<2	0	0
2 – 20	36	45
21 – 40	20	25
41 – 60	15	18.7
61 – 80	9	11.2

Duration of the disease at the time of presentation varied from 2 months to 49 years and the average disease duration was 7.4 ± 9.9 years. Most cases (56.2%) were less than 5 years duration, regardless of sex. Around 18.8% patients had family history of vitiligo. First degree relatives (parents/ brother/ sister/ children) were affected in 10% of the study population and second degree relatives (grand parents/ maternal and / or paternal uncle/aunt) in 8.8% of patients. The details regarding the family history of vitiligo are shown in table 2.

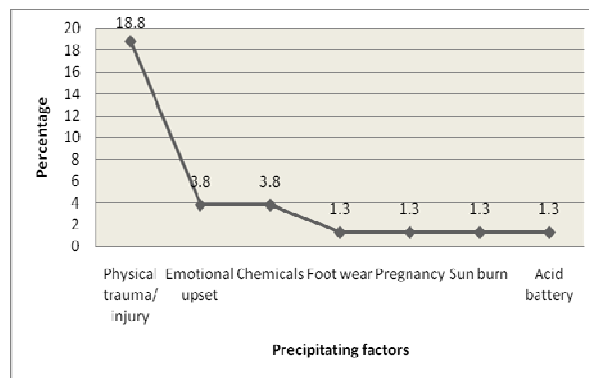
**Table 2: Findings of family history of vitiligo patients**

Relationship with patient	Number	Percentage
Parents	5	6.3
Brother	1	1.3
Children	2	2.5
Paternal grand parents	3	3.8
Maternal grand parents	2	2.5
Maternal/ Paternal uncle or aunt	2	2.5
Negative family history	65	81.3

Major precipitating factor of vitiligo was found to be physical trauma/ injury (18.8%). Others included emotional upset (3.8%), chemicals / drugs (3.8%), footwear (1.3%), pregnancy (1.3%) etc which is shown in table 3.

**Table 3: Factors precipitating vitiligo lesions**

Precipitating factors	Number	Percentage
Physical trauma/ injury	15	18.8
Emotional upset	3	3.8
Chemicals	3	3.8
Footwear	1	1.3
Pregnancy	1	1.3
Sun burn	1	1.3
Acid battery	1	1.3



**Fig. 1: Graphical presentation of factors precipitating vitiligo**

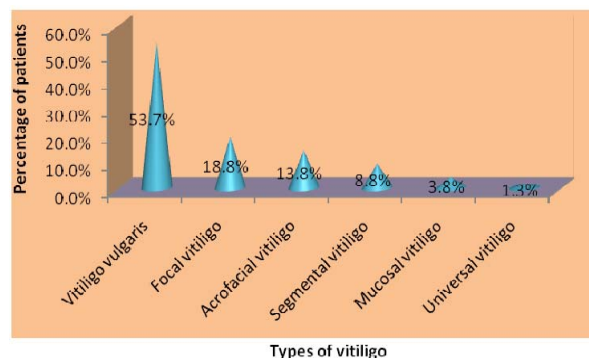
Associated systemic and cutaneous diseases that were observed in the vitiligo patients are listed in Table 4.

**Table 4: Findings of associated diseases with vitiligo**

Associated diseases	Number	Percentage
Thyroid disorders	17	21.3
Diabetes mellitus	11	13.8
Alopecia areata	10	12.5
Leukotrichia	5	6.3
Cardiac problems	5	6.3
Hypertension	4	5
Atopic dermatitis	3	3.8
Diabetes + hypertension	2	2.5
Pernicious anemia	2	2.5
Rheumatoid arthritis	1	1.3
Bronchial asthma	1	1.3
Tinea cruris	1	1.3
Pruritus	1	1.3

Associated autoimmune / endocrine disorders were present in 38.8% of the patients. In these, thyroid disorder was most common and reported in 21.3% patients, diabetes mellitus in 13.8% of the patients, pernicious anemia in 2.5% of patients, rheumatoid arthritis in 1.3% of patients etc. Among other systemic diseases, cardiac problem was present in 6.3%; hypertension was in 5% of the patients. Association of Koebner phenomenon was observed in 20% of the patients. The associated cutaneous diseases noted in this study were Alopecia areata (12.5%), leukotrichia (6.3%), atopic dermatitis (3.8%), pruritus and tinea cruris in 1.3% of patients each. Lesions of vitiligo showing leukotrichia were observed in about 6.3% patients.

The distribution pattern of lesions which denotes the clinical types of vitiligo is shown in Table 5. Vitiligo vulgaris / generalized vitiligo was the most common (53.7%) morphological pattern. Other patterns seen were focal vitiligo (18.8%), acrofacial vitiligo (13.8%), segmental vitiligo (8.8%), mucosal vitiligo (3.8%), and universal vitiligo (1.3%).



**Fig. 2: Graphical presentation of distribution of morphological types of vitiligo**

**Table 5: Distribution pattern of morphological types of vitiligo**

Clinical types	Number	Percentage
Vitiligo vulgaris	43	53.7
Focal vitiligo	15	18.8
Acrofacial vitiligo	11	13.8
Segmental vitiligo	7	8.8
Mucosal vitiligo	3	3.8
Universal vitiligo	1	1.3



**Fig. 3: Distribution of vitiligo lesions on the distal parts of fingers of a 33 year old male patient**

The most common site of onset of vitiligo lesion was lower limbs (42.5%), followed by face (27.5%), upper limbs (13.8%), finger tips (7.5%), trunk (3.8%), scalp (2.5%), and genital mucosa (2.5%) in the descending order of frequency.



**Fig. 4: Distribution of vitiligo lesions on the extensor surface of lower limbs (feet, soles) of a 48 year old male patient.**

Various drug and non drug modalities used for the management of vitiligo were studied and the details are listed in Table 6.

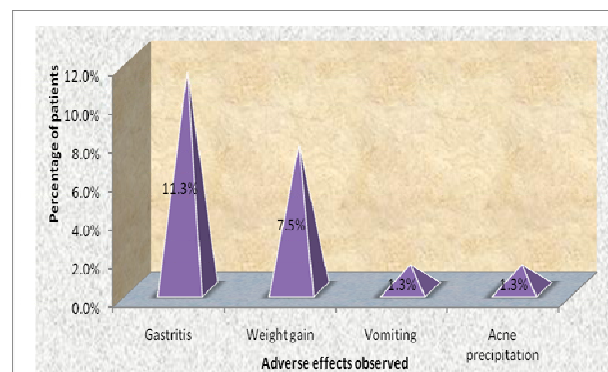
**Table 6: Treatment pattern of vitiligo**

Treatment modality	Drug/ treatment	Number	Percentage
Topical therapies	Topical tacrolimus	55	68.8
	Topical corticosteroid	43	53.7
	Topical psoralen	39	48.8
	Sunscreen lotion	5	6.3
Systemic therapies	Tab. B complex	32	40
	T. corticosteroid (Pulse therapy)	28	35
Phototherapy	Narrow band ultraviolet B (NBUVB)	22	27.5
Surgical Repigmentation	Autologus melanocyte Transplantation	4	5
	Epidermal suction blister grafting	2	2.5

In this study we found out that both drug and non drug treatment modalities are employed for vitiligo. Topical and systemic methods are utilized in drug treatment. Other modalities, especially in stable vitiligo and localized lesions, surgical manipulations like autologus transplantation and epidermal suction blister grafting, are also carried out in this study center. The three most common first line treatments were topical tacrolimus (68.8%), topical corticosteroids (53.7%), and topical psoralen in 48.8% of the patients. Combination therapy may subsequently be employed during the treatments of patients. Oral corticosteroid in pulse therapy (OMP- oral mini pulse) form was given to 35% of the patients with progressive disease for stabilization. Narrow band ultraviolet B (NBUVB) was used in 27.5% patients. Around 5.0% of the patients had undergone for autologus melanocyte transplantation and 2.5% for epidermal suction blister grafting.

Most of the patients tolerated the treatments well except a few. Out of the total of 80 patients, only 21.3% of patients experienced minor side effects to the treatment. Most common side effect observed in this study was gastric irritation (11.3%) followed by weight gain (7.5%), precipitation of acne (1.3%), and vomiting (1.3%). Gastritis, weight gain and acneiform eruptions are mainly due to corticosteroids, while one patient had vomiting after first dose of

phototherapy. No skin atrophy or any other local adverse effects at the lesional sites has been reported.



**Fig. 5: Graphical presentation of adverse effects experienced by the patients with current therapy**

## DISCUSSION

The prevalence of vitiligo is high in India. The relative prevalence varies between 0.46 to 8.8%.<sup>3</sup> In this study the prevalence was found to be 1.3%. The varying ethnic backgrounds of the population residing in different geographic regions with varying environmental conditions may contribute to the wide variation in the prevalence of vitiligo in India.

The female to male ratio of vitiligo patients observed in this study was found to be nearly equal (1.1:1). This means that this disease has no predilection for any gender. Arycan et al<sup>8</sup> and Rajpal et al<sup>4</sup> reported a female to male ratio of 1.1:1, whereas others reported 0.9:1,<sup>9</sup> 1.6:1,<sup>3</sup> and 1.22:1.<sup>10</sup> In this study vitiligo was found to be more common in the age group of 2 – 20 years which is in agreement with other reports.<sup>1,2,6</sup> In 45% of patient's age at onset was less than 25 years, consistent with most reports from India<sup>3,4,11</sup> and from other countries.<sup>8,9,12</sup> The mean age of onset of disease was reported to be 25.6 years,<sup>3</sup> 23.3 years<sup>13</sup> and 18.9 years<sup>9</sup> in various studies. In this study the mean age at onset was 29.6 ± 20.6 years. All these findings indicate that vitiligo predominantly affects a younger population.

The duration of the disease varied widely from 2 months to 49 years, with the mean duration of 7.4 ± 9.9 years in this study. Most of the cases (56.2%) were less than 5 years in duration regardless of sex, which corresponds to the study done by Hann et al.<sup>14</sup> A majority (62.5%) of our patients had progressive vitiligo at the time of presentation. Hann et al<sup>15</sup> also reported that 88.8% of their patients showed a progression in the disease.

There was a family history of vitiligo in 18.8% patients; first degree relatives were affected in 10% of patients. Vitiligo has a polygenic or autosomal dominant inheritance pattern with incomplete penetrance and variable expression.<sup>3,16</sup> Familial occurrence has been reported to be in the range of 6.3% to 30%<sup>3,16</sup> whereas other studies reported 13%,<sup>15</sup> 18.9%<sup>12</sup> and even 1.6%.<sup>9</sup> Positive family history is considered to be a poor prognostic factor for vitiligo.<sup>3</sup>

The precipitating factors were noticed in twenty five (31.3%) patients. Physical trauma or injury being the most common factor (18.8%). Various studies undertaken to determine the factors precipitating vitiligo include emotional stress, sun burn, major illness, surgical procedure, pregnancy, parturition and physical trauma.<sup>10</sup> However Slominski et al<sup>17</sup> point out that several environmental factors including stress, extreme exposure to pesticides, sunlight etc have been implicated in the etiology of vitiligo.

Many lesions in hairy areas showed leukotrichia and such lesions were seen in 6.3% of the patients in this study. Leukotrichia is considered to be a poor prognostic factor. Leukotrichia was seen in 43.5% of South Korean patients<sup>15</sup> and in 11.5% of Indian patients.<sup>18</sup> Koebner phenomenon was seen in 20% of our patients. Koebner phenomenon was reported to occur in as many as 33% of vitiligo patients.<sup>3</sup>

Vitiligo vulgaris (53.7%) was the most common clinical type in this study. This was followed by focal vitiligo, acrofacial vitiligo, segmental, mucosal and universal vitiligo in the descending order of frequency. Kovacs<sup>19</sup> also reported that generalized vitiligo is the commonest presentation. Handa and Kaur<sup>18</sup> reported that vitiligo vulgaris was the commonest type seen followed by focal vitiligo and segmental vitiligo. The frequency of distribution of clinical types of vitiligo varies in different studies. However, with the present state of our knowledge it is difficult to comprehend the mechanisms and determinants underlying varying clinical patterns of vitiligo seen in different patients.<sup>12</sup>

The lower limbs were found to be the site initially developing depigmentation in majority (42.5%) of patients in this study. Face (27.5%), hands / upper limbs (13.8%), finger tips (7.5%) were the next commonest site followed by trunk (3.8%), scalp and genital regions (2.5%). This is in concordance with the studies by Mutairi et al,<sup>12</sup> Chanda et al,<sup>11</sup> and Martis et al.<sup>10</sup> However it is at variance with Handa and Kaur<sup>18</sup> in which the sites of onset were the face, trunk, and legs in descending order of frequency.

Association of vitiligo with other diseases/ abnormalities has also been a subject of great interest. We also observed an association of vitiligo with cutaneous diseases like atopic dermatitis (3.8%), alopecia areata (12.5%), and pruritus (1.3%) and with, systemic disorders like diabetes mellitus (13.8%), thyroid disorders (21.3%), hypertension (5.0%), pernicious anemia, bronchial asthma, rheumatoid arthritis etc. Vitiligo has been reported in association with numerous cutaneous and systemic disorders.<sup>10</sup> Handa and Kaur<sup>18</sup> observed atopic/nummular eczema in 1.4%, alopecia areata in 0.4%, bronchial asthma in 0.7%, diabetes mellitus in 0.6% and thyroid disease in 0.5% of their patients.

The association of vitiligo with thyroid disorders was 21.3% in our study, which was reported to be 0.5% to 23% by Liu et al,<sup>9</sup> 12% by Gopal et al,<sup>16</sup> 4.4% by Arycan et al.<sup>8</sup> Diabetes mellitus was found in 13.8% of patients in this study, but the reported values were 1% to 7%,<sup>16</sup> 7.1%,<sup>8</sup> 1%<sup>15</sup> and 9%.<sup>10</sup> Hypertension was found to be 5% in our study, whereas the reported values were 4%,<sup>10</sup> 0.7%,<sup>3</sup> 0.5%,<sup>20</sup> and 1.37%.<sup>16</sup> Pernicious anemia and bronchial asthma were found to be 2.5% and 1.3%, and incidence of rheumatoid arthritis was found to be 1.3% in our study. Pernicious anemia coexisting with vitiligo was reported to be 0.9%<sup>8</sup> and 0.4%<sup>21</sup> in previous studies. Reported values of bronchial asthma were 1.76%,<sup>8</sup> 0.7%,<sup>3</sup> 0.3%,<sup>9</sup> and while for rheumatoid arthritis 0.3%,<sup>9</sup> 0.10%.<sup>20</sup> Atopic dermatitis was reported to be 3.4% by Hann et al,<sup>14</sup> 2% by Martis et al.<sup>10</sup> Frequency of alopecia areata in vitiligo was found to be 3%,<sup>22</sup> 1.4%,<sup>21</sup> and 1%<sup>10</sup> by other authors.

Clinically apparent deafness or any ocular abnormality was not observed in any of the patients in our study. Auditory disability and ocular involvement in vitiligo patients has attracted attention, because it is known that the inner ear contains melanocytes and also the pigment epithelium of the retina and the choroid are rich in melanocytes.<sup>12</sup> Since vitiligo affects all active melanocytes, auditory and ocular problems can result in patients with vitiligo.<sup>19</sup>

In this study, the treatment modalities used can be divided into topical, systemic, phototherapy, and surgical repigmentation techniques. The three most common treatments used were topical tacrolimus (68.8%), topical corticosteroids (53.7%), and topical psoralen (48.8%). Oral corticosteroid minipulse therapy was used only for those with progressive disorder (35%). NBUVB was used for 27.5% patients and surgical manipulations (7.5%) were done for stable vitiligo and localized lesions. Most of the studies reported that topical corticosteroids are the most commonly used treatment option.<sup>23</sup> Ping et al<sup>21</sup> reported that the most commonly used treatments were topical corticosteroids (70.2%), topical tacrolimus (51%) and phototherapy (23.8%). In phototherapy commonly used option was Narrow Band UVB (10.6%). According to Rajpal et al<sup>4</sup> the most commonly used treatment modalities were Bath PUVA therapy (in which patient lies in a bath tub containing 0.75% topical psoralen for 20 minutes, and later exposes to UVA source, either in a UVA chamber or to natural sunlight) and corticosteroids.

In this study the main adverse effects noted with the therapy were a transient weight gain in 7.5% patients, gastric irritation in 11.3% patients, nausea or vomiting and precipitation of acne in 1.3% patients each. Huda et al<sup>24</sup> reported the following adverse effects with phototherapy and oral minipulse steroid therapy. Examples were weight gain in 14% patients, nausea in 12% patients, gastric irritation and acneiform eruption in 8% of patients each. Majid et al<sup>25</sup> reported weight gain in 14.3%, gastric irritation in 4.5%, acne precipitation in 2.8% of their patients. Nausea / Vomiting occurred after the first dose of NBUVB therapy. Transient weight gain, and gastric irritation are mainly due to systemic corticosteroid pulse therapy (Betamethasone 5mg) while topical steroid (Mometasone) caused acneiform eruptions.

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